Pediatr Nephrol (2012) 27:1605–1829
DOI 10.1007/s00467-012-2232-7

ABSTRACTS

The 45th Annual Meeting on September 6th – 8th 2012, Krakow, Poland

ORAL PRESENTATIONS

OP1 - BLOOD PRESSURE VARIABILITY AND ARTERIAL STIFFNESS IN CHILDREN WITH ESSENTIAL HYPERTENSION AND DIABETES MELLITUS TYPE 1

TEREZIE SULAKOVA[1], JANA CERNA[1], JANUSZ FEBER[2]
[1]DEP. OF PEDIATRICS, UNIVERSITY HOSPITAL OSTRAVA AND DEP. OF CLINICAL STUDIES, FACULTY OF MEDICINE UNIVERSITY OF OSTRAVA, THE CZECH REPUBLIC
[2]DEP. OF PEDIATRICS, CHILDREN´S HOSPITAL OF EASTERN ONTARIO AND UNIVERSITY OF OTTAWA, OTTAWA, CANADA

Introduction: An increased blood pressure variability (BPV) and arterial stiffness have been considered as risk factors for cardiovascular health in adults. The goal of our study was to compare the BPV and arterial stiffness in hypertensive diabetic and non-diabetic children with normotensive children.
Material and methods: We retrospectively analyzed ambulatory blood pressure monitoring (ABPM) records in 106 children (49 boys), median age=14.32 years. Patients were categorized into 4 groups: normotensive diabetics (33, NTDM), hypertensive diabetics (24, HTNDM), normotensive non-diabetics (27, NT), and hypertensive non-diabetics (22, HTN). BPV were analyzed using the 24 h standard deviation (SD) of mean arterial pressure (MAP); to account for BP dipping we also calculated the weighted SD (wSD) as mean of day and night MAP SD corrected for the number of hours included in each subperiod. Arterial stiffness was evaluated as arterial ambulatory stiffness index (AASI).
Results: The mean 24 h SD MAP was significantly higher in HTN compared to NTDM, HTNDM, and NT (12.2±2.2, 9.4±1.8, 9.5±2.2, and 10.3±2.1, respectively; $p<0.0001$). However, wSD MAP was significantly different only in primary HTN compared to NTDM and NT (9.3±1.7 vs. 7.3±1.1 and 7.5±1.4, respectively; $p=0.004$). In contrast to BPV, the AASI was increased in both HTNDM a HTN patients as compared to NT (0.36±0.15 and 0.37±0.17 vs. 0.23±0.15, respectively; $p=0.005$).
Conclusions: In conclusion, diabetic and non-diabetic hypertensive patients have increased arterial stiffness, but only hypertensive non-diabetic patients have increased variability. This may be due to altered baroreceptor sensitivity in patients with primary hypertension.

These Abstracts are not sponsored by outside commercial interests. They are funded entirely by the publisher.

OP2 - HYPERTENSION IN CHILDREN AND ADOLESCENTS AFTER KIDNEY TRANSPLANTATION

JUUSO TAINIO, ERIK QVIST, TUULA HÖLTTä, CHRISTER HOLMBERG, TIMO JAHNUKAINEN, HANNU JALANKO
CHILDREN'S HOSPITAL, UNIVERSITY OF HELSINKI AND HELSINKI UNIVERSITY CENTRAL HOSPITAL

Introduction: Arterial hypertension is a major risk factor for cardiovascular disease after kidney transplantation (RTx). This study was conducted to evaluate the blood pressure (BP) profiles, risk factors, and outcome in children and adolescents 5–10 years after RTx.
Material and methods: We retrospectively reviewed the 24-hour ambulatory blood pressure measurement (ABPM) results in 117 RTx patients (aged 5.9–20.8 years), 42 heart or liver transplantation recipients (aged 6.1–20.4 years), and 44 patients (aged 8.8–18.7 years) with essential hypertension and compared their BP profiles (BP index, BP load and nocturnal dipping). The accuracy of office BP results in 104 RTx and 39 heart or liver transplantation patients were assessed in relation to the ABPM.
Results: ABPM revealed mild to moderate masked hypertension in 38/69 (55 %) RTx patients without antihypertensive medication and in 36/48 (75 %) patients with

antihypertensive medication. Office BP measurement was consistent with ABPM only in 56 % of the patients. Hypertensive BP levels occurred in 38 % and 61 % of the RTx patients during daytime and nighttime, respectively. The prevalence of increased BP load was higher than abnormal BP index and 62 % of the patients showed blunted dipping. The BP profiles were not significantly different in the Tx groups and those with essential hypertension. Decreased kidney function was a significant risk factor for hypertension in RTx patients (OR 2.7, 95 % confidence interval 1.1–6.7, p= 0.03), as was high urate level (OR 2.6, 95 % confidence interval 1.1–6.5, p=0.04). On the other hand, the relation of removal of the native kidneys, age >5 years at transplantation, cyclosporine trough concentration >80 μg/l, or methylprednisolone daily dose >0.05 mg/kg to hypertension was insignificant.

Conclusions: The results show that ABPM often reveals hypertensive BP levels in RTx patients, even in patients on antihypertensive medication, and regular ABPM monitoring is recommended.

OP3 - Dyslipidaemia in children with end-stage renal disease

MARJOLEIN BONTHUIS[1], KARLIJN J VAN STRALEN[1], TIMO JAHNUKAINEN[2], GUIDO F LAUBE[3], LUDMILA PODRACKA[4], TOMAS SEEMAN[5], MANISH D SINHA[6], KAY TYERMAN[7], TIM ULINSKI[8], FRANZ SCHAEFER[9], KITTY J JAGER[1], ENRICO VERRINA[10]

[1]*ESPN/ERA-EDTA REGISTRY, ACADEMIC MEDICAL CENTER, UNIVERSITY OF AMSTERDAM, AMSTERDAM, THE NETHERLANDS*

[2]*HOSPITAL FOR CHILDREN AND ADOLESCENTS, UNIVERSITY OF HELSINKI, HELSINKI, FINLAND*

[3]*UNIVERSITY CHILDREN'S HOSPITAL, ZURICH, SWITZERLAND*

[4]*FACULTY OF MEDICINE, PJ SAFARIK UNIVERSITY, KOSICE, SLOVAK REPUBLIC*

[5]*UNIVERSITY HOSPITAL MOTOL, 2ND SCHOOL OF MEDICINE, CHARLES UNIVERSITY PRAGUE, PRAGUE, CZECH REPUBLIC*

[6]*EVELINA CHILDREN'S HOSPITAL, GUYS AND ST THOMAS NHS FOUNDATION TRUST, LONDON, UNITED KINGDOM*

[7]*ST. JAMES'S UNIVERSITY HOSPITAL, LEEDS, UNITED KINGDOM*

[8]*ARMAND TROUSSEAU HOSPITAL, L'ASSISTANCE PUBLIQUE–HôPITAUX DE PARIS (APHP), PARIS, FRANCE*

[9]*UNIVERSITY OF HEIDELBERG, HEIDELBERG, GERMANY*

[10]*GASLINI CHILDREN'S HOSPITAL, GENOA, ITALY*

Introduction: Data on dyslipidaemia in end-stage renal disease mainly originate from adult patients or small paediatric studies. We aimed to describe the prevalence of dyslipidaemia and potential determinants associated with lipid measures in a large cohort of paediatric ESRD patients.

Material and methods: Within the ESPN/ERA-EDTA registry data on lipid measures were available for 1378 patients aged 2–17 years from 17 different countries from the year 2000 onwards. Dyslipidaemia was defined as triglycerides >130 mg/dl, HDL cholesterol <40 mg/dl, or non-HDL cholesterol >160 mg/dl, no age- and sex-dependent values were used. Analyses were performed using linear mixed models adjusting for potential confounders.

Results: Dyslipidaemia was present in 57 % of patients. Hypertriglyceridaemia was found in 70 % of PD, 61 % of HD, and 39 % of transplanted patients. 36 % of HD patients, 25 % of PD patients and 14 % of transplanted patients displayed low HDL values, and elevated non-HDL levels were found in 42 % of PD patients, 18 % of HD patients, and 14 % of transplanted patients. Among transplanted patients, only triglyceride levels were inversely associated with graft function. In patients with an eGFR<29 mL/min/1.73 m2 the mean triglyceride level was 138 mg/dl (95%CI: 118–161) compared to 106 mg/dl among those with eGFR> 90 mL/min/1.73 m2. Use of cyclosprine instead of tacrolimus resulted in significantly higher triglyceride (12 mg/dl 95%CI: 6–18, p<0.05) and non-HDL levels (20 mg/dl 95%CI: 15–25, p<0.05). Furthermore, non-HDL levels were 22 mg/dl (95%CI: 16–64, p<0.05) higher among users of sirolimus as compared to non-users, all adjusted for age, sex, time since transplantation, eGFR, and year of transplantation.

Conclusions: Dyslipidaemia is present in more than half of the European paediatric ESRD patients. Graft function and different types of immunosuppressants affected triglyceride levels. Considering its association with cardiovascular morbidity and mortality, dyslipidaemia should receive close attention in the treatment of children with ESRD.

OP4 - ALTERED ARTERIAL MORPHOLOGY AND FUNCTION IN CHILDREN WITH CKD: ROLE OF MINERAL-BONE DISORDER

ANKE DOYON[1], BETTINA SCHMIEDCHEN[2], AYSUN BAYAZIT[3], NUR CANPOLAT[4], ALI DUZOVA[5], DANIELA KRACHT[6], MIECZYSLAW LITWIN[7], ANNA NIEMIRSKA[7], BETUL SOZERI[8], RENE ZELLER[9], ALI ANARAT[3], SALIM CALISKAN[4], SEVGI MIR[8], RUKSHANA SHROFF[10], ANETTE MELK[6], ELKE WÜHL[1], FLORIAN SCHWEIGERT[2], UWE QUERFELD[9], FRANZ SCHAEFER[1], AND THE 4C STUDY CONSORTIUM[1]

[1]*CENTER FOR PEDIATRICS AND ADOLESCENT MEDICINE HEIDELBERG, GERMANY*

[2]UNIVERSITY OF POTSDAM, GERMANY
[3]CUKUROVA UNIVERSITY ADANA, TURKEY
[4]CERRAHPASA UNIVERSITY ISTANBUL, TURKEY
[5]HACETTEPE UNIVERSITY ANKARA, TURKEY
[6]HANNOVER MEDICAL SCHOOL, GERMANY
[7]CHILDREN'S MEMORIAL HEALTH INSTITUTE WARSAW, POLAND
[8]EGE UNIVERSITY IZMIR, TURKEY
[9]CHARITE CHILDREN'S HOSPITAL BERLIN, GERMANY
[10]GREAT ORMOND STREET HOSPITAL LONDON, UK

Introduction: The Cardiovascular Comorbidity in Children with CKD (4C) study prospectively explores morphological and vascular aspects of CKD and their associations to various laboratory and clinical risk factors. Here we present key results of the baseline vascular assessment.
Material and methods: 733 CKD patients aged 6–17 years with eGFR between 10 and 45 ml/min/1.73 m2 have been enrolled to the study in 55 centers of 12 European countries. The morphology and function of the large arteries are followed by regular assessment of carotid intima media thickness (IMT) and pulse wave velocity (PWV). Standardized sonographic IMT and oscillometric PWV measurements are performed by eight jointly trained observers. Central laboratory analyses include measurements of eGFR, Ca, P, PTH and 25-OH-Vitamin D levels. Potential effectors/covariates of PWV and IMT are assessed by multivariate analysis.
Results: IMT was elevated above the 95th percentile for age in 43 %, and PWV in 16 % of children irrespective of eGFR. IMT was positively associated with age ($p<0.0001$), blood pressure ($p<0.0001$), serum phosphorus levels ($p<0.0007$), and inversely with serum 25OH-D ($p<0.01$) and serum calcium levels ($p<0.03$). PWV was independently associated with age ($p<0.0001$), blood pressure ($p<0.0001$) and serum phosphorus ($p<0.0014$), but not with serum calcium or 25OH-D. PTH was not associated with either IMT or PWV.
Conclusions: When adjusting for age and BP, serum phosphorus levels are linked to morphological (IMT) and functional (PWV) vascular alterations in children with advanced CKD. Low vitamin D levels appear to additionally increase the risk of early intima-media thickening in paediatric CKD.

OP5 - Malnutrition-Inflammation-Atherosclerosis Complex in Children Undergoing Chronic Dialysis

NUR CANPOLAT[1], MEHMET TASDEMIR[1], LALE SEVER[1], AYSE AGBAS[1], MINE KUCUR[2], GULSEREN PEHLIVAN[1], SALIM ÇALIŞKAN[1]
[1]ISTANBUL UNIVERSITY, CERRAHPASA MEDICAL FACULTY, DEPARTMENT OF PEDIATRIC NEPHROLOGY
[2]ISTANBUL UNIVERSITY, CERRAHPASA MEDICAL FACULTY, DEPARTMENT OF BIOCHEMISTRY

Introduction: Inflammation is associated with malnutrition and protein energy wasting in dialysis patients. There are several overlaps between inflammation and malnutrition with regards to their pathogenetic pathways and their effects on the development of cardiovascular disease. The aim of the present study was to evaluate malnutrition-inflammation-atherosclerosis complex in children receiving chronic dialysis.
Material and methods: Thirty-three patients (18 PD and 15 HD), ages ranging from 5.7 to 19.9 years were enrolled in the study. Nutritional status was assessed by measuring midarm circumference (MAC), triceps skinfold (TSF), midarm muscle circumference (MAMC), and multi-frequency bioimpedance analysis. The presence of inflammation was evaluated by serum C-reactive protein (CRP) and Interleukin 6 (IL-6) levels. The measurement of intima-media thickness (IMT) in the common carotid artery was performed to assess atherosclerosis.
Results: The mean weekly Kt/V was 2.68±0.84 in PD patients; mean single pool Kt/V was 1.8±0.62 in HD patients. Neither anthropometric measurements nor the results of bioimpedance analysis differed between PD and HD patients. The standard deviation (SD) score of body mass index (BMI) was below −2 in a total of nine patients (4PD and 5HD); these patients were defined to be malnourished. Malnourished patients had lower TSF and lower body fat percentage as compared to normally nourished patients (4.52± 0.97 mm vs. 10.0±5.97 mm, $p=0.001$ and 17.9±6.06 vs. 25.5±10.4, $p=0.032$, respectively). There was a statistically significant inverse correlation between SD scores of BMI and the duration of renal replacement therapy ($r=-0.387$, $p=0.026$). Neither CRP nor IL-6 was associated with BMI SD scores. A total of 16 patients (8PD, 8HD) showed an increased height-specific SD score (>2SD) of the carotid IMT. Higher SD scores of carotid IMT were associated with decreased lean tissue index ($\beta=-0.494$, $p=0.006$) and higher CRP levels ($\beta=0.141$, $p=0.016$) in the entire study group.
Conclusions: Children undergoing chronic dialysis are at higher risk for accelerated atherosclerosis which in this study is closely associated with both poor nutritional status and inflammation.

OP6 - Pulse Wave Velocity in Healthy European Children: Reference Values and Role of Body Dimensions

ELKE WÜHL, FOR THE 4C REFERENCE STUDY CONSORTIUM
PEDIATRIC NEPHROLOGY, CENTER FOR PEDIATRICS AND ADOLESCENT MEDICINE, UNIVERSITY OF HEIDELBERG, GERMANY

Introduction: Pulse wave velocity (PWV), a measure of aortic stiffness, is a powerful independent predictor of

cardiovascular morbidity and mortality in adults. Experience with PWV in children is limited due to methodological challenges and lacking paediatric reference data. Recently, a largely observer-independent, easily applicable oscillometric technology has become available that facilitates PWV assessment in the paediatric setting. We performed a collaborative study in 4 European countries to establish normative paediatric PWV charts and assess the anthropometric covariates of pulse wave velocity in healthy school children and adolescents.

Material and methods: PWV was measured in 1,000 healthy boys and girls aged 6 to 18 years by 7 jointly trained observers in Germany, Turkey, Poland and the United Kingdom using the Vicorder device according to a standardized protocol. The mean of three consecutive measurements was used for further analysis. Height, weight, systolic and diastolic blood pressure (BP) were measured. The LMS method was used to construct percentile charts.

Results: The distribution of PWV was skewed towards higher levels and did not differ significantly between sexes, nor by country of residence. PWV increased with age (r= 0.54) and body size (height: r=0.52, weight: r=0.54, body surface area (BSA): r=0.55), and was positively and independently correlated with height SDS and BMI SDS. PWV was also correlated with absolute, but not with standardized systolic or diastolic BP. Reference percentiles (pct) were constructed relative to age, and to body surface area for application in diseased populations with abnormal height and/or weight for age. The 5th pct increased from 3.6 to 4.6, the 50th pct from 4.4 to 5.9 and the 95th pct from 5.1 to 6.6 m/s across the age range studied.

Conclusions: PWV increases with age across childhood and tends to be higher in children who are tall and/or heavy for age. Our European reference charts allow valid assessment of PWV in healthy and diseased pediatric cohorts, accounting for differences in age and relative body size.

OP7 - Frequency and Outcome of Anti-factor H Autoantibody Associated Hemolytic Uremic Syndrome (HUS) in Indian children

ARVIND BAGGA[1], MARIE-AGNES DRAGON-DUREY[2], SAVITA SAINI[1], PANKAJ HARI[1], AMIT DINDA[1], ADITI SINHA[1], ASHIMA GULATI[1]

[1]*ALL INDIA INSTITUTE OF MEDICAL SCIENCES, NEW DELHI, INDIA*

[2]*APHP, HôPITAL EUROPéEN GEORGES POMPIDOU, LABORATOIRE D'IMMUNOLOGIE, UNIVERSITé PARIS DESCARTES, PARIS, FRANCE*

Introduction: Autoantibodies to complement-factor H (CFH) are incriminated in pathogenesis of atypical HUS (aHUS) in 5-11 % patients in European cohorts. We report a high frequency of this condition in Indian children including details on therapy & outcomes.

Material and methods: During 2007–11, patients with HUS (microangiopathic hemolytic anemia, platelets <150,000/mm3, creatinine >1.5 mg/dL) were prospectively screened by ELISA for anti-CFH IgG antibodies. Anti-CFH titer >100 AU/mL was considered positive. Patients with antibody-associated HUS received supportive treatment, plasma therapy, IV immunoglobulin (IVIG) and immunosuppressive agents. Outcome was assessed as renal death (estimated GFR <15 mL/min/1.73 sq.m or needing dialysis >3-months from onset).

Results: Of 97 patients with HUS, 57 (58.7 %) were positive for anti-CFH antibodies, mean titer 4243±849 AU/mL. The mean age was 8.4±3.3 yr; diarrheal prodrome and low C3 were present in 5 % and 64 % respectively. Kidney biopsy (n= 28) showed fibrin-rich thrombi in glomerular capillaries & arterioles. Multiplex ligation-dependant probe amplification showed 88 base-pair deletion in CFHR1/3 genes. Therapies included plasma-exchanges (30), plasma-infusions (10) and IVIG (15). Following initial therapy with prednisolone and IV cyclophosphamide (23) or rituximab (4), maintenance agents included mycophenolate mofetil or azathioprine. Plasma-exchanges resulted in 89 % reduction in antibody titer (mean difference 1015±712 AU/mL; P<0.001). At 13.0± 14.1 months, renal death occurred in 18 (38 %) patients. Risk factors for renal death were creatinine ≥5 mg/dL at presentation (HR 16.1; 95 % CI 1.9-138.1; P=0.011) & dialysis requirement ≥4 weeks (P<0.001). Initial & maintenance immunosuppression prevented renal death (HR 0.21; P=0.025) and relapses (HR 0.14; P=0.085) respectively. For every 4 patients treated, one relapse was prevented.

Conclusions: A high proportion of children with HUS in India show presence of anti-CFH antibodies. Patients with severe renal failure are at risk of rapid progression to end-stage renal failure. Appropriate immunosuppression is useful in enabling renal recovery and preventing relapses.

OP8 - IDENTIFICATION AND CHARACTERIZATION OF A RARE GENE VARIANT IN CONGENITAL INTERSTITIAL LUNG FIBROSIS AND NEPHROTIC SYNDROME

NAYIA NICOLAOU[1], COERT MARGADANT[2], SIETSKE KEVELAM[1], MARC LILIEN[3], MICHIEL OOSTERVELD[3], ROEL GOLDSCHMEDING[4], ALBERTIEN VAN EERDE[1], ROLPH PFUNDT[5], PAULIEN TERHAL[1], NINE KNOERS[1], ARNOUD SONNENBERG[2], KIRSTEN RENKEMA[1]

[1]*DEPARTMENT OF MEDICAL GENETICS, UNIVERSITY MEDICAL CENTER UTRECHT*

[2]*DIVISION OF CELL BIOLOGY, NETHERLANDS CANCER INSTITUTE, AMSTERDAM*

[3]DEPARTMENT OF PEDIATRIC NEPHROLOGY, UNIVERSITY MEDICAL CENTER UTRECHT
[4]DEPARTMENT OF PATHOLOGY, UNIVERSITY MEDICAL CENTER UTRECHT
[5]DEPARTMENT OF HUMAN GENETICS, RADBOUD UNIVERSITY MEDICAL CENTER, NIJMEGEN

Introduction: A newborn female presented with interstitial lung fibrosis and developed nephrotic syndrome before age 3 months. She had unilateral kidney hypoplasia with hydronephrosis, glomerulosclerosis, pulmonary hypoplasia, and alveolar glycogenosis, leading to death at 7 months due to respiratory insufficiency. Nothing was known about the origin of this phenotype. The purpose of this study was to describe the clinicopathologic findings and unravel their genetic cause.
Material and methods: Screening for known nephrotic syndrome-causing gene variants was performed and genome-wide screening for CNVs and homozygous regions was done using Affymetrix 250 K SNP array in the affected child and unaffected parents. We sequenced the coding region of the strongest candidate gene within the identified homozygous region of 20 Mb in the affected child, the unaffected parents, and 192 healthy control individuals for the identified gene variant. Functional interaction studies were performed in order to characterize the variant identified.
Results: A novel homozygous missense variant identified in the patient was inherited from the heterozygous unaffected parents and was not found in 384 control chromosomes. The variant leads to an amino acid substitution in a gene essential for basement membrane development. Expression of the protein was absent. Striking similarities were seen between the gene knockout mouse model and the patient's phenotype. In vitro characterization studies demonstrated intracellular retention of the variant protein. No variants were identified in the known nephrotic syndrome genes.
Conclusions: We report a novel human gene variant, causing congenital interstitial lung fibrosis and nephrotic syndrome. This is the first report on the genetic background of this developmental disease, but is also the first clinical phenotype associated with a mutation in this gene in humans. Our findings have major implications for our understanding of basement membrane development. They enable the design of genetic screening tests to facilitate diagnosis and genetic counselling for patients and their relatives

OP9 - EFFECTIVENESS OF A TWICE DAILY THERAPY FOR CYSTINOSIS ON WBC CYSTINE

DESCHENES GEORGES[1], DOHIL RANJAN[2], LEVTCHENKO ELENA[3], GREENBAUM LAURENCE[4], LANGMAN CRAIG[5], NIAUDET PATRICK[7], COCHAT PIERRE[8], CORNELISSEN ELIZABETH[11], MORIN DENIS[9], SARWAL MINNIE[10], RIOUX PATRICE[6]

[1]APHP-ROBERT-DEBRE, PARIS
[2]UNIVERSITY OF CALIFORNIA, SAN DIEGO
[3]UNIVERSITY HOSPITAL LEUVEN
[4]EMORY UNIVERSITY, ATLANTA
[5]FEINBERG SCHOOL OF MEDICINE, CHICAGO
[6]RAPTOR PHARMACEUTICAL CORPORATION, NOVATO CALIFORNIA
[7]APHP-NECKER, PARIS
[8]HOPITAL FEMME MERE ENFANT, LYON
[9]CHU MONTPELLIER, FRANCE
[10]STANFORD UNIVERSITY, USA
[11]RADBOUD UNIVERSITY, NIJMEGEN

Introduction: Cystinosis is an autosomal recessive inborn error of metabolism in which the transport of cystine out of lysosomes is reduced or absent secondary to a mutation in the transporter gene. Cystagon® is an immediate-release formulation of cysteamine bitartrate (a cystine-depleting agent) that must be taken in strict 6 hour intervals. A new delayed-release formulation of cysteamine bitartrate (RP103) has been recently developed and demonstrated to have a bioequivalence of efficacy administered every 12 hours based on the level of White Blood Cell (WBC) cystine.
Material and methods: A phase 2b study was completed in order to assess the pharmacokinetic (PK), WBC cystine levels (PD), safety and tolerability of RP103, compared to Cystagon® in 9 patients with cystinosis. The RP103-03 phase 3 study was a randomized, crossover, PK and PD study to determine the safety and efficacy RP103. The primary aim of the study was to demonstrate that at steady-state, patients receiving every 12 hour treatment of RP103 can maintain a comparable depletion of WBC cystine levels not different than when receiving Cystagon® every 6 hours. Patients who completed the RP103-03 study were invited to enroll in "a long-term, open-label, safety and efficacy study of RP103 in patients with nephropathic cystinosis". Three additional studies were designed as bioequivalence studies when drug has to be administered with food.
Results: Twice-a-day dosing of RP103 allows controlling WBC cystine similarly to four-times-a-day dosing with Cystagon®. As expected, both compounds have comparable Adverse Event profile, with mostly gastro-intestinal side-effects. Sprinkling the content of RP103 capsules on apple compote has the same effectiveness on WBC cystine as RP103 whole capsules. However, since food (especially protein and fat) interacts with cysteamine absorption, new recommendations will be discussed.
Conclusions: RP103, a new formulation of cysteamine bitartrate that allows to prevent any nocturnal delivery of the drug, gives a similar maintenance of WBC cystine depletion

OP10 - A new European federation of associations of patients with genetic renal diseases: FEDERG (FEDeration of European patients with Renal Genetic diseases).

RENAULT DANIEL[1], PIRSON YVES[2], CHAUVEAU DOMINIQUE[3], COCHAT PIERRE[4], LOIRAT CHANTAL[5]
[1]AIRG-FRANCE
[2]CLINIQUES UNIVERSITAIRES SAINT-LUC, BRUXELLES, BELGIUM
[3]CHU RANGUEIL, TOULOUSE, FRANCE
[4]HOSPICES CIVILS DE LYON & UNIVERSITé DE LYON
[5]HôPITAL ROBERT DEBRé, PARIS, FRANCE

Introduction: Renal Genetic Diseases (RGD) although of rare occurrence except for dominant polycystic kidney disease, account altogether for about 10 % of patients with ESRD in Europe. Their economic burden is significant since the costs of medical treatment (orphan drugs) and renal replacement therapy reaches 0.2 % of national healthcare budgets. In addition to the clinical consequences of kidney disease by itself, RGD may impact both quality of life and relationships within the whole family, especially with respect to genetic counseling, pregnancy, and all consequences of inheritance.
Material and methods: Significant advances have been achieved during the recent years, both in the diagnosis and the treatment of some RGD. In this fast moving field of knowledge and clinical achievements, patients associations have and will increasingly have an important role in informing and helping patients, in participating to improvement of their quality of life, in advocating the cause of rare diseases and in supporting clinical research.
Results: An initiative is taken to create a European federation of patients, called FEDERG (FEDeration of European patients with Renal Genetic diseases). FEDERG aims at gathering the numerous associations devoted to RGD, thus providing enough voice and room to the smallest ones and given them more empowerment within the European community: better inform, help and advocate, support research, better represent patients and foster the development of national associations.
Conclusions: The creation of FEDERG will be officially announced in May 2012 during a dedicated meeting held at the 49th Congress of ERA-EDTA in Paris and should be finalized by early 2013. Pediatric nephrologists are warmly invited to widespread this information to all patient groups concerned by RGD and possibly interested to join the initiative.

OP11 - Systemic Complement activation and acquired MCP deficiency at acute phase of typical hemolytic uremic syndrome

SELLIER-LECLERC ANNE-LAURE[1], LAHOCHE ANNIE[2], HARAMBAT JéRôME[3], TSIMARATOS MICHEL[4], BAUDOUIN VéRONIQUE[5], LOIRAT CHANTAL[5], FRéMEAUX-BACCHI VéRONIQUE[6]
[1]DEPARTMENT OF PEDIATRIC NEPHROLOGY, FEMME MèRE ENFANT HOSPITAL, HCL LYON, FRANCE.
[2]DEPARTMENT OF PEDIATRIC NEPHROLOGY, JEANNE DE FLANDRES HOSPITAL, LILLE, FRANCE
[3]DEPARTMENT OF PEDIATRIC NEPHROLOGY, CENTRE HOSPITALIER UNIVERSITAIRE DE BORDEAUX, BORDEAUX, FRANCE.
[4]DEPARTMENT OF PEDIATRIC NEPHROLOGY,LA TIMONE HOSPITAL, AP-HM MARSEILLE, FRANCE.
[5]DEPARTMENT OF PEDIATRIC NEPHROLOGY, ROBERT DEBRé HOSPITAL, AP-HP, PARIS, FRANCE
[6]LABORATORY OF IMMUNOLOGY, EUROPEAN GEORGES POMPIDOU HOSPITAL, AP-HP PARIS, FRANCE.

Introduction: Clinical manifestations of Shiga-like toxin producing Escherichia coli (STEC) infection in children vary from gastroenteritis to hemolytic uremic syndrome (HUS) and represent a Public Health problem. The various mechanisms of vascular endothelial lesions induced by STEC do not explain the variability of clinical symptoms. It is urgent to find out new risk factors, that will open the way to new therapeutic. Mutations or polymorphisms in genes of the complement alternative pathway regulatory proteins have been demonstrated as risk factors for aHUS, not associated with STC infection.
Material and methods: Here, we investigated complement in children STEC-HUS patients during acute disease. Eighty patients (44 girls) were included in this French multicenter prospective study.
Results: Patient age was 3.9 (0.6-13.8) years. Thirty children presented with only minimal renal involvement (37.5 %) (group A) and extra-renal epuration was required for 50 patients (group B). The mean duration of dialysis period in group B was 9.8 days (2–43). Extra renal manifestations were observed in 21/50 patients (42 %): central nervous system involvement (14), severe hemorrhagic colitis (15), pancreatic involvement (5, one with diabetes) and one cardiogenic shock. No end stage renal failure and no fatal issue were observed. Eight children received plasmapheresis (1 in group A) and 12 were treated with eculizumab (1 in group A). Six children (7 %) presenting with low C3 (2 in group A) and 37/51 (72 %) had a decreased cell-surface expression of CD46 at the acute phase.
Conclusions: In STEC-HUS, systemic alternative pathway activation and decreased MCP expression were detected. Advances in our understanding of the pathogenesis of atypical HUS suggest that complement inhibitiors such as eculizumab may be used as treatment for the disease. Therefore eculizumab offer hope that the prognosis for STEC-HUS will improve in future years.

OP12 - NEP- SYNDROME: A NEW GENETIC CONDITION WITH NEPHROTIC SYNDROME, EPIDERMOLYSIS BULLOSA AND PULMONARY DISEASE BASED ON INTEGRIN α3 MUTATION

GIUSEPPINA SPARTA'[1], CRISTINA HAS[2], DIMITRA KIRITSI[2], LISA WEIBEL[3], ALEXANDER MOELLER[4], VIRGINIA VEGA-WARNER[5], AOIFE WATERS[6], YINGHONG HE[2], YAIR ANIKSTER[7], PHILIPP ESSER[2], BEATE K. STRAUB[8], INGRID HAUSSER[9], DETLEF BOCKENHAUER[6], BENJAMIN DEKEL[10], FRIEDHELM HILDEBRANDT[1], LEENA BRUCKNER-TUDERMAN[2], GUIDO F. LAUBE[1]

[1]*DEPARTMENT OF PAEDIATRIC NEPHROLOGY OF THE CHILDREN'S HOSPITAL ZÜRICH SWITZERLAND*

[2]*DEPARTMENT OF DERMATOLOGY OF THE UNIVERSITY FREIBURG MEDICAL CENTER*

[3]*DEPARTMENT OF PAEDIATRIC DERMATOLOGY OF THE CHILDREN'S HOSPITAL ZÜRICH SWITZERLAND*

[4]*DEPARTMENT OF PAEDIATRIC PULMONOLOGY OF THE CHILDREN'S HOSPITAL ZÜRICH SWITZERLAND*

[5]*DEPARTMENT OF PAEDIATRICS OF THE UNIVERSITY OF MICHIGAN, ANN ARBOR, USA*

[6]*UCL INSTITUTE OF CHILD HEALTH AND GREAT ORMOND STREET HOSPITAL FOR CHILDREN NHS TRUST, LONDON UK*

[7]*METABOLIC DISEASE UNIT, EDMOND & LILY SAFRA CHILDREN'S HOSPITAL SHEBA MEDICAL CENTER, SACKLER SCHOOL OF MEDICINE, TEL AVIV UNIVERSITY, ISRAEL*

[8]*DEPARTMENT OF PATHOLOGY, UNIVERSITY OF HEIDELBERG, GERMANY*

[9]*DEPARTMENT OF DERMATOLOGY UNIVERSITY OF HEIDELBERG, GERMANY*

[10]*THE PAEDIATRIC STEM CELL RESEARCH INSTITUTE AND DIVISION OF PAEDIATRIC NEPHROLOGY, EDMOND & LILY SAFRA CHILDREN'S HOSPITAL, SHEBA MEDICAL CENTER, SACKLER SCHOOL OF MEDICINE, TEL AVIV UNIVERSITY, ISRAEL*

Introduction: Integrin α3 is a transmembrane integrin receptor subunit mediating signals between cells and their microenvironment. Mutations in integrin genes are associated with different human disorders. We report 3 infants with congenital nephrotic syndrome, skin fragility and interstitial lung disease, who were homozygous for mutations in the Integrin α3 gene (ITGA3).

Material and methods: Patient 1 was the index case in whom the genetic defect was discovered, detailed histological evaluation was performed and the complex phenotype was described. Subsequently, two other children with similar clinical features and ITGA3 mutations were identified. From all 3 patients and their parents the genomic DNA was extracted from peripheral-blood leukocytes and the coding region and exon/intron boundaries of the ITGA3 gene were analyzed, as were other candidate genes.

Results: Patient 1 revealed a homozygous mutation c.1173_1174del in exon 8 of ITGA3 histologically leading to a loss of Integrin α3 in the kidney, skin and lung and profound abnormalities of the basement membrane in these clinically affected organs. Although skin fragility initially was mild, it provided clues to the diagnosis. Patients 2 and 3 were homozygous for the ITGA3 mutations c.1538-1 G>A, in intron 11, and c.1883 G>C, p.Arg628Pro in exon 14, respectively. The ITGA3 mutations in all patients were associated with a complex phenotype consisting of congenital nephrotic syndrome accompanied with end stage renal failure, during follow-up worsening epidermolysis bullosa and severe interstitial lung disease leading to increasing oxygen consumption. Although patients survived neonatal period, severe and worsening multi-organ involvement led to a lethal course.

Conclusions: We identified three patients with homozygous mutations of the ITGA3-gene associated with disrupted basement membrane structures in these organs clinically leading to nephrotic syndrome, epidermolysis bullosa and pulmonary disease (NEP-syndrome). These new mutations reflect the impact and indispensability of Integrin α3 concerning the organization of basement membranes and its clinical impact.

OP13 - LIVING DONOR RENAL TRANSPLANTATION IN CHILDREN: RESULTS OF EARLY VS. LATE WITHDRAWAL OF CORTICOSTEROID IMMUNOSUPPRESSION

ÁNGEL ALONSO, MARISOL DOS SANTOS, LAURA ESPINOSA, CARMEN GARCíA MESEGUER, MARTA MELGOSA, CARLOTA FERNáNDEZ, ANTONIA PEñA, MERCEDES NAVARRO

PEDIATRIC NEPHROLOGY SERVICE. HOSPITAL LA PAZ. MADRID. SPAIN

Introduction: Post-transplantation corticosteroid use is associated with metabolic, cardiovascular, skeletal, ophthalmological and growth complications. Different studies have suggested that late corticosteroid withdrawal might increase rejection risk; possibly, early withdrawal might not have these effects and could improve growth.

Material and methods: The effects of two different corticosteroid suppression protocols were studied for the first two years post-transplant in 23 consecutive pediatric living donor transplant recipients. Corticosteroids were withdrawn during the first year in 12 patients (Group A) and during the first week in 11 (Group B). In both groups, age, retransplantation, incompatibility, cytomegalovirus risk and primary disease are similar. Maintenance immunosuppression employs tacrolimus and micophenolate in both groups while

induction employed basiliximab in Group A and antithymocytic globulin in Group B.

Results: No patients or grafts have been lost and each group has only had one rejection episode. The glomerular filtration rate (GFR) at the end of follow up is similar in both groups whether estimated by creatinine (101 versus 111 ml/min./1.73 m2) or by cistatin C (80 versus 84 ml/min./1.73 m2). The groups showed no significant differences in so far as cytomegalovirus infection (33 % and 18 %), poliomavirus urine elimination (16 % and 9 %) or Epstein Barr virus replication (58 % and 63 %). Hemoglobin was lower in Group B on days: 7, 9.2 versus 10.6 g/dl; 15, 9.1 vs. 11.1 g/dl; 30, 10.2 vs 11.1 g/dl; and 60, 10.1 vs 11.4 g/dl. Group B required more post-transplant transfusions (54 % vs 16 %) and had a lower total neutrophil count, but without clinical repercussions. The growth rate was better in Group B than A (monthly delta Z score 0.035 versus 0.016).

Conclusions: Quick corticosteroid withdrawal therapy is safe at short and mid term. There is a slight improvement in the growth rate if withdrawal is during the first week. Initial anemia is frequent if early withdrawal is associated with antithymocytic globulin induction.

OP14 - Skeletal Findings in the First 12 Months Following Initiation of Glucocorticoid Therapy for Pediatric Nephrotic Syndrome

JANUSZ FEBER[1], VERONIQUE PHAN[2], TOM BLYDT-HANSEN[3], STEVEN ARORA[4], LORRAINE BELL[5], GUIDO FILLER[6], JOANNE GRIMMER[6], DIANE HEBERT[7], JULIAN P. MIDGLEY[8], MAURY PINSK[9], BRIAN LENTLE[10], MARY ANN MATZINGER[1], NAZIH SHENOUDA[1], LEANNE M. WARD[1], AND THE CANADIAN STOPP CONSORTIUM[11]

[1]*UNIVERSITY OF OTTAWA, OTTAWA, ON, CANADA*
[2]*UNIVERSITE DE MONTREAL, MONTREAL, QC, CANADA*
[3]*UNIVERSITY OF MANITOBA, WINNIPEG, MB, CANADA*
[4]*MCMASTER UNIVERSITY, HAMILTON, ON, CANADA*
[5]*MCGILL UNIVERSITY, MONTREAL, QC, CANADA*
[6]*UNIVERSITY OF WESTERN ONTARIO, LONDON, ON, CANADA*
[7]*UNIVERSITY OF TORONTO, TORONTO, ON, CANADA*
[8]*UNIVERSITY OF CALGARY, CALGARY, AB, CANADA*
[9]*UNIVERSITY OF ALBERTA, EDMONTON, AB, CANADA*
[10]*UNIVERSITY OF BRITISH COLUMBIA, VANCOUVER, BC, CANADA*
[11]*CANADIAN PEDIATRIC BONE HEALTH WORKING GROUP, OTTAWA, ON, CANADA*

Introduction: Children with nephrotic syndrome (NS) may develop vertebral fractures (VF). We analyzed the incidence of VF and lumbar spine bone mineral density (LSBMD) during 1 year of glucocorticoid (GC) therapy as part of the pan Canadian multicenter prospective study (STeroid-associated Osteoporosis in the Pediatric Population - STOPP).

Material and methods: VF were characterized by the Genant semi-quantitative method on baseline (within 37 days of GC initiation) and 12 month spine radiographs. An incident VF was defined as an increase in the Genant grade by at least one compared to baseline. LSBMD was evaluated by dual energy x-ray absorptiometry at baseline, 3, 6 and 12 months.

Results: We studied 65 children from GC initiation to 12 months (age range 2.3 to 17.9 years; 55 % boys). 3/65 children (5 %) had a single, asymptomatic incident VF in the mid-thoracic region at 1 year. The LSBMD Z-score was significantly lower than the healthy average at baseline (-0.5 ± 1.1) and at 3 months (-0.6 ± 1.0; $p=0.001$), but not at 12 months (-0.3 ± 1.2; $p=0.066$). 16/65 (25 %) had LSBMD Z-scores≤-1 at 12 months, but the total quantity ($p=0.35$) and duration ($p=0.33$) of GC therapy were similar to those with LS BMD Z-scores>-1 at 1 year. However, in these 16 children each additional g/m2 of cumulative GC received in the first 3 months was associated with a reduction in LSBMD Z-score of 0.48 at 12 months (95 % CI, -0.83 to -0.12; $p=0.008$; controlling for age, gender and BMI). This relationship was not observed in the rest of the cohort ($p=0.50$).

Conclusions: In children with GC-treated NS at 12 months after GC initiation, the incidence of VF was low and LSBMD Z-scores were>-1.0 in the majority. However, 25 % of children had persistent LS BMD Z-scores deficits that were inversely associated with cumulative GC exposure in the first 3 months.

OP15 - HSP27 AS A NOVEL BIOCOMPATIBILITY MARKER IN CHILDREN ON CHRONIC DIALYSIS

KINGA MUSIAŁ, DANUTA ZWOLIŃSKA
DEPARTMENT OF PEDIATRIC NEPHROLOGY, WROCŁAW MEDICAL UNIVERSITY, POLAND

Introduction: Intracellular heat shock protein (Hsp) 27 acts anti-apoptotically, unabling the binding of death receptor Fas to its ligand FasL. However, the potential role of extracellular Hsp27 is unknown. There are no data on relations between Hsp27, sFas/sFasL system, and its regulators, matrix metalloproteinases (MMPs) and their tissue inhibitors (TIMPs), in children or adults on chronic dialysis, either. The aim of our study was to evaluate serum concentrations of Hsp27, sFas, sFasL, MMP-7 and TIMP-1 in children on chronic dialysis. We searched for differences between various dialysis modalities, analyzed the impact of a single dialysis session on those parameters and their correlations

with markers of inflammation (hsCRP) or endothelial dysfunction (sE-selectin).

Material and methods: 19 patients on hemodialysis (HD) and 22 children on automated peritoneal dialysis (APD) were examined. 30 age-matched healthy children served as controls. Serum concentrations of Hsp27, sFas, sFasL, MMP-7, TIMP-1 and sE-selectin were assessed by ELISA, hsCRP – by nephelometry.

Results: Median values of Hsp27, sFas, sFasL, MMP-7 and TIMP-1 were significantly elevated in all dialyzed patients vs. controls, the highest values being observed in subjects on HD. Although a single HD session decreased the concentrations of Hsp27, they were still elevated vs. those in APD children. Concentrations of sFas, sFasL, MMP-7 and TIMP-1 diminished after the session to the values lower than those in APD patients. sFas, sFasL, MMP-7 and TIMP-1 correlated with Hsp27 concentrations in patients on dialysis, whereas no connections between Hsp27, markers of inflammation or endothelial dysfunction, independent of the group, were observed.

Conclusions: Children on chronic dialysis are prone to Hsp27 dysfunction, more pronounced in patients on hemodialysis. A single HD session modifies Hsp27 concentrations, clearly distinguishing its values from those in APD patients. Obtained results suggest the role for Hsp27 as a marker of biocompatibility, independent of inflammation and endothelial dysfunction, in children on chronic dialysis.

OP16 - Assessment of Water-, Salt and Nutritional Status by Multifrequency Body Impedance Analysis in Children on Hemodialysis

ARIANE ZALOSZYC[1], CLAUS PETER SCHMITT[2], BETTI SCHAEFER[2], RéMI SALOMON[3], SAOUSSEN KRID[3], MICHEL FISCHBACH[1]

[1]*NEPHROLOGY DIALYSIS TRANSPLANTATION CHILDREN'S UNIT, UNIVERSITY HOSPITAL HAUTEPIERRE, STRASBOURG, FRANCE*

[2]*CENTER FOR PEDIATRIC AND ADOLESCENT MEDICINE, UNIVERSITY OF HEIDELBERG, GERMANY*

[3]*PEDIATRIC NEPHROLOGY, HôPITAL NECKER-ENFANTS MALADES, PARIS, FRANCE*

Introduction: Hypertension, fluid and sodium overload and protein-energy-wasting substantially contribute to long term cardiovascular morbidity and mortality of dialysis patients. In clinical routine accurate assessment of the water, sodium and nutritional status, however, is still challenging. Bioelectrical impedance analysis at 50 different frequencies between 5 kHz and 1 MHz, using the Body Composition Monitor (BCM®, Fresenius), is a non-invasive, simple and fast tool for the determination of the different body compartments, but has not systematically been applied in children with CKD5D.

Material and methods: We retrospectively analyzed 615 BCM measurements in 24 pediatric hemodialysis patients, age 15.8 (2.4-26.1) years, from three pediatric centers, performed within one year.

Results: Ten patients (42 %) had increased mean arterial blood pressure predialysis, 4 patients (17 %) also after dialysis. All 10 patients were on antihypertensives. BCM demonstrated predialytic hyperhydration in 5 out of the 24 patients, two of them had elevated blood pressure. Out of the 19 patients classified by BCM as normohydrated, 8 patients were hypertensive. Intracellular water content was neither changed in normo- nor in hypertensive patients. Mean Kt/V urea per hemodialysis session was 1.39 (0.7-2.2). Mean BCM derived Lean Tissue Index (LTI) was 13.5 (9.8-17.2) kg/m²; 8 patients were below the 10th LTI percentile of healthy children. LTI correlated with serum albumin (r=0.46) and prealbumin (r=0.65), but not with BMI (r=0.19).

Conclusions: Hypertension and protein energy wasting is still prevalent in pediatric hemodialysis patients. Our BCM findings of normohydration in hypertensive patients together with the absence of intracellular water changes during dialysis, consistent with isonatric fluid removal, indicate the importance not only of volume but also of sodium overload. Normohydrated hypertensive patients should benefit from stepwise sodium removal by reduction of dialysate sodium levels. BCM furthermore gives an innovative estimate of the nutritional status in pediatric dialysis patients.

OP17 - Kidney transplantation in infancy has a relatively good outcome

HUIB DE JONG[1], ENRICO VERRINA[2], FRANZ SCHAEFER[3], KITTY JAGER[4], KARLIJN VAN STRALEN[4]

[1]*DEPARTMENT OF PAEDIATRIC NEPHROLOGY, UMC ST RADBOUD, NIJMEGEN, THE NETHERLANDS*

[2]*DEPARTMENT OF PAEDIATRIC NEPHROLOGY, GASLINI CHILDREN'S HOSPITAL, GENOA, ITALY*

[3]*CENTER FOR PEDIATRICS AND ADOLESCENT MEDICINE, UNIVERSITY OF HEIDELBERG, GERMANY*

[4]*ESPN/ERA-EDTA REGISTRY, ACADEMIC MEDICAL CENTER, UNIVERSITY OF AMSTERDAM, AMSTERDAM, THE NETHERLANDS*

Introduction: Although the first years after kidney transplantation comprise a challenging period in infancy (children <3 years), once this period is overcome previous studies have suggested a better outcome compared to the children and adolescent age groups. We studied possible factors associated with better outcome, such as i) primary renal disease, ii) gender, iii) year of transplantation.

Material and methods: We included 6036 patients aged less than 18 years from 25 countries from the ESPN/ERA-

EDTA Registry between 1995 and 2010. Of this population almost 494 children were less than 3 years of age at transplantation.

Results: In the first year of life graft survival is closely associated with recipient age. Conversely, beyond the first post-transplant year the youngest age group has the least graft losses resulting in a graft survival curve that is superior to other age groups after 4–8 years post kidney transplantation. When correcting for gender, primary renal disease and year of transplantation by cox regression analysis the youngest age group had a significantly better graft survival. The children younger than 3 years used a smaller number of immunosuppressive drugs than the older age groups.

Conclusions: Graft survival in infants is better compared to other age groups irrespective of primary renal disease, gender and year of transplantation. By contrast, the immunosuppression needed was lowest in the young age group. Our data are in accordance with the NAPRTCS report 2010 showing that patients younger than 2 years of age had significantly lower rejection rates. These data suggest that less medication toxicity or better transplant tolerance could be possible reasons for relatively good graft survival in the youngest age group.

OP18 - Carotis intima-media thickness in children with kidney disease – Cross sectional study

ARIANNA DéGI[1], ANDREA KERTI[1], ATTILA J SZABó[1], PéTER SALLAY[1], ÉVA KIS[1], ORSOLYA CSEPREKáL[2], GEORGE S REUSZ[1]

[1]*FIRST DEPARTMENT OF PEDIATRICS, SEMMELWEIS UNIVERSITY*

[2]*FIRST DEPARTMENT OF INTERNAL MEDICINE, SEMMELWEIS UNIVERSITY*

Introduction: Cardiovascular (CV) morbidity is increased in kidney diseases as the nephrotic syndrome (NS) and even after successful renal transplantation (RTX). Carotis intima-media thickness (cIMT) and central pulse wave velocity (PWV) are known as surrogate CV markers in adults. Our aim was to investigate cIMT and PWV in NS and RTX children.

Material and methods: 36 RTX (16.45±4.04 years, 24 males) and 15 NS (10.18±3.6 years, 9 males) children were involved in the study. cIMT was investigated by B mode ultrasonography. Central PWV was measured by applanation tonometry. Standard deviation scores (SDS) were calculated.

Results: cIMT exceeded the 95th percentile in 13 children in the RTX and 4 in the NS group. In RTX patients there was a strong correlation between cIMT SDS and calcium-phosphate product, serum 25OH vitamin D and LDL-C levels ($r=0.46$; -0.93; 0.55 respectively; $p<0.05$). Patients on vitamin D therapy had lower cIMT and PWV SDS values (−0.45±2.02 vs. 1.29±2.0; -0,01±0,93 vs 1,47±0,99; $p<0.05$). In NS patients cIMT SDS correlated significantly with serum total cholesterol, triglyceride and total protein levels ($r=0.60$; 0.53; -0.54 respectively; $p<0.05$). Patients with low albumin levels had elevated cIMT SDS values (2.69±1.39 vs. 1.19±1.06; $p<0.05$).

Conclusions: Subclinical atherosclerosis is present in pediatric renal transplant recipients and children with nephrotic syndrome. After RTX vitamin D supplementation could reduce the CV risk. In NS children adequate lipid-lowering therapy could have great importance to halt the progression of atherosclerosis. The study was supported by the grants OTKA 83431; 100909; LP2011-008/2011 TÁMOP-4.2.2/B-10/1-2010-0013 and TÁMOP-4.2.1/B-09/1/KMR-2010-0001

OP19 - Increased platelet count and aggregability due to urinary loss of PACAP in nephrotic syndrome

BENEDICTE ENEMAN[1], KATHLEEN FRESON[2], BERT VAN DEN HEUVEL[1], CHRIS VAN GEET[2], ELENA LEVTCHENKO[1]

[1]*DEPARTMENT OF GROWTH AND REGENERATION, KULEUVEN*

[2]*DEPARTMENT OF MOLECULAR AND VASCULAR BIOLOGY, KULEUVEN*

Introduction: Thrombotic complications occurring in up to 15 % of patients represent a severe burden in nephrotic syndrome (NS). The underlying mechanisms are mainly unraveled in regard of venous thrombosis, while elevated blood platelet count and hyperaggregability increase the risk of arterial thrombosis. A role of the neuropeptide PACAP (pituitary adenylate cyclase-activating polypeptide) as an inhibitor of megakaryocyte maturation and platelet function has recently been established. PACAP interferes with the regulation of apoptosis in megakaryocytes, via stimulation of NFκB signaling. We assumed that urinary losses of PACAP bound to ceruloplasmin in NS might lead to PACAP deficiency, leading to thrombocytosis and increased platelet reactivity. The aim of this study was to investigate plasma PACAP levels in relation to blood platelet counts and aggregability in patients with congenital NS (CNS).

Material and methods: Four patients with CNS of the Finnish type, aged 0.5-19 months were tested. Plasma and urinary levels of PACAP were measured semi-quantitatively by western blot.

Results: All patients had plasma PACAP deficiency (14-40 % of control, $p<0.001$) and excessive urinary PACAP excretion. In one patient aged 19 months both kidneys were removed as a routine treatment of CNS. Plasma PACAP levels progressively increased during the first days after

nephrectomy and blood platelet count normalized. In analogy to PACAP deficient mice, an increased platelet aggregation response to collagen was found in a patient in nephrotic state, while platelets from the sibling after bilateral nephrectomy showed normal reactivity towards collagen.
Conclusions: Our observation provides new insights on the mechanisms of arterial thrombosis in NS and is a proof-of-principle that PACAP deficiency exists in CNS. In analogy to mice, PACAP deficiency seems to play an important role in the thrombocytosis and platelet hyperaggregability in CNS. When confirmed in larger studies, PACAP replacement or stimulation of PACAP receptors might become a valuable therapeutic option for prevention of arterial thrombosis in CNS.

OP20 - IGM BINDING ON T LYMPHOCYTES PREDICTS STEROID DEPENDENCE IN CHILDREN WITH IDIOPATIC NEPHROTIC SYNDROME

MARINA VIVARELLI, MANUELA COLUCCI, FRANCESCO EMMA
BAMBINO GESù CHILDREN'S HOSPITAL, IRCCS

Introduction: Idiopathic nephrotic syndrome (INS) is the most frequent glomerular disease in childhood and responds to steroids in >80 % of cases. However, some children have a complicated course that is characterized by steroid dependence (SDNS). To date, the etiology of INS remains unclear, although several lines of evidence implicate a T cell dysregulation, while response to rituximab suggests a role of B cells.
Material and methods: In the course of analysis of the phenotype of T and B cells in INS children, we have observed that certain patients present an unexpected amount of IgM deposition on the surface of their T lymphocytes (CD5pos/CD19neg cells). To further investigate the significance of this finding, we have collected PBMCs from children with steroid-sensitive INS at onset, prior to any treatment, and have analyzed by cytofluorimetry their T and B cell phenotype.
Results: Between 2008 and 2011, 44 patients were recruited for this study. All responded to steroids within 4 weeks, and were followed for at least 6 months. 78 healthy donor and 25 age-matched control samples were used to define the normal range, expressed as Mean Fluorescence Intensity [MFI], of IgM staining of T lymphocytes. Patients with INS had more prominent IgM staining ($p<0.003$); 15/44 (34 %) were above the 97th percentile for controls. By multivariate analysis, the intensity of IgM staining at onset, prior to any treatment, was highly predictive of early relapse (Hazard Ratio 1.64 [1.23-2.20] per 100 MFI, $p=0.001$). Except for children with lupus nephritis and few patients with membranous nephropathy, screening of other glomerulopathies showed no significant IgM staining of T lymphocytes. In the past 3 years, 23 SDNS patients received rituximab; most had negative T cell IgM staining while CD20 cells were depleted.
Conclusions: Taken together, these results suggest a role of IgM T cell deposition in inducing steroid dependence in INS patients.

OP21 - Understanding the renal pathogenesis of diarrhoea associated haemolytic uraemic syndrome: the role of the podocyte

LINDSAY KEIR[1], ANNA RICHARDS[2], ROBERT SPOONER[3], GAVIN WELSH[1], SIMON SATCHELL[1], RICHARD COWARD[1], MOIN SALEEM[1]
[1]*ACADEMIC RENAL UNIT, UNIVERSITY OF BRISTOL*
[2]*QUEENS MEDICAL RESEARCH INSTITUTE, UNIVERSITY OF EDINBURGH*
[3]*LIFE SCIENCES, UNIVERSITY OF WARWICK*

Introduction: Diarrhoea-associated haemolytic uraemic syndrome (D+HUS) is the leading cause of paediatric acute renal failure. It occurs after infection by Shiga toxin (stx) producing bacteria. There is no direct treatment. HUS was considered an endothelial disease until an inducible podocyte-specific VEGFA knockdown mouse also developed the pathological signature: glomerular thrombotic microangiopathy (TMA). Stx binds cellular Gb3 receptors. Human podocytes express Gb3 and show reduced VEGFA production following stx2 treatment. Atypical HUS is caused by mutations in alternative complement pathway proteins, particularly Factor H. Eculizumab, a drug that blocks complement, is used to treat atypical HUS and experimentally in D+ HUS. We hypothesize that podocytes, VEGFA and complement regulators play a co-ordinated role in the renal pathogenesis of D+HUS.
Material and methods: Gb3 expression on human glomerular cells was investigated. Cellular Stx1 sensitivity was determined using a radio-labelled protein synthesis assay. Glomerular endothelial cell (GEnC) complement regulator expression was analysed. GEnC were treated to remove surface Factor H and then exposed to serum free media +/−VEGFA. After 24 hrs, surface-bound and secreted Factor H was measured. A functional complement activation assay was used to test VEGF-A treated and untreated GEnC. The readout was C3d and C4d deposition, determined by flow cytometry.
Results: Human glomerular cells express Gb3 and are stx1 sensitive. Podocytes are 2.6-fold more sensitive to stx1 than GEnC($p<0.002$). GEnC express complement regulators and expression is increased by VEGF-A. VEGF-A upregulates GEnC surface-bound and secreted factor H ($p<0.0001$).

Functionally, GEnC treated with VEGF-A showed 30 % less C3d and C4d deposition compared to untreated cells.
Conclusions: Podocytes are exquisitely sensitive stx1 targets. Reduced podocyte VEGFA decreases GEnC complement regulator expression making the glomerular endothelium vulnerable to complement-mediated attack. This evidence supports a central role for podocyte injury and complement mediated endothelial cell damage in the pathogenesis of D+HUS; suggesting a role for complement blockade in D+HUS treatment.

OP22 - REGULATORY T CELLS (TREG) AND TRYPTOPHAN/KYNURENINE PATHWAY IN IgA NEPHROPATHY

ELISA LOIACONO[1], DAVIDE DEFEDELE[2], M. PAOLA PUCCINELLI[2], ROBERTA CAMILLA[1], RACHELE GALLO[1], LICIA PERUZZI[1], CRISTIANA ROLLINO[3], GIULIETTA BELTRAME[3], MICHELA FERRO[3], LUCA VERGANO[1], FEDERICA CAMPOLO[1], ALESSANDRO AMORE[1], ROSANNA COPPO[1]
[1]*NEPHROLOGY, DIALYSIS, TRANSPLANTATION, R.MARGHERITA HOSPITAL, TURIN, ITALY*
[2]*DIAGNOSTIC SERVICES, DIAGNOSTIC DEPARTMENT, R.MARGHERITA HOSPITAL, TURIN, ITALY*
[3]*NEPHROLOGY AND DIALYSIS, G.BOSCO HOSPITAL, TURIN, ITALY*

Introduction: IgA nephropathy (IgAN) is due to immune dysregulation with persistent T cell response to common mucosal antigens. We aimed at investigating regulatory T-cells (Treg), which play an essential role in down-regulating immune response. We assessed also the activity of the metabolic enzyme indoleamine 2,-dioxygenase (IDO), an inducer and amplifier of Treg functions.
Material and methods: PBMC were isolated from 27 children with IgAN (12.7±3.7 years old), with e-GFR 141± 35 ml/min/1.73 m2 and proteinuria 0.61±1.37 g/day, and from 30 healthy controls (HC). The protocol included the measurement in Taqman of mRNA expression of the Treg regulation-associated gene forkhead box P3 (Foxp3) and the assessment of IDO activity as change in the ratio between tryptophan (Trp) and its catabolic product kynurenine (Kyn) (simultaneously determined using isocratic RP-HPLC method with UV detection). Kyn/Trp ratio was also calculated.
Results: The transcriptional level of Foxp3 was significantly lower in patients with IgAN versus HC (0.96±0.60 vs 1.26±0.65, P=0.036). Trp levels were similar in IgAN patients and HC, but Kyn, its catabolic product, resulted significantly increased (2.55±0.62 vs 2.02±0.32, P= 0.0087) and so was the Kyn/Trp ratio (5.28±1.78 vs 3.72 ±0.55 in HC, P=0.0018). No correlation was found with proteinuria, nor with eGFR. No correlation was found with possible TReg modulator factors, including Toll-Like Receptors (TLR 3-4-9).
Conclusions: In patients with IgAN there is a defective transcription of mRNA encoding for Foxp3, hence a likely defective Treg activity, in spite of an hyperactivity of the IDO enzyme which is expected to trigger Tregs. Environmental causes have been reported to induce Foxp3 Treg to undergo phenotypic changes, including conversion, plasticity or reprogramming to rapidly adopt a pro-inflammatory phenotype. Mechanisms inhibiting Tregs in IgAN in spite of IDO pathway activation deserve further investigations.

OP23 - NEXT GENERATION SEQUENCING IS AN EFFECTIVE METHOD OF ANALYSING LARGE NUMBERS OF GENES IN THE UK STUDY OF STEROID RESISTANT NEPHROTIC SYNDROME (SRNS) IN CHILDHOOD

HUGH MCCARTHY, AGNIESZKA BIERZYNSKA, MATT WHERLOCK, GAVIN WELSH, MOIN SALEEM
UNIVERSITY OF BRISTOL

Introduction: SRNS in childhood in the UK is rare but has a high morbidity with an estimated 350 affected and over 100 on the end stage program. Advances in understanding of the genetic basis and molecular biology of this condition have not been mirrored by clinical advances. The UK cohort of SRNS in childhood has been developed, in the first instance to correlate detailed phenotype with genotype.
Material and methods: DNA was extracted from the blood samples of 23 patients in the cohort and 1 podocyte cell line known to have a mutation for PLCe1, with full ethical approval. A Roche Nimblegen Sequence Capture Array (12x135K capability) was used to capture exons of the 478 genes of interest. Sequencing was performed on an Illumina GAIIx sequencer. Bioinformatics was performed using CLC Bio genomics workbench software. Comparison was made with previously undertaken Sanger sequencing of NPHS1, 2 and exons 10, 11 of WT1 of five patients.
Results: 97 % of reads mapped to the reference sequence and 76 % of reads were on target genes. On average, 185 nonsynonymous single nucleotide polymorphisms (SNPs) were identified per patient (average of 10 novel/patient). On average, 6 deletion insertion polymorphisms were found per patient. Homozygous or compound heterozygous pathogenic mutations were identified in 20 % of sporadic cases and 38 % of familial, including a rare compound heterozygous mutation in COQ2 (phenotype an isolated nephropathy). In one family of three siblings with a homozygous NPHS1 mutation, phenotype appeared altered by the addition of a 3rd allelic hit in WT1 in two. Of the 25 SNPs identified in preliminary Sanger sequencing, 24 were detected with NGS.

All other changes of note detected by NGS were subsequently confirmed with Sanger sequencing.

Conclusions: NGS appeared effective in analysing known nephrotic genes and other of interest. Detection rate of pathogenic mutations was similar to that previously reported. Genotype phenotype correlation in the extended cohort will allow for development of prognostic variants which could potentially be used in the early clinical setting.

OP24 - WT1 screening in nephrotic syndrome – lessons from PodoNet

BEATA S. LIPSKA[1], PARASKEVAS IATROPOULOS[2], BRUNO RANCHIN[3], JIRI DUSEK[4], FATIH OZALTIN[5], ANETTE MELK[6], JUTTA GELLERMANN[7], AUGUSTINA JANKAUSKIENE[8], AMIRA PECO-ANTIC[9], ALEKSANDRA ZUROWSKA[10], ANNA WASILEWSKA[11], GIANLUCA CARIDI[12], BASSAM SAEED[13], ANNA MOCZULSKA[14], RADOVAN BOGDANOVIC[15], OZLEM ERDOGAN[16], MARIA SZCZEPAńSKA[17], MUKADDES KALYONCU[18], HALINA BORZECKA[19], AGNES TRAUTMANN[20], FRANZ SCHAEFER[20], PODONET CONSORTIUM[21]

[1]*DEPARTMENT OF BIOLOGY AND GENETICS, MEDICAL UNIVERSITY OF GDAńSK, POLAND*

[2]*CLINICAL RESEARCH CENTRE FOR RARE DISEASES "ALDO E CELE DACCO", MARIO NEGRI INSTITUTE FOR PHARMACOLOGICAL RESEARCH, BERGAMO, ITALY*

[3]*DEPARTMENT OF PEDIATRICS, EDOUARD-HERRIOT HOSPITAL, LYON, FRANCE*

[4]*DEPARTMENT OF PEDIATRICS, UNIVERSITY HOSPITAL MOTOL, PRAGUE CZECH REPUBLIC*

[5]*PEDIATRIC NEPHROLOGY AND RHEUMATOLOGY, HACETTEPE UNIVERSITY FACULTY OF MEDICINE, ANKARA, TURKEY*

[6]*PAED. KIDNEY, LIVER AND METABOLIC DISEASE, MHH CHILDREN´S HOSPITAL, HANNOVER, GERMANY*

[7]*DEPARTMENT OF PEDIATRIC NEPHROLOGY, CHARITé UNIVERSITY CHILDREN'S HOSPITAL, BERLIN, GERMANY*

[8]*VILNIUS UNIVERSITY CHILDREN`S HOSPITAL, VILNIUS, LITHUANIA*

[9]*DIVISION OF PEDIATRIC NEPHROLOGY, UNIVERSITY CHILDREN'S HOSPITAL, BELGRADE, SERBIA*

[10]*DEPARTMENT OF PEDIATRIC AND ADOLESCENT NEPHROLOGY, MEDICAL UNIVERSITY OF GDANSK, POLAND*

[11]*DEPARTMENT OF PEDIATRIC NEPHROLOGY UNIVERSITY OF BIALYSTOK, POLAND*

[12]*LABORATORY ON PHYSIOPATHOLOGY OF UREMIA, G. GASLINI CHILDREN HOSPITAL, GENOA, ITALY*

[13]*DEPARTMENT OF PEDIATRIC NEPHROLOGY, KIDNEY HOSPITAL OF DAMASCUS, SYRIA*

[14]*DIALYSIS UNIT, DEPARTMENT OF PEDIATRIC NEPHROLOGY, JAGIELLONIAN UNIVERSITY MEDICAL COLLEGE, CRACOW, POLAND*

[15]*DEPARTMENT OF NEPHROLOGY, INSTITUTE OF MOTHER AND CHILD HEALTHCARE, BELGRADE, SERBIA*

[16]*SAMI ULUS CHILDREN´S HOSPITAL, ANKARA, TURKEY*

[17]*DIALYSIS DIVISION FOR CHILDREN, DEPARTMENT AND CLINICS OF PEDIATRICS MEDICAL UNIVERSITY OF SILESIA IN KATOWICE, POLAND*

[18]*PEDIATRIC NEPHROLOGY DEPARTMENT, FACULTY OF MEDICINE, KARADENIZ TECHNICAL UNIVERSITY, TRABZON TURKEY*

[19]*PEDIATRIC NEPHROLOGY, MEDICAL UNIVERSITY OF LUBLIN, LUBLIN POLAND*

[20]*DIVISION OF PEDIATRIC NEPHROLOGY, CENTER FOR PEDIATRICS AND ADOLESCENT MEDICINE, HEIDELBERG, GERMANY*

[21]*WWW.PODONET.ORG*

Introduction: Despite recent advantages in molecular diagnosis of hereditary nephrotic syndrome (HNS), there are no clear indications for WT1 screening in patients presenting without extrarenal manifestations. WT1 mutations are characterized by considerable differences in phenotypic expression and incomplete penetration. Accordingly, we have analyzed phenotypic spectrum of WT1-associated HNS so as to propose guidelines for screening and clinical management.

Material and methods: Molecular analysis of exons 8–9 of WT1 gene was performed in 726 steroid-resistant NS patients enrolled in the Podonet registry.

Results: 47 (6.5 %) mutations: 19 intronic (I; Frasier type) and 28 exonic (E; Denys-Drash type) were detected. Patients with exonic mutations were significantly younger at diagnosis (3.1 vs 7.0 years; $p<0.001$) and had lower 5 years renal survival rates (37 % vs. 88 %; $p<0.001$). 20 (43 %; 9E, 11I) patients had apparently idiopathic HNS at the time of referral, however mild structural abnormalities including isolated cryptorchidism, horseshoe kidney or VUR were present in 5 of them. Idiopathic cases were mostly genotypic females (90 %). 16 (34 %; 15E, 1I) had Wilms tumor. Usually, patients presented signs of NS within 2 years from cancer diagnosis, however 20 % developed NS more than 10 years later. 7 % (3I) had other cancers, namely gonadoblastoma and lymphoma. 12 (26 %; 5E, 7I) exhibited some degree of sexual ambiguity. All of them had 46,XY karyotype, however 5 were phenotypically females. Structural abnormalities of genitourinary tract were present in 41 % patients of both genders. FSGS was the most common

histopathological finding (52 %), DMS being present in 28 % and GGS in 11 %.

Conclusions: Our findings substantiate WT1 testing also in non-syndromic HNS patients, regardless of age at diagnosis or histological subtype. Detailed gynecological and endocrinological examination along with karyotyping and oncological surveillance is indicated in all WT1-positive patients to detect mild phenotypic abnormalities. Wilms tumor cases should have regular proteinuria check-up for at least 15 years after cancer diagnosis.

OP25 - The role of the Sigma-1 receptor – Akt - eNOS pathway in renal ischemia/reperfusion injury.

NORA F BANKI[1], ADAM HOSSZU[1], ZSUZSANNA ANTAL[2], SANDOR KOSZEGI[1], LASZLO WAGNER[3], RENATA GELLAI[1], LILLA LENART[1], ADAM VANNAY[4], VERONIKA MULLER[5], ATTILA J SZABO[2], TIVADAR TULASSAY[2], ANDREA FEKETE[1]

[1]SE-MTA „LENDULET" DIABETES RESEARCH GROUP, SEMMELWEIS UNIVERSITY, BUDAPEST

[2]1ST DEPT. OF PEDIATRICS, SEMMELWEIS UNIVERSITY, BUDAPEST

[3]DEPT. OF TRANSPLANT SURGERY, SEMMELWEIS UNIVERSITY, BUDAPEST

[4]SE-MTA NEPHROLOGY RESEARCH GROUP, SEMMELWEIS UNIVERSITY, BUDAPEST

[5]DEPT. OF PULMONOLOGY, SEMMELWEIS UNIVERSITY, BUDAPEST

Introduction: The protective role of a novel pathway, the Sigma-1 receptor (S1R)-Akt-endothelial nitrogen monoxide synthase (eNOS) axis has been recently described in heart ischemia/reperfusion (IR) injury. In renal IR we previously showed that S1R agonists are protective, however the exact mechanism is still unknown. Here in renal IR we studied the effect of S1R agonist fluvoxamine (FLU) and antagonist NE-100 on the S1R-Akt-eNOS signaling pathway.

Material and methods: Male Wistar rats were treated i.p. with FLU (20 mg/bwkg; FLU), FLU and NE-100 (20 mg/bwkg and 1 mg/bwkg; FN) or vehicle (VEH). 30 minutes after the treatment animals were harvested (T30') or subjected to renal ischemia for 50 minutes followed by 2 (T2) or 24 (T24) hours of reperfusion. Sham-operated, untreated animals served as controls (C) (n=10/group). The renal S1R-Akt-eNOS proteins were analyzed by Western blot and immunofluorescence microscopy.

Results: 30 min after FLU treatment renal Akt and eNOS expression were elevated compared to C. After IR both proteins continually increased with time (C vs. T2 vs. T24). While at T2 there was no difference among the groups, at T24 renal Akt and eNOS protein levels were higher in the VEH group compared to FLU. NE-100 diminished all effects of FLU. S1R expression remained unchanged in the different groups. S1R-Akt-eNOS were co-localized in renal tubular cells. In C and after FLU treatment a nucleus-associated staining was observed, while in VEH and FN groups S1R-Akt-eNOS showed a more cytoplasmic localization.

Conclusions: The S1R-Akt-eNOS axis could be a novel pathway in the pathophysiology of renal IR injury. The S1R agonist FLU might exert its renoprotective effect by altering these proteins.

OP26 - Sigma-1 receptor agonist treatment is protective against renal ischemia/reperfusion injury.

ADAM HOSSZU[1], NORA F. BANKI[1], ZSUZSANNA ANTAL[2], SANDOR KOSZEGI[1], LASZLO WAGNER[3], AGNES PROKAI[2], RENATA GELLAI[1], LILLA LENART[1], ADAM VANNAY[4], VERONIKA MULLER[5], ATTILA SZABO[2], TIVADAR TULASSAY[2], ANDREA FEKETE[1]

[1]SE-MTA „LENDULET" DIABETES RESEARCH GROUP, SEMMELWEIS UNIVERSITY, BUDAPEST

[2]1ST DEPT. OF PEDIATRICS, SEMMELWEIS UNIVERSITY, BUDAPEST

[3]DEPT. OF TRANSPLANT SURGERY, SEMMELWEIS UNIVERSITY, BUDAPEST

[4]SE-MTA NEPHROLOGY RESEARCH GROUP, SEMMELWEIS UNIVERSITY, BUDAPEST

[5]DEPT. OF PULMONOLOGY, SEMMELWEIS UNIVERSITY BUDAPEST

Introduction: Ischemia/reperfusion (IR) injury is a severe complication of various clinical situations. Fluvoxamine (FLU) has been shown to be protective against heart IR injury through activating the Sigma-1 receptor (S1R). However there is no data about the potential effect of S1R agonists in renal IR injury. In renal IR we studied the effect of S1R agonist FLU and antagonist NE-100 on the postischemic survival, the structural and functional kidney damage.

Material and methods: Uninephrectomized male Wistar rats were treated i.p. with FLU (20 mg/bwkg; FLU), FLU and NE-100 (20 mg/bwkg and 1 mg/bwkg; FN) and vehicle (VEH) 30 minutes before the 50 minute renal ischemia. Sham-operated animals served as controls (C) (n=10/group). We observed postischemic survival and analyzed structural kidney damage and the deterioration of renal function in the 24th hour of reperfusion. We studied the alteration of renal capillary diameter and structural damage in vivo using muliphoton microscopy.

Results: FLU treatment improved postischemic survival. Deterioration of renal function and renal structural damage

was milder in FLU treated animals. This was characterized by the more preserved integrity of the tubular brush border and nuclei as well as less prominent hyaline accumulation. The reduced capillary diameter after IR was increased by FLU treatment (C: 9.86±1.23 μm; VEH: 8.29±1.29 μm; FLU: 10.73±0.67 μm). NE-100 suspended all effects of FLU.

Conclusions: The S1R agonist FLU –used as an antidepressant chronically without notable side-effects – could have a renoprotective effect in IR. We suspect the improvement of renal perfusion and the role of the S1R behind this effect.

OP27 - EARLY DETECTION OF ACUTE KIDNEY INJURY. IS IT POSSIBLE?

MERYEM BENZER[1], HARİKA ALPAY[1], ÖZGÜR BAYKAN[2], ABDULLAH ERDEM[3], İBRAHİM HALİL DEMİR[3]

[1]*MARMARA UNIVERSITY MEDICAL FACULTY, DEPARTMENT OF PEDIATRIC NEPHROLOGY*

[2]*MARMARA UNIVERSITY MEDICAL FACULTY, DEPARTMENT OF BIOCHEMISTRY*

[3]*DR SIYAMI ERSEK THORACIC AND CARDIOVASCULAR SURGERY TRAINING AND RESEARCH HOSPITAL, DEPARTMENT OF PEDIATRIC CARDIOLOGY*

Introduction: We aimed to investigate early detection of contrast-induced-nephropathy (CIN) by new biochemical markers and the relationship between those markers and body composition determined by bioimpedance method before angiography.

Material and methods: The study included 91 patients (8.7 ±4.29 years) who had been undergone elective cardiac angiography and 50 healthy age-sex matched controls (9.49±3.85 years). Blood-urea-nitrogen(BUN), serum(s) creatinine, s-cystatin-C, s-sodium, and s-neutrophil-gelatinase-associated-lipocalin (NGAL) and urinary N-acetyl-β-glucosaminidase (NAG) with creatinine were measured before and at 6-12-24 hours after radiocontrast media administration in patients and all were taken once in controls. Body-composition-monitoring (BCM) was performed in all cases.

Results: Serum creatinine and glomerular filtration rate (GFR) were not significant between patients and controls. Serum cystatin-C increased significantly after 12 hours. Serum NGAL and urinary NAG/creatinine ratio increased in the first six hours. During the 24-hour follow-up, acute kidney injury (AKI) developed in 18 patients. In this AKI group (A-1), the sixth hour sodium median and serum cystatin-C levels were significantly higher than those that did not develop AKI (A-0). The median lean tissue index (LTI) of patients was higher than the controls (p=0.027). Extracelluler water (ECW) and intracelluler water (ICW) measurements, after adjusting for body area, were not different between patients and controls. The median FTI of A-1 group was significantly higher than A-0 (p=0.044).

Conclusions: We conclude that in the first 24 hours, creatinine and creatinine-based GFR are not adequate for early detection of CIN but increase in s-cystatin C, s-NGAL and urinary NAG/creatinine ratios are found promising markers for early diagnosis of AKI. Fat and lean tissue of the body as well as the water composition are thought to be important in the development of AKI.

OP28 - Critical value of plasma creatinine in premature neonates: a predictive factor for mortality and long-term developmental morbidity. Results from LIFT cohort.

BRUEL ALEXANDRA[1], FLAMANT CYRIL[2], ROUSSEY-KESLER GWENAELLE[1], ROZE JEAN-CHRISTOPHE[2], DENIZOT SOPHIE[2], SIMEONI UMBERTO[3], ALLAIN-LAUNAY EMMA[1]

[1]*PEDIATRICS DEPARTMENT, NANTES UNIVERSITY HOSPITAL, FRANCE*

[2]*NEONATAL INTENSIVE CARE, NANTES UNIVERSITY HOSPITAL, FRANCE*

[3]*NEONATAL INTENSIVE CARE, APHM, MARSEILLE, FRANCE*

Introduction: The aim of this study was to define critical values of highest serum creatinine (HSCr) observed between the 3rd and the 30th day of life according to gestational (GA) in very preterm infants.

Material and methods: 1074 very preterm infants (230 with GA of 24–27 w, 246 of 28–29 w; 598 of 30–32 w) hospitalized in our NICU between January1, 2003 and December 31, 2008, with at least one or more serum creatinine available were included in this study. Data were extracted and analyzed from a prospective clinical and biochemical data bank. Surviving infants (n=999) were enrolled in follow-up after parental written consent (n=886) and examined at 2 years of age (n=791). Critical values of serum creatinine were defined as the 90th percentile values of HSCr observed among infants with optimal 2 years outcome for each group of GA. Renal failure was defined as a HSCr over the critical value according to GA.

Results: HSCr was closely predictive for mortality (area under the receiver-operating-characteristic curve=0.74 (95%CI:0.66-0.82) in 24-27w, 0.79 (95%CI:0.63-0.94) in 28–29 and 0.79 (95%CI:0.62-0.95) in 30-32w). Critical value of HSCr obtained among surviving infants with 2 years optimal outcome were 140, 100 and 85 μmol/L (n=388) respectively for each group of GA. For all groups, renal failure was associated to mortality with a specificity of

0.88 (95%CI:0.86-0.90) and a sensitivity of 0.55 (95%CI:0.43-0.65), to non optimal 2 years outcome with a specificity of 0.90 (95%CI:0.86-0.91) and a sensitivity of 0.20 (95%CI:0.14-0.27). After adjustment for known risk factors of renal failure, renal failure was significantly associated with mortality (aOR= 5.8 (95%CI:3.0-11.0), p=0.001) and non optimal 2 years outcome (aOR=1.8 (95%CI:1.05-3.1), p=0.03).
Conclusions: Critical values of HSCr of 140, 100 and 85 μmol/L for respectively 24–27, 28–29 and 30-32w were significantly associated to mortality and morbidity in this cohort.

OP29 - Biomarkers of acute kidney injury in pediatric cardiac surgery

AMIRA PECO-ANTIC[1], IRENA VUKICEVIC[2], JELENA KOTUR[3], DJORDJE HERCOG[2], VLADIMIR MILOVANOVIC[2], JASMINA IVANISEVIC[3], IVANA IVANISEVIC[1], MILICA MILJKOVIC[3], NIKOLA KOCEV[1]
[1]*MEDICAL FACULTY, UNIVERSITY OF BELGRADE, BELGRADE, SERBIA*
[2]*UNIVERSITY CHILDREN'S HOSPITAL, BELGRADE, SERBIA*
[3]*FACULTY OF PHARMACY, UNIVERSITY OF BELGRADE, BELGRADE, SERBIA*

Introduction: Acute kidney injury (AKI) is common after pediatric cardiac surgery. It is still diagnosed by measuring serum creatinine (sCr) although this is unreliable indicator during acute changes of kidney function. New biomarkers that can identify subjects with early AKI are needed to facilitate appropriate treatment. Objective of this study was to test the role of serum Cystatin C (sCC), serum and urine neutrophil gelatinase-associated lipocalin (s/u NGAL), urine kidney injury molecule 1 (KIM1) and urine liver fatty acid-binding protein (L-FABP) as biomarkers for early AKI in children undergoing cardiopulmonaly bypass (CPB).
Material and methods: We performed a prospective single-center evaluation of sCC, sNGAL, uNGAL, KIM 1 and L-FABP at 0, 2, 6, 24, 48 and 72 postoperative hours in a cohort of children undergoing CPB during cardiac surgery. Patients with pre-existing chronic renal failure or congenital renal anomalies were excluded from further analysis. AKI was defined as a≥50 % increase in sCr from the preoperative value within 48 h.
Results: Of the 107 patients 12 patients (11.2 %) developed AKI; 4 of them needed acute dialysis treatment. In AKI compared to no AKI group, sCC at 2 h, sNGAL at 6-72 h and uNGAL at 2-72 h were significantly increased, as well as CPB, aortic cross clamp time and length of hospital stay. The best accuracy for diagnosis of AKI had uNGAL at 2 h with an area under the receiver operator curve (AUC ROC) of 0.925 while those for sCC at 2 h, sNGAL at 6–72 h and uNGAL at 6–72 h were moderate (AUC ROC 0.729-0.869).
Conclusions: Urine and serum NGAL and sCC identify AKI early (at 2–6 hours) post CPB.

OP30 - FIRST EXPERIENCE WITH PRISMAFLEX HF 20 SET IN AN INFANT OF 5 KILOGRAMS BODY WEIGHT

MARIA TERESA SARAVO[1], CARMEN LUBRANO[1], MICHELE SAGLIANO[1], GABRIELE MALGIERI[1], UGO GRAZIANO[2], ANTONINO MUSUMECI[3], CARMINE PECORARO[1]
[1]*DEPARTMENT OF NEPHROUROLOGY, CHILDREN'S HOSPITAL SANTOBONO, NAPLES, ITALY*
[2]*DEPARTMENT OF SURGERY, CHILDREN'S HOSPITAL SANTOBONO, NAPLES, ITALY*
[3]*DEPARTMENT OF CARDIOLOGY, UNIVERSITY FEDERICO II, NAPLES, ITALY*

Introduction: Prismaflex HF20® is a disposable set (Gambro Industries) used in infants with renal failure. It allows for blood and fluid flow rate adaptation and balance control compatible with treatments of small infants. Used in conjunction with the Prismaflex® device (Gambro, Lund, Sweden) it is a promising approach for RRT in infants or toddlers with body weight≥8 Kilograms.
Material and methods: We report our experience investigating the performance of this system (the combination of the Prismaflex machine on the Prismaflex HF20®) in a girl with body weight ≤5 Kilograms.
Results: B.L. is a girl born at 39 weeks gestation, B.W. 2,400 g; at the fourth day of life a subtotal small bowel resection due to massive necrosis was performed. A nephrotic syndrome with progressive decrease of renal function developed. A kidney biopsy, performed at 20 days of life, revealed a Diffuse Mesangial Sclerosis, the molecular analysis of DNA showed an homozygous mutation in WT1 gene. Due to the inability to perform peritoneal dialysis (a peritoneal catheter was inserted at the same time of the central vascular catheter, but it was not working, may be due to the previous abdominal surgery) twin single lumen 6.5 F Tesio catheters in right internal jugular vein were inserted. At 1 month of age and with a body weight 2,850 g, B.L. started daily Hemodiafiltration using Prisma M10®set on the Prisma® device. At 8 months of age and with a body weight 4,850 g, HDF with Prismaflex®HF20 on Prismaflex®device was started. The filter membranes consisted of polyarylethersulfone (PAES) hollow fibers, the effective membrane surface area is 0.2 m2. The extracorporeal volume is 60 ml. Overall 139 treatment sessions were performed over 8 months time: 6 sessions a week during the first 6 months (when parenteral feeding was exclusive

because of intestinal malabsorption due to postsurgical short bowel syndrome) and then 4 sessions a week when a mixed enteral and parenteral feeding system was adopted. Duration of each HDF session was 3.5-4.0 hours, according to the prescribed fluid balance. Treatment monitoring included patient weight change and fluid balance, treatment efficacy, number of interventions and alarms. Desired fluid balance according to the prescribed weight loss was achieved in 81 % sessions, UF volume was 200÷300 ml for session. Treatment efficacy was monitored by urea and creatinine serum levels at the start of RRT (79±13 and 7.33±0.7 mg/dl) and their decrease after 4 hours (30±4 and 3.0±0.5 mg/dl). Main complication was hypotension. The clinical course and the dialysis efficacy were similar with both dialysis systems (M10 filter on Prisma and HF20 on Prismaflex, respectively): mean Qb was 25 ml/min with both treatments, meanwhile Qd was 1.500 ml/hour and Uf was 30–70 with M10 and 850 ml/hour and 50–100 with HF20, respectively.
Conclusions: Prismaflex HF20 disposable set in conjunction with the prismaflex device can be used successfully for RRT in infants with body weight lesser than 8 Kilograms and as small as 5 Kilograms.

OP31 - Endothelial progenitor cells accelerate endothelial regeneration after shiga toxin-induced injury

NEYSAN RAFAT[1], FARNOOSH FATHALIZADEH[1], KATHRIN PLOTNICKI[1], CHRISTIAN BETZEN[1], VOLKER ECKSTEIN[2], ANGELIKA BIERHAUS[3], BURKHARD TÖNSHOFF[1]
[1]*DEPARTMENT OF PEDIATRICS I, UNIVERSITY CHILDREN'S HOSPITAL HEIDELBERG*
[2]*FACS CORE FACILITY, DEPARTMENT OF MEDICINE V, UNIVERSITY HOSPITAL HEIDELBERG*
[3]*DEPARTMENT OF MEDICINE I AND CLINICAL CHEMISTRY, UNIVERSITY HOSPITAL HEIDELBERG*

Introduction: Endothelial injury with consecutive microangiopathy plays a central role in the pathogenesis of the hemolytic-uremic syndrome (HUS). An accelerated regeneration of this damage would lead to improved perfusion, oxygen supply and organ function. In the present study we therefore examined the potential of endothelial progenitor cells (EPC) as a new treatment strategy for shiga toxin-induced endothelial lesions in an in vitro-model.
Material and methods: Monolayers of human umbilical vein endothelial cells (HUVEC) were sensitized with TNF-α and then incubated with various concentrations of shiga toxin 2 (Stx2) [1 ng/l - 1 μg/l] for 48 hours. Endothelial damage was detected by a cell-based assay (ApoToxGlo Triplex-Assay, Promega) for cell viability, cell cytotoxicity and apoptosis. EPC were isolated from cord blood by Ficoll-density gradient centrifugation and cell sorting using the antibodies CD34 and CD133. Under dynamic flow conditions, Stx2-damaged monolayers were treated with EPC and captured by video microscopy over a period of 3–7 days. The regenerative potential of EPC was assessed in comparison to Stx2-damaged but untreated monolayers.
Results: Pretreatment of HUVEC with TNF-α lead to an upregulation of the Stx-surface receptor Globotriaosylceramid (Gb3). The following incubation with Stx2 induced a time- and concentration-dependent decrease of cell viability and an increase of cytotoxicity and apoptosis of HUVEC. Subsequent co-incubation with EPC (10^4-10^5 cells/ml) under dynamic flow conditions lead to a significant ($p<0.05$) improvement of cell viability as well as a decrease in cytotoxicity and apoptosis in comparison to untreated monolayers.
Conclusions: These results demonstrate that EPC accelerate endothelial regeneration after Stx2-induced damage in vitro and could potentially play a role in the treatment of HUS.

OP32 - A HIGH FREQUENCY OF GENOMIC DISORDERS IN PATIENTS WITH CONGENITAL KIDNEY MALFORMATIONS

SIMONE SANNA-CHERCHI[1], KRZYSZTOF KIRYLUK[1], KATELYN E BURGESS[1], MONICA BODRIA[2], MATTHEW G SAMPSON[3], DEXTER HADLEY[3], SHANNON N NEES[1], ROEL STERKEN[1], MIGUEL VERBITSKY[1], VLADIMIR J LOZANOVSKI[4], ANNA MATERNA-KIRYLUK[5], BRITTANY J PERRY[1], ALBA CARREA[2], CORRADO MURTAS[2], NADICA RISTOSKA-BOJKOVSKA[4], MARCIN ZANIEW[5], HANA FLOGELOVA[6], PATRICIA L WENG[1], ADELA ARAPOVIC[7], KRISTINA DRNASIN[8], GIANLUCA CARIDI[2], VINICIO GOJ[9], RICHARD P LIFTON[10], MARIJAN SARAGA[7], ANNA F DOMINICZAK[11], LORETO GESUALDO[12], ZORAN GUCEV[4], LANDINO ALLEGRI[13], ANNA LATOS-BIELENSKA[5], DANIELE CUSI[14], FRANCESCO SCOLARI[15], VELIBOR TASIC[4], HAKON HAKONARSON[3], GIAN MARCO GHIGGERI[2], ALI G GHARAVI[1]
[1]*COLUMBIA UNIVERSITY, NY, USA*
[2]*G. GASLINI INSTITUTE, GENOA, ITALY*
[3]*UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA, USA*
[4]*UNIVERSITY CHILDREN'S HOSPITAL, SKOPJE, MACEDONIA*
[5]*POLISH REGISTRY OF CONGENITAL MALFORMATIONS, POZNAN, POLAND*
[6]*PALACKY UNIVERSITY, OLOMOUC, CZECH REPUBLIC*
[7]*UNIVERSITY OF SPLIT, SPLIT, CROATIA*
[8]*PEDIATRIC OUTPATIENT CLINIC, SOLIN, CROATIA*
[9]*FATEBENEFRATELLI HOSPITAL, MILAN, ITALY*
[10]*YALE UNIVERSITY, NEW HAVEN, USA*
[11]*UNIVERSITY OF GLASGOW, GLASGOW, UNITED KINGDOM*

[12]UNIVERSITY OF FOGGIA, ITALY
[13]UNIVERSITY OF PARMA, ITALY
[14]UNIVERSITY OF MILAN, MILAN, ITALY
[15]UNIVERSITY OF BRESCIA AND MONTICHIARI HOSPITAL, ITALY

Introduction: Congenital defects of the kidney and urinary tract (CAKUT) are a major cause of pediatric kidney failure. The molecular diagnosis in the majority of these cases is unknown. Data from cytogenetic studies suggest that submicroscopic structural abnormalities may contribute to the disease pathogenesis.
Material and methods: Genome-wide search for copy number variations (CNVs) was performed with high-density Illumina arrays. We examined the burden of large rare CNVs in 192 patients with renal agenesis and hypodysplasia (RHD). We next searched for known and novel genomic disorders and replicated findings in 330 RHD cases from two independent cohorts (total of 522 RHD cases). Comparisons were made with 13,839 population controls genotyped with equal or higher resolution arrays.
Results: CNV size was significantly larger in 192 RHD cases compared to 4,733 ethnicity-matched controls, based on every standard metric examined (e.g. average CNV size 366.1 kb in RHD vs. 197.1 kb in controls, P=1.5 x 10–6). This excess of large CNVs was attributable to known and novel genomic disorders. Altogether, we detected CNVs diagnostic of 34 known genomic disorders, such as renal cyst and diabetes syndrome, in 55/522 RHD cases (10.5 %); these disorders were present in 0.2 % of 13,839 population controls (P=1.2 x 10–58). Another 32 RHD patients (6.1 %) harbored large gene-disrupting CNVs that were absent or extremely rare in the 13,839 population controls (frequency <0.14 %), identifying 38 potential novel or rare genomic disorders for this trait. The genomic imbalances were detected in RHD patients with and without extra-urinary tract defects.
Conclusions: Up to 16.6 % of patients with congenital kidney defects have a molecular diagnosis attributable to a genomic disorder. A search for genomic structural variants is indicated in this patient population to diagnose their specific genomic disorders, conduct adequate genetic counseling, and individualize medical care.

OP33 - Prevalence of HNF1beta gene mutations in children with various types of cystic kidney diseases

MICHAL MALINA, PETRA DUšáTKOVá, JIří DUšEK, KVěTA BLáHOVá, JAN LéBL, ONDřEJ CINEK, ŠTěPáNKA PRůHOVá, TOMáš SEEMAN
DEPARTMENT OF PAEDIATRICS, 2ND FACULTY OF MEDICINE, CHARLES UNIVERSITY IN PRAGUE AND UNIVERSITY HOSPITAL MOTOL, PRAGUE, CZECH REPUBLIC

Introduction: Hepatocyte nuclear factor beta (gene HNF1B), is an essential transcription factor for kidney and pancreas development. Mutations in HNF1B are known to cause broad spectrum of kidney pathology including kidney cystic diseases, and also a subtype of maturity onset diabetes of the young (MODY5). The aim of the study was to analyze the HNF1B gene in a large cohort of children coming from a registry of patients assumed to have polycystic kidney disease, predominantly ADPKD.
Material and methods: In total 106 Czech patients were investigated for the HNF1B gene: 104 children from a registry of polycystosis and 2 children with symptoms of renal cyst and diabetes (RCAD). Direct sequencing and MLPA analysis were used.
Results: The HNF1B gene anomalies were detected in 5 cases. One case of RCAD had whole gene heterozygous deletion, second carried R165H missense mutation. From the polycystosis group, one child had IVS1-1 G>C mutation and two carried whole gene heterozygous deletion. Interestingly, two children with deletion are maintaining good renal function, one of them complete. All other patients had severely impaired kidney function (CKD 2–5), two needed kidney transplantation.
Conclusions: Children with mutations in HNF1B can clinically mimic various genetically determined polycystic kidney diseases. In our case, the presentation ranged from straightforward RCAD to more indiscernible cases, which were clinically diagnosed as classical autosomal recessive (2 cases) or dominant (1 case) polycystosis. These findings suggest HNF1B analysis should not be omitted in patients with clinical signs and family history of kidney polycystosis. The study was supported by grants NT11402 and MZ NT11457.

OP34 - INVESTIGATION OF THE EFFECTS OF BONE MARROW-DERIVED MESENCHYMAL STEM CELLS IN THE CHRONIC CYCLOSPORINE NEPHROTOXICITY

IPEK AKIL[2], ARDA BOZGUL[2], SEDA VATANSEVER[1], ELGIN TURKOZ ULUER[1], BURCU KARA[1], MAHMUT OZKUT[1]
[1]DEPT. OF HISTOLOGY, MANISA, TURKEY
[2]CELAL BAYAR UNIVERSITY, DEPT. OF PEDIATRIC NEPHROLOGY, MANISA, TURKEY

Introduction: Cyclosporine A (CsA) is a powerful immunosuppressant which is used for allogenic transplantation and nephrotic syndrome treatment. Idiosyncratic chronic nephrotoxicity is the most important side effect limiting use of CsA. Mesenchymal stem cells are often used because they have the advantage of being able to be used autologous, not causing ethical problems and being able to be got from

more sources. In this study, the aim was to evaluate the effects of experimental mesenchymal stem cells on chronic CsA nephrotoxicity.

Material and methods: Forty young adult Wistar rats were included. Rats in the group 1 had 15 mg/bw/day subcutaneous cyclosporine for 60 days. Rats in the group 2 had CyA by the same way and 60 days later were administered bone marrow derived mesencyhmal stem cells. Rats in the group 3 had only bone marrow derived mesenchymal stem cells. Rats in the group 4 were as control. All rats were scarified at the end of 67th day and all renal tissues were examined histologically and immunohistochemically (TGF-β1, TGF-β3, collagen-1, Brd-U, CD4).

Results: Arteriolopathy and tubular atrophy in group 2 were less than group 1. Increase in tubulointerstitial mononuclear cells was higher in both group 1 and 2 compared to other two groups, but there were no significant difference between group 1 and 2. This was thought to be due to inflammatory cells infiltrating tubulointerstitial area caused by CsA and/or mesenchymal stem cells migrating here. Increase in positive marking with Brd-U staining supports our thought of some of these cells was administered mesenchymal stem cells. We suggested mesenchymal stem cells contributed to tubular regeneration following migration to injured area. In group 3 and 4 there was no finding suggesting tubular atrophy, fibrosis and arteriolopathy. Immunohistochemically, in group 2, staining with TGF-β1 and TGF-β3 were significantly decreased compared group 1. This in turn was showing favorable effects of mesenchymal stem cells on tubulointerstitial fibrosis.

Conclusions: In conclusion, we showed that histopathologic findings caused by experimental chronic CsA nephrotoxicity can be reversed by bone marrow derived mesenchymal stem cells.

OP35 - Exome sequencing identifies dominant alleles causing obstructive uropathy and other congenital anomalies

SIMONE SANNA-CHERCHI[1], KATELYN E BURGESS[1], SHANNON N NEES[1], NATALIA PAPETA[1], MURIM CHOI[2], ROSEMARY V SAMPOGNA[1], MONICA BODRIA[3], BRITTANY J PERRY[1], PATRICIA L WENG[1], VLADIMIR J LOZANOVSKI[4], ANNA MATERNA-KIRYLUK[5], NADICA RISTOSKA-BOJKOVSKA[4], LORETO GESUALDO[6], ZORAN GUCEV[4], LANDINO ALLEGRI[7], ANNA LATOS-BIELENSKA[5], FRANCESCO SCOLARI[8], ROBERTO RAVAZZOLO[9], KRZYSZTOF KIRYLUK[1], IAIN DRUMMOND[10], QAIS AL-AWQATI[1], VIVETTE D D'AGATI[11], VELIBOR TASIC[4], RICHARD P LIFTON[2], GIAN MARCO GHIGGERI[3], ALI G GHARAVI[1]

[1]*DIVISION OF NEPHROLOGY, COLUMBIA UNIVERSITY, NEW YORK*

[2]*DEPARTMENT OF GENETICS, YALE UNIVERSITY, NEW HAVEN*

[3]*DIVISION OF PEDIATRIC NEPHROLOGY, G. GASLINI INSTITUTE, GENOA, ITALY*

[4]*DIVISION OF PEDIATRIC NEPHROLOGY, UNIVERSITY CHILDREN'S HOSPITAL, SKOPJE, MACEDONIA*

[5]*POLISH REGISTRY OF CONGENITAL MALFORMATIONS, POZNAN, POLAND*

[6]*DEPARTMENT OF BIOMEDICAL SCIENCES, UNIVERSITY OF FOGGIA, ITALY*

[7]*DIVISION OF NEPHROLOGY, UNIVERSITY OF PARMA, ITALY*

[8]*DIVISION OF NEPHROLOGY, HOSPITAL OF MONTICHIARI, ITALY*

[9]*LABORATORY OF MOLECULAR GENETICS, G. GASLINI INSTITUTE, GENOA, ITALY*

[10]*DEPARTMENT OF GENETICS, MASSACHUSETTS GENERAL HOSPITAL, BOSTON*

[11]*DEPARTMENT OF PATHOLOGY, COLUMBIA UNIVERSITY, NEW YORK*

Introduction: Kidney and urinary tract malformations are the most common cause of pediatric end-stage renal failure. Despite epidemiological evidence for a strong hereditary component to these traits, the underlying genetic mutations still remain elusive in the majority of cases. We sought to identify additional alleles responsible for familial obstructive uropathy using a combination of linkage analysis and whole exome sequencing.

Material and methods: We ascertained one multigenerational family with obstructive uropathy and other congenital kidney malformations segregating as an autosomal dominant trait with incomplete penetrance. We performed genome-wide linkage analysis using the Affymentrix 10 K arrays, combined to whole exome capture followed by next-generation massive parallel sequencing using the Illumina HiSeq. We validated results in additional 468 patients. Immunohistochemistry, co-localization studies and morpholino knock-down in Zebrafish were conducted to explore the functional role of the novel gene.

Results: Linkage analysis identified 5 loci with maximum expected LOD score of 1.5 in in the family, confining the disease gene to <3 % of the genome. Exome sequencing identified >14,000 single nucleotide polymorphisms (SNPs) per sample, ~600 of which were novel. A total of 24 novel, potentially pathogenic variants were found. Two were localized to the previously identified linkage intervals and were segregating with the disease but only one, a splice site mutation, was absent in controls. We identified 14 additional independent rare variants, including a premature termination mutation, in the 468 additional patients sequenced. Localization studies showed diffuse expression in adult and

developing kidney, and knock-down in Zebrafish resulted in embryonic lethality due to severe developmental defects.
Conclusions: Combining linkage analysis to exome sequencing we identified a novel gene for autosomal dominant obstructive uropathy and congenital kidney malformations.

OP36 - Muscarinic acetylcholine receptor M3 (CHRM3) mutation causes congenital bladder disease and a prune-belly-like syndrome

STEFANIE WEBER[1], HOLGER THIELE[2], SEVGI MIR[3], MOHAMMAD REZA TOLIAT[2], BETUL SOZERI[3], HEIKO REUTTER[4], MARKUS DRAAKEN[4], MICHAEL LUDWIG[4], PETER FROMMOLT[2], HELEN M STUART[5], KARL PETER SCHLINGMANN[6], WILLIAM NEWMANN[9], ROLF BEETZ[7], PETER F HOYER[1], MARTIN KONRAD[6], FRANZ SCHAEFER[8], PETER NÜRNBERG[2], ADRIAN S WOOLF[5]
[1]*PEDIATRICS II, UNIVERSITY CHILDREN'S HOSPITAL ESSEN, 45122 ESSEN, GERMANY*
[2]*COLOGNE CENTER FOR GENOMICS, UNIVERSITY OF COLOGNE, 50931 COLOGNE, GERMANY*
[3]*UNIVERSITY CHILDREN'S HOSPITAL IZMIR, 35030 IZMIR, TURKEY*
[4]*INSTITUTE OF HUMAN GENETICS, UNIVERSITY OF BONN, 53127 BONN, GERMANY*
[5]*DEVELOPMENTAL BIOMEDICINE RESEARCH GROUP, SCHOOL OF BIOMEDICINE, MANCHESTER ACADEMIC HEALTH SCIENCES CENTRE, UNIVERSITY OF MANCHESTER AND CENTRAL MANCHESTER UNIVERSITY HOSPITALS NHS FOUNDATION TRUST, M13 9PT MANCHESTER, UNITED KINGDOM*
[6]*UNIVERSITY CHILDREN'S HOSPITAL MÜNSTER, 48149 MÜNSTER, GERMANY*
[7]*UNIVERSITY CHILDREN'S HOSPITAL MAINZ, 55131 MAINZ, GERMANY*
[8]*PEDIATRIC NEPHROLOGY, UNIVERSITY CHILDREN'S HOSPITAL HEIDELBERG, 69120 HEIDELBERG, GERMANY*
[9]*DEVELOPMENTAL BIOMEDICINE RESEARCH GROUP, SCHOOL OF BIOMEDICINE, MANCHESTER ACADEMIC HEALTH SCIENCES CENTRE, UNIVERSITY OF MANCHESTER AND CENTRAL MANCHESTER UNIVERSITY HOSPITALS NHS FOUNDATION TRUST, M13 9PT MANCHESTER, UNITED KINGDOM*

Introduction: Congenital bladder dysfunction with bladder outlet obstruction (BOO) is a relevant cause of progressive renal failure in children. In rare cases BOO can be associated with a prune-belly syndrome (PBS), characterized in its complete form by megacystis, cryptorchidism and hypoplasia of the abdominal wall musculature. Familial occurrence of PBS has been described among siblings in some pedigrees. Applying a genome-wide, SNP-based linkage analysis we recently identified two regions of homozygosity (Chr1q41-q44, Chr11p11) in a consanguineous family of Turkish origin with 4 affected boys (BOO/PBS).
Material and methods: We now applied exon capture and next generation sequencing-technologies to identify the causative gene defect in this family.
Results: In the critical interval on Chr1q41-q44 we identified a homozygous frameshift mutation in CHRM3 (c.1173_1184delinsT;p.Pro392Alafs*43), cosegregating with the recessive phenotype within the family. CHRM3 encodes for the muscarinic acetylcholine receptor M3, the major receptor involved in mediating urinary bladder contraction upon micturition. M3 belongs to the family of G protein-coupled receptors with 7 transmembrane domains and p.Pro392Alafs*43 induces a premature stop codon within the third cytosolic loop, relevant for M3 function. Immunohistochemistry and RT-PCR-based analyses demonstrate expression of human M3/CHRM3 in the developing bladder and renal epithelia but not in the abdominal wall musculature. The phenotype of children with CHRM3 mutation confirms the important role of M3 during the fetal development of the detrusor muscle.
Conclusions: Recessive mutations in CHRM3 [MIM 118494] can be associated with congenital bladder dysfunction and a prune-belly like syndrome. This is the first identified mutation of a human muscarinic acetylcholine receptor and the first monogenic defect in children with a prune-belly like syndrome. Bladder dysfunction is likely to persist in individuals with CHRM3 mutation thoughout life, constituting an important risk factor for the progression of renal insufficiency.

OP37 - Adult height after childhood onset renal replacement therapy in Europe: an ESPN/ERA-EDTA Registry study

JEROME HARAMBAT[1], MARJOLEIN BONTHUIS[1], KARLIJN J. VAN STRALEN[1], GEMA ARICETA[2], NINA BATTELINO[3], TIMO JAHNUKAINEN[4], ANA RITA SANDES[5], KITTY J. JAGER[1], CHRISTIAN COMBE[6], ENRICO VERRINA[7], FRANZ SCHAEFER[8]
[1]*ESPN/ERA-EDTA REGISTRY, ACADEMIC MEDICAL CENTER, AMSTERDAM*
[2]*UNIVERSITY HOSPITAL DE CRUCES, BARRACALDO, SPAIN*
[3]*UNIVERSITY CHILDREN'S HOSPITAL, LJUBLJANA, SLOVENIA*
[4]*UNIVERSITY CHILDREN'S HOSPITAL, HELSINKI, FINLAND*
[5]*UNIVERSITY HOSPITAL DE SANTA MARIA, LISBON, PORTUGAL*

[6]NEPHROLOGY UNIT, UNIVERSITY HOSPITAL BORDEAUX, FRANCE
[7]GASLINI CHILDREN'S HOSPITAL, GENOA, ITALY
[8]UNIVERSITY CHILDREN'S HOSPITAL, HEIDELBERG, GERMANY

Introduction: Growth and final height are of major concern in children with end-stage renal disease. Our aim was to describe the distribution of adult height of patients who started renal replacement therapy (RRT) during childhood, and to identify determinants of final height in a large cohort of RRT children using data from the ESPN/ERA-EDTA registry.
Material and methods: A total of 1577 patients from 16 European countries who started RRT before 19 years of age and reached final height between 1990 and 2010 were included. Standard Deviation Scores (SDS) for height were calculated according to recent national growth charts whenever available, or to newly developed Northern and Southern Europe growth charts for those countries where recent growth reference data are unavailable. Linear regression analyses were performed to calculate adjusted mean final height SDS and to investigate the relationship between height and potential determinants after adjustments for possible confounders.
Results: The median final height SDS was −1.64 (IQR −2.64 to −0.78). Boys reached a median final height of 168 cm and girls a median final height of 155 cm. The proportion of patients who attained a normal adult height was 60 %. Final height increased significantly over time from −2.21 SDS (IQR −3.41 to −1.24) in children who started RRT before 1990 to −1.71 (IQR −2.75 to −0.86) in children starting RRT in 1990–1999, and −1.33 (IQR −2.30 to −0.46) in those commencing RRT from 2000. Older age at start of RRT, more recent period of start of RRT, fewer number of RRT modalities, cumulative percent time on a functioning graft and higher height SDS at initiation of RRT were independently associated with a higher final height SDS, while patients with CAKUT and metabolic disorders had a lower final height compared with other primary renal diseases.
Conclusions: Despite substantial improvement over time, final height remains suboptimal in ESRD children and may impact self-esteem and quality of life in adulthood.

OP38 - Impact of perinatal nutrition on kidney function at five years in very low birth-weight children

VIEUX RACHEL[1], GALU SORANA[1], SOW AISSATA[1], GUILLEMIN FRANCIS[2], HASCOET JEAN-MICHEL[1]
[1]MATERNITE REGIONALE UNIVERSITAIRE NANCY
[2]NANCY UNIVERSITY - EA 4360 APEMAC

Introduction: Low birth-weight is a risk factor of hypertension and renal failure in adulthood. Some symptoms may be diagnosed in childhood allowing a better monitoring. We aimed to determine the impact of perinatal factors on renal function in five year-old preterm-born children.
Material and methods: Prospective longitudinal study of preterm-born children followed-up from birth to five years. Neonatal renal function was evaluated weekly for one month. Then it was measured at four and five years. Five year-old full-term children (EDEN study) composed the control group. The primary outcome was renal function at five years: blood pressure (BP), estimated glomerular filtration rate (eGFR), albuminuria. Multivariate analysis was performed with multiple linear regression models.
Results: 168 children were included aged 5.1±0.1 years. 133 preterm-born children, born at (mean±SD): 29.2±1.4 weeks gestation, birth-weight: 1216±336 grams; 35 full-term children aged five. Systolic BP (sBP) was 97.5±7.1 mmHg in preterm-born children versus 92.2±8.1 mmHg in full-term controls, p=0.0001. In preterm-born children, sBP increased by (β±σ): 2.2±1.0 mmHg for each gram/kg increase in proteins/day on day 28, and decreased by −3.0±1.4 in case of bronchopulmonary dysplasia, after adjustment on gender and height at five years. eGFR was 176.3±37.1 mL/min/1.73 m² at five in preterm-born children. It was significantly decreased when children had presented hyaline membrane disease or necrotising enterocolitis, respectively (β±σ): -17.6±6.7 and −25.7±10.4 mL/min/1.73 m². eGFR at five was not associated with neonatal nutrition. Urine albumin/creatinine ratio was: 1.3±2.8 mg/mmol in preterm-born children vs. 1.1±0.8 mg/mmol in full-terms. 14.4 % preterm-born children had an albumin ratio >2 mg/mmol vs. 11.1 % full-terms, p=0.7. Renal volume, absolute or relative, at five years was negatively correlated to protein intakes from day 14 onwards in the neonatal period: R=−0.69, p=0.006.
Conclusions: Protein intakes in the neonatal period are associated to an increased BP and decreased renal volume in five year-old preterm-born children.

OP39 - Vitamin D as a new regulator of iron metabolism: vitamin D suppresses hepcidin in vitro and in vivo

JUSTINE BACCHETTA[1], JOSHUA J ZARITSKY[2], JESSICA L SEA[2], RENE F CHUN[2], ELIZABETA NEMETH[2], THOMAS GANZ[2], MARK WESTERMAN[3], ISIDRO B SALUSKY[2], MARTIN HEWISON[2]
[1]HOSPICES CIVILS DE LYON ET UNIVERSITE DE LYON, FRANCE
[2]UCLA, LOS ANGELES, USA
[3]INTRINSIC LIFE, LA JOLLA, USA

Introduction: Recent reports have shown improved hemoglobin levels and decreased ESA requirements with vitamin D repletion in CKD patients. We examined the effects of vitamin D on expression and production of hepcidin (Hep),

the iron-regulatory peptide hormone responsible for iron sequestration and anemia by posttranslational downregulation of ferroportin (Fp), the sole known exporter of iron from cells to the systemic circulation. In CKD, Hep levels are increased due to decreased renal clearance and inflammation.

Material and methods: We utilized rtPCR techniques to assess Hep mRNA production along with immunohistochemistry to stain for FP in peripheral blood mononuclear cells (PBMC) isolated from healthy donors and in monocytes (PDM) isolated from the dialysate of patients undergoing peritoneal dialysis.

Results: When treated with active 1,25-dihydroxyvitamin D (5 nM) or with precursor 25-hydroxyvitamin D (100 nM) for 6 hours in HS10%, PBMC and PDM showed decreased expression of Hep. Chromatin immunoprecipitation revealed decreased recruitment of the RNA polymerase II within the promoter of the human Hep gene after treatment with 1,25D, pointing to direct effects of 1,25D on Hep transcription. Immunohistochemistry showed that PBMC and PDM expressed Fp, with membrane enhancement after treatment with 1,25D. Finally we observed a 50 % decrease in serum hepcidin by competive ELISA which persisted for 72 hours in 7 healthy human subjects after a single oral dose of vitamin D (100,000 IU).

Conclusions: For the first time, these results both in vitro and in vivo indicate that vitamin D is a potent suppressor of Hep in humans. We propose that these findings provide a clinically relevant mechanism by which vitamin D supplementation can improve anemia management in CKD patients.

OP40 - Systolic dysfunction measured by Speckle Tracking Echocardiography in children with ESRD

NIKKI J. SCHOENMAKER[2], IRENE M. KUIPERS[1], JOHANNA H. VAN DER LEE[3], NICO A. BLOM[1], JAAP H. GROOTHOFF[2]

[1]*PEDIATRIC CARDIOLOGY, EMMA CHILDREN'S HOSPITAL AMC*

[2]*PEDIATRIC NEPHROLOGY, EMMA CHILDREN'S HOSPITAL AMC*

[3]*PEDIATRIC CLINICAL EPIDEMIOLOGY, EMMA CHILDREN'S HOSPITAL AMC*

Introduction: In young adults with End-stage renal disease (ESRD) abnormal left ventricular geometry and function are predictors of cardiovascular morbidity and mortality. Early identification of systolic dysfunction might help to identify patients at risk. Speckle tracking echocardiography (STE) is able to reveal early abnormalities in LV systolic function prior to manifestation of hypertrophy in adults. We aimed to compare the assessment of LV systolic function using conventional echocardiography, Tissue Doppler imaging (TDI) and STE in children with ESRD and healthy controls.

Material and methods: 27 children with ESRD and 21 healthy control subjects, matched for body surface area (BSA), were included. Indicators of LV systolic function were shortening fraction (FS%), LV- and intraventricular septum peak systolic annular velocity (LV-S and IVS-S), and global longitudinal strain, measured by conventional echocardiography, TDI, and STE, respectively. These indicators were compared in the ESRD and control group using linear regression analysis to adjust for possible confounders

Results: After adjustment for age and gender, there were no significant differences between the ESRD patients and the healthy controls for FS%, LV-S and IVS-S measured by conventional echocardiography and TDI, respectively. Global longitudinal strain measured by STE was significantly lower in ESRD patients compared to the control subjects, mean difference [95%CI] 2.7 [1.2-4.2], p=0.001).

Conclusions: Measured by STE children with ESRD have significantly decreased LV systolic function compared to healthy matched controls. STE is more sensitive to detect decreased systolic function than conventional echocardiography and TDI. Longitudinal studies are necessary to evaluate the progression of cardiac dysfunction in these children.

OP41 - Eculizumab therapy for atypical hemolytic uremic syndrome (aHUS) in pediatric patients: efficacy and safety outcomes from a retrospective study

THERESE JUNGRAITHMAYR[1], SAMHAR AL-AKASH[2], JEAN-CLAUDE DAVIN[3], RALPH GRUPPO[4], JOEL HERNANDEZ[5], CRAIG LANGMAN[6], ANNE-LAURE LAPEYRAQUE[7], MARIE ALICE MACHER[8], NANCY RODIG[9], JULIUS SHERWINTER[10], GIACOMO SIMONETTI[11], JODI SMITH[12], COURTNEY THORNBURG[13], ELKE WÜHL[14], RAMON VILALTA[15]

[1]*INNSBRUCK MEDICAL UNIVERSITY, INNSBRUCK, AUSTRIA*

[2]*DRISCOLL CHILDREN'S KIDNEY CENTER, CORPUS CHRISTI, USA*

[3]*EMMA CHILDREN'S HOSPITAL, AMSTERDAM, NETHERLANDS*

[4]*CINCINNATI CHILDREN'S HOSPITAL MEDICAL CENTER, CINCINNATI, USA*

[5]*SACRED HEART CHILDREN'S HOSPITAL, SPOKANE, USA*

[6]*FEINBERG SCHOOL OF MEDICINE, NORTHWESTERN UNIVERSITY AND CHILDREN'S MEMORIAL HOSPITAL, CHICAGO, USA*

[7]*CHU SAINTE-JUSTINE, MONTRéAL, CANADA*

[8]*HôPITAL ROBERT DEBRé – APHP, PARIS, FRANCE*

[9]*CHILDREN'S HOSPITAL, BOSTON, USA*

[10]CHILDREN'S HEALTHCARE OF ATLANTA, ATLANTA, USA
[11]UNIVERSITY CHILDREN'S HOSPITAL, INSELSPITAL AND UNIVERSITY OF BERN, BERN, SWITZERLAND
[12]CHILDREN'S HOSPITAL AND REGIONAL MEDICAL CENTER, SEATTLE, USA
[13]DUKE UNIVERSITY MEDICAL CENTER, DURHAM, USA
[14]CENTER FOR PEDIATRIC AND ADOLESCENT MEDICINE, UNIVERSITY OF HEIDELBERG, HEIDELBERG, GERMANY
[15]HOSPITAL VALL D'HEBRON, BARCELONA, SPAIN

Introduction: aHUS is a rare, genetic, and life-threatening disease driven by chronic, uncontrolled complement activation that results in multi-organ damage caused by thrombotic microangiopathy (TMA). Despite plasma exchange/infusion (PE/PI), patients with aHUS have a poor prognosis, with 33 %-40 % progressing to end-stage renal disease or death with first clinical aHUS manifestation. Within a year of diagnosis, 65 % of aHUS patients require dialysis, have permanent renal damage, or die. Chronic treatment with eculizumab, a humanized, monoclonal anti-C5 antibody that selectively inhibits terminal-complement activation, was demonstrated to be safe and effective in 2 prospective clinical trials of adult/adolescent aHUS patients. Our objective was to assess the efficacy/safety of eculizumab therapy in pediatric aHUS patients within a medical-practice setting.
Material and methods: Retrospective data collection analysis of 19 aHUS patients aged <18y (<12y [n=15]; 12-17y [n=4]) who received eculizumab outside of clinical trials from 2007–2009.
Results: At baseline, 8/19 patients (42 %) had platelet counts <150×10^9/L, 13/19 (68 %) had estimated glomerular filtration (eGFR) levels <60 mL/min/1.73 m^2, and 10/19 (53 %) had an identified genetic complement mutation. Eculizumab reduced systemic TMA as demonstrated by platelet count normalization in 17/19 patients (89 %), achievement of TMA event-free status (no PE/PI, no dialysis, and no decrease in platelet count >25 % for ≥12wk) in 13/19 (68 %), and reduced TMA intervention rate (PE/PI or new dialysis events/patient/d) from a median [range] of 0.31 [0–2.38] pretreatment to 0 [0–0.08] during eculizumab therapy. 9/19 patients (47 %) demonstrated eGFR improvement ≥15 mL/min/1.73 m^2; 4/8 (50 %) eliminated need for dialysis during eculizumab treatment. Eculizumab was well tolerated.
Conclusions: In this pediatric population (aged <18y), eculizumab treatment reduced TMA, improved kidney function (eliminating dialysis in 50 % of patients [4/8] and reducing need for PE/PI), and was well tolerated. These findings, consistent with those from adult/adolescent trials, support the role of eculizumab as the standard of care for aHUS.

OP42 - DISTRIBUTION AND DETERMINANTS OF SERUM VITAMIN D CONCENTRATIONS IN EUROPEAN CHILDREN WITH CHRONIC KIDNEY DISEASE

ANKE DOYON[1], BETTINA SCHMIEDCHEN[2], AYSUN BAYAZIT[3], NUR CANPOLAT[4], ALI DUZOVA[5], DANIELA KRACHT[6], MIECZYSLAW LITWIN[7], ANNA NIEMIRSKA[7], BETUL SOZERI[8], RENE ZELLER[9], BRUNO RANCHIN[10], ALI ANARAT[3], SALIM CALISKAN[4], SEVGI MIR[8], ANETTE MELK[6], ELKE WÜHL[1], FLORIAN SCHWEIGERT[2], UWE QUERFELD[9], FRANZ SCHAEFER[1], AND THE 4C CONSORTIUM[1]
[1]CENTER FOR PEDIATRICS AND ADOLESCENT MEDICINE HEIDELBERG, GERMANY
[2]UNIVERSITY OF POTSDAM, GERMANY
[3]CUKUROVA UNIVERSITY ADANA, TURKEY
[4]CERRAHPASA UNIVERSITY ISTANBUL, TURKEY
[5]HACETTEPE UNIVERSITY ANKARA, TURKEY
[6]HANNOVER MEDICAL SCHOOL, GERMANY
[7]CHILDRENS MEMORIAL HEALTH INSITUTE WARSAW, POLAND
[8]EGE UNIVERSITY IZMIR, TURKEY
[9]CHARITE CHILDRENS HOSPITAL BERLIN, GERMANY
[10]HOPITAL FEMME MERE ENFANT, UNIVERSITE DE LYON, FRANCE

Introduction: The Europe-wide Cardiovascular Comorbidity in Children with CKD (4 C) study prospectively explores risk factors for early cardiovascular disease in pediatric Chronic Kidney Disease (CKD). As Vitamin D (VitD) deficiency is common in children with CKD and experimental work suggests a role of VitD in vascular health we analyzed the factors affecting VitD levels and the substitution practice in different regions of Europe.
Material and methods: Serum 25OH-VitD levels were assessed in 456 children from 55 European centers with CKD stages IIIb-V. Differences of serum 25OH-VitD levels according to CKD stage, season, oral VitD supplementation and regional sunlight intensity were evaluated by ANOVA. The influence of VitD, serum phosphorus and serum calcium on iPTH levels were assessed by multivariate analysis.
Results: 25OH-VitD levels were significantly higher in patients with VitD supplementation (16.2±16.2 vs 12.3±7.8 ng/ml, $p<0.003$) and in the summer season (16.5±9.9 vs 13.2±15.7, $p<0.01$). 25OH-VitD levels were significantly higher in CKD stage V than in stages III and IV (19.2±25.4 ng/ml vs 14.4±8.3 ng/ml and 13.3±10.3 ng/ml, $p<0.005$). VitD was most frequently administered in children with CKD-V ($p<0.002$). VitD supplementation rates differed regionally, being lowest in Turkey (47 % vs 74 % in other countries, $p<0.0001$). Surprisingly, even when adjusting for eGFR and VitD supplementation, serum 25OH-VitD levels were inversely associated with sunlight intensity at the place of living. Higher iPTH values were

independently associated with severe VitD deficiency (<10 ng/ml, p<0.05), higher serum phosphorus (p<0.02) and lower serum calcium levels (p<0.0001).

Conclusions: VitD supplementation is effective in raising serum 25OH-VitD levels. In addition, 25OH-VitD levels show major regional variation independent of VitD supplementation and the degree of renal failure. Low 25OH-VitD levels are predictive of serum iPTH independent of serum calcium and phosphorus. Further evaluation is needed to identify the optimal supplementation dosage and the influence of VitD metabolism on cardiovascular functions.

OP43 - Novel C3 mutation p.Lys65Gln in aHUS affects complement factor H binding

ELENA VOLOKHINA[1], DINEKE WESTRA[1], XIAOGUANG XUE[2], PIET GROS[2], NICOLE VAN DE KAR[1], LAMBERT VAN DEN HEUVEL[1]

[1]*RADBOUD UNIVERSITY NIJMEGEN MEDICAL CENTRE, NIJMEGEN, THE NETHERLANDS*

[2]*UTRECHT UNIVERSITY, UTRECHT, THE NETHERLANDS*

Introduction: Atypical hemolytic uremic syndrome (aHUS) is associated with mutations affecting complement proteins and regulators and with autoantibodies against complement factor H (CFH). Approximately half of the aHUS patients progress to end-stage renal disease. DNA analysis of the risk factor genes is important for prognosis of aHUS recurrence after renal transplantation.

Material and methods: Mutational screening of C3 encoding the central complement component was performed by Sanger sequencing in 70 aHUS patients. Mutated and wild type recombinant C3b proteins were produced and their affinity to CFH was analyzed by ELISA.

Results: A single novel missense change p.Lys65Gln in C3 was found in three aHUS patients. The alteration leads to decreased binding of C3b to CFH in vitro. All three patients acquired the illness as adults and had a first aHUS episode after renal transplantation or suffered recurrence of the disease after transplantation.

Conclusions: The novel C3 change was found in three aHUS patients. It results in decreased C3b binding to CFH and thus might lead to impaired C3b inactivation in vivo. The p.Lys65Gln is likely to be associated with aHUS after kidney transplantation and, therefore, might be an important prognostic factor.

OP44 - ACUTE PRESENTATION AND LONG-TERM FOLLOW-UP IN PEDIATRIC PATIENTS WITH ATYPICAL HEMOLYTIC UREMIC SYNDROME (AHUS)

MAGDALENA RIEDL[1], JOHANNES HOFER[1], ALEJANDRA ROSALES[1], REINHARD WÜRZNER[1], THERESE JUNGRAITHMAYR[1]

[1]*MEDICAL UNIVERSITY INNSBRUCK*

[2]*GEMEINSCHAFT FÜR PäDIATRISCHE NEPHROLOGIE*

Introduction: The atypical HUS (aHUS) is associated with a dysfunction of the alternative pathway of the complement system, leading to thrombotic microangiopathy (TMA). Long-term prognosis is poor.

Material and methods: Since 2002 the international aHUS registry investigates the role of complement in aHUS and long-term outcome by collecting clinical data and analyzing TMA and complement activity parameters. Here we present data of 100 pediatric aHUS patients at diagnosis, the 1 year follow-up of 79 patients and the 5 year follow-up of 26 patients. Mutations were detected in 17 patients, FH antibodies in 23 patients. Results are given in mean±standard deviation.

Results: During acute phase the hemoglobin value dropped to 6.0±1.4 mg/dl, the platelet count to 50.7±43.8x109 and mean creatinine was elevated to 4.1±3.1 mg/dl. Oliguria/anuria was seen in 60 % (mean duration: 12±15 days) of patients. Dialysis was performed in 62 % (mean duration: 28±46 days) of patients, of which 20 % remained on dialysis. Arterial hypertension was seen in 78 %. Other organ involvement was reported as follows: gastrointestinal (41 %), CNS (27 %), cardiac (8 %) and pancreas (6 %). Treatment of first episode included plasma therapy in 66 % - plasma infusions (PI, 44 %), plasma exchange (PE, 46 %) - and Eculizumab in 2 %. HUS recurrence in the first year was reported in 68 % of the patients. The first recurrence occurred in mean after 3.1± 3.3 months. One year after diagnosis any sequel was reported in 75 % of children, this included arterial hypertension in 64 %, dialysis/transplantation in 33 %, chronic renal insufficiency in 18 % and proteinuria in 59 %. 49 % of the patients had a normal renal function, but proteinuria was reported in 41 % of them. Five years after HUS onset 88 % had signs of renal sequelae, like arterial hypertension in 80 %, impaired renal function or dialysis in 38 % and proteinuria in 52 %. During the observation period 8 patients died, in 4 cases due to cardiopulmonary insufficiency or multi-organ failure.

Conclusions: In the acute phase aHUS presents as a multisystem disorder, but in the long term impaired renal function is the main concern. New treatment options give hope to improve long-term outcome in patients with atypical HUS.

OP45 - Efficacy and safety of eculizumab in 10 children with atypical hemolytic uremic syndrome (aHUS)

FILA MARC[1], ADRA ANNE LAURE[2], KWON THERESA[1], BAUDOUIN VERONIQUE[1], FISCHBACH MICHEL[3], SALOMON REMI[4], TAQUE SOPHIE[5], FREMEAUX BACCHI VERONIQUE[6], DESCHENES GEORGES[1], LOIRAT CHANTAL[1]

[1]*PEDIATRIC NEPHROLOGY UNIT, CHU ROBERT DEBRé, APHP, PARIS VII UNIVERSITY, PARIS, FRANCE*

[2]PEDIATRIC NEPHROLOGY UNIT, CHRU DE MONTPELLIER, MONTPELLIER,NIMES UNIVERSITY, MONTPELLIER, FRANCE
[3]UNIVERSITY HOSPITAL HAUTEPIERRE, STRASBOURG, FRANCE.
[4]CHU NECKER ENFANTS MALADES, APHP, PARIS V UNIVERSITY, PARIS, FRANCE
[5]PEDIATRIC UNIT. CHU RENNES, RENNES 1 UNIVERSITY, RENNES, FRANCE
[6]IMMUNOLOGY DEPARTMENT, HôPITAL EUROPEEN GEORGES POMPIDOU, PARIS, FRANCE

Introduction: Prognosis of aHUS a disease of complement dysregulation is poor, with one third of pediatric patients progressing to end stage renal disease or death within the first year after onset. Plasmatherapy has been first line treatment until recently. The efficiency of eculizumab, a humanized monoclonal anti-C5 antibody, has been suggested by approximately 25 case reports and the preliminary results of 2 prospective trials in adults.
Material and methods: We report the outcome of 10 aHUS children (median age: 2 years, range: [0.2-17]) treated off-trials with eculizumab (mutation in factor H (CFH), n=4; factor I, n=1; C3: n=1; anti-CFH antibodies, n=1; no mutation identified, n=3).
Results: 6 patients received long term plasmatherapy prior to eculizumab (disease duration 392 days, [161–5870], relapses in 5, vascular access difficulties/plasma intolerance in 4), 4 patients received eculizumab for the first episode of aHUS (disease duration: 11 days [1–31], prior plasmatherapy in 3). At baseline, median serum creatinine (Screat) was 212 μmol/l [47–594], with 6 patients requiring dialysis. Complete inhibition of complement hemolytic activity (CH50≤ 10 %), was maintained until day 7 after the first, second, third and fourth injection in 6, 1, 2 and 1 patients respectively. Platelet count normalized within the first week of treatment in 3/4 thrombocytopenic patients. Median follow up under eculizumab was 274 days [53–756] At last follow up, all patients were free of dialysis and median S creat was 36 μmol/l [24–167]. Proteinuria decreased in 5/6 proteinuric patients at baseline, and was unchanged in 1. Antihypertensive therapy was reduced in 6/9 patients. Only one patient (no complement abnormality identified) presented relapses under eculizumab despite CH50< 10 %. Eculizumab was stopped in 2 patients owing to allergic manifestations. No severe infection was observed
Conclusions: Eculizumab was efficient in 9/10 children with aHUS, was well tolerated and thus has the potential to be the new standard of care for aHUS.

OP46 - International audit of investigation and initial therapy of diarrhoea negative (atypical) HUS

SALLY JOHNSON[12], JELENA STOJANOVIC[12], GEMA ARICETA[2], MARTIN BITZAN[13], NESRIN BESBAS[3], DIANA KARPMAN[4], MICHELLE FRIELING[6], DANIEL LANDAU[5], CRAIG LANGMAN[14], CHRISTOPH LICHT[6], CARMINE PECORARO[8], MAGDELENA RIEDL[11], EKATERINI SIOMOU[15], NICOLE VAN DE KAR[9], JOHAN VAN DE WALLE[10], CHANTAL LOIRAT[7], C MARK TAYLOR[1]
[1]BIRMINGHAM CHILDREN'S HOSPITAL
[2]HOSPITAL DE CRUCES, BARAKALDO
[3]HACETTEPE UNIVERSITY, ANKARA
[4]LUND UNIVERSITY
[5]SOROKA MEDICAL CENTER, BEER SHEVA
[6]THE HOSPITAL FOR SICK CHILDREN, TORONTO
[7]ASSISTANCE PUBLIQUE-HOPITAUX DE PARIS
[8]SANTOBONO CHILDREN'S HOSPITAL, NAPLES
[9]UNIVERSITY MEDICAL CENTER ST RADBOUD, NIJMEGEN
[10]UNIVERSITY HOSPITAL GENT
[11]MEDIZINISCHE UNIVERSITäT INNSBRUCK
[12]GREAT NORTH CHILDREN'S HOSPITAL, NEWCASTLE UPON TYNE
[13]MONTREAL CHILDREN'S HOSPITAL
[14]CHILDREN'S MEMORIAL HOSPITAL, CHICAGO
[15]UNIVERSITY HOSPITAL OF IOANNINA

Introduction: On behalf of The European Paediatric Study Group for HUS (in collaboration with colleagues from North America). The consensus-based guideline on investigation and initial therapy of diarrhoea-negative (atypical) HUS (Ariceta Pediatr Nephrol 2009) invited international audit to test its validity. This is timely given the emergence of eculizumab for treatment of atypical HUS (aHUS).
Material and methods: Questionnaire to paediatric nephrologists in 13 countries regarding acceptance of the guideline and details of its application to new aHUS episodes July 2009-December 2010.
Results: 71 patients were reported. There was intention to use the guideline in 59. Infectious precipitating events were identified in 27, including 6 Influenza H1N1. Genetic and/or acquired complement abnormalities were reported in 33/53 (62 %) patients tested. There was geographic variation in the use, extent and rapidity of complement investigations. At 33 days (endpoint of guideline): Dialysis dependent n=12; Failure to enter haematological remission n=8; Mortality n=0. Subgroups devised according to treatment received: (i) Full guideline plasma exchange (PEX) over 33 days n=5; (ii) PEX >300 ml/kg in first 5 days (representing intensive, early PEX) n=8; (iii) Lower doses of PEX n=8; (iv) Plasma infusion only n=12; (v) No plasma therapy n=12. Serious

complications of PEX were frequent (including central venous catheter/thrombosis).

Conclusions:

The guideline was broadly accepted and the investigation scheme widely used. Influenza H1N1 emerged as a precipitant of HUS. Variation in the availability and extent of complement genomic investigation was notable. As regards the outcome of treatment, subgroup analysis is not empowered to confirm benefit of plasma therapy. The incidence of dialysis dependence at day 33 (17 %) was lower than the reported incidence of end-stage renal disease after first aHUS episode from registry data. This unique cohort provides important data regarding contemporary experience and management of aHUS and will be a useful baseline against which newer treatments can be compared.

OP47 - ATYPICAL HUS AND ECULIZUMAB TREATMENT: EXPERIENCE OF A TERTIARY CENTER

NESRIN BESBAS, BORA GULHAN, SEZA OZEN, REZAN TOPALOGLU, ALI DUZOVA, CIGDEM YILDIZ, FATIH OZALTIN

HACETTEPE UNIVERSITY

Introduction: Atypical hemolytic uremic syndrome (aHUS) is a rare, life-threatening disease caused by complement system dysregulation leading to uncontrolled complement activation. Eculizumab, a humanized monoclonal anti-C5 antibody, has proven to be effective in patients with aHUS.

Material and methods: Here, we present our experience with 4 different aHUS patients and eculizumab usage in them.

Results: The first patient was diagnosed in newborn period. Eculizumab was first introduced when he was 7-month old after 5th disease recurrence, which resulted in full remission for 11 months. The second, 4-year-old patient presented with steroid resistant nephrotic syndrome and macroscopic hematuria in whom renal biopsy was compatible with membranoproliferative glomerulonephritis. He developed aHUS when he was 6-year-old. Plasma exchange induced remission that was maintained by FFP infusions for 1 year. Three disease recurrences were observed in which FFP infusions failed to induce remission again. Therefore, eculizumab had to be administered with a success. The third 16-year-old patient was diagnosed in another center where plasma exchange therapies were unsuccessful. Therefore, the patient was referred to our center. Eculizumab was administered immediately but no improvement in renal and hematological parameters was observed. A renal biopsy was performed late in the course in which thrombotic microangiopathy was absent although glomerular scarring and fibrosis were present likely associated with aHUS. The forth 9-year-old patient was diagosed in another center where FFP infusions yielded to remission however the patient was hospitalized again due to disease recurrence 2 weeks later. Re-administration of FFP caused a hypersensitivity reaction therefore eculizumab was started in our center following premedication. However, anapylaxis occured after getting half of the total eculizumab dosage. Nevertheless this yielded full remission for 2 weeks.

Conclusions: In conclusion, eculizumab seems to be effective in selected aHUS patients if administered early. On the other hand, severe side effects including anaphylaxis should be taken into consideration.

OP48 - Factor H antibody associated atypical HUS: 1 year follow up data from the international Innsbruck HUS-Net aHUS registry

JOHANNES HOFER[1], MAGDALENA RIEDL[1], THOMAS GINER[1], ALEJANDRA ROSALES[1], VERENA JELLER[1], REINHARD WÜRZNER[2], JACEK PIETRZYK[3], DOROTHEA DROZDZ[3], THERESE JUNGRAITHMAYR[1]

[1]*CHILDRENS UNIVERSITY CLINIC INNSBRUCK, PEDIATRICS I*

[2]*MEDICAL UNIVERSITY INNSBEUCK, DEPARTMENT FOR HYGIENE*

[3]*CHILDRENS UNIVERSITY CLINIC KRAKAU, POLAND*

Introduction: Antibodies against complement factor H (FH Ab) have been reported in aHUS patients. The role of FH Ab in disease onset, progression and treatment is of critical interest for physicians and patients dealing with this unsolved problem. At present, evidence based therapy recommendations are missing.

Material and methods: We comment on 16 patients with FH Ab associated aHUS from the Innsbruck HUS-Net registry (www.hus-online.at). Patients were followed from the beginning of the acute phase, with recording on patient's therapy and clinical progression over a period of 1 year.

Results: Patients show a median age at disease onset of 7 years. All patients presented with hemolytic anemia (mean hemoglobin: 5,8 g/l), thrombocytopenia (mean platelet count: 33,2 x 109/μl) and elevated creatinine levels (mean: 458 μmol/l). Only 37 % of the patients showed decreased C3 levels and 15 % decreased Factor H levels. Within the follow up period of 1 year 25 % of the patients developed renal insufficiency, 33 % showed ESRD, and 67 % showed at least one episode of recurrence. Using supportive therapy without plasmatreatment or immunosuppression 2/2 patients presented with disease recurrence, 6/7 patients recurred under plasmatherapy without additional immunosuppression and only 2/7

patients with plasmatherapy followed by immunosuppression developed recurrence.

Conclusions: CFH Ab positivity is a distinct pathogenetic aHUS subgroup mainly of pediatric patients. Testing for CFH Ab as soon as possible is mandatory, as in positive cases this has important impact on prognosis and the recommended therapy. Following our results and the literature a recommendation for the use of plasmatherapy as induction followed by a maintenance immunosuppression can be given. Nevertheless, treatment responses are heterogeneous and the choice of immunosuppressive agent, the dosages and the timing of initiation and withdrawal are still a matter of speculation.

OP49 - IDENTIFICATION OF SUBGROUPS AT HIGH RISK OF GRAFT FAILURE AFTER PAEDIATRIC RENAL TRANSPLANTATION

DANILO LOFARO[1], AMEEN ABU-HANNA[4], KITTY JAGER[3], FRANZ SCHAEFER[5], ENRICO VERRINA[6], KARLIJN VAN STRALEN[2]

[1]*KIDNEY AND TRANSPLANTATION RESEARCH CENTRE. DEPT. NEPHROLOGY, ANNUNZIATA HOSPITAL, COSENZA, ITALY.*

[2]*ESPN/ERA-EDTA REGISTRY, DEPT. OF MEDICAL INFORMATICS, AMC, UNIVERSITY OF AMSTERDAM, AMSTERDAM, THE NETHERLANDS.*

[3]*ERA-EDTA REGISTRY, DEPT. OF MEDICAL INFORMATICS, AMC, UNIVERSITY OF AMSTERDAM, AMSTERDAM, THE NETHERLANDS.*

[4]*DEPT. OF MEDICAL INFORMATICS, AMC, UNIVERSITY OF AMSTERDAM, AMSTERDAM, THE NETHERLANDS.*

[5]*DEPT. OF PEDIATRIC NEPHROLOGY, UNIVERSITY HOSPITAL, HEIDELBERG, GERMANY*

[6]*DEPT. OF PEDIATRIC NEPHROLOGY, GASLINI CHILDREN'S HOSPITAL, GENOA, ITALY*

Introduction: Kidney transplantation (Tx) is the treatment of choice for children on renal replacement therapy (RRT). However, graft loss remains an important problem and may affect the choice for living versus deceased donation and timing of transplantation. Therefore, the aim of this analysis is to identify special subgroups of patients with different graft survival among a large sample of European paediatric Tx recipients.

Material and methods: 7839 paediatric Tx recipients included in the ESPN/ERA-EDTA Registry were analyzed. Factors under study were gender, age at start RRT, age at transplantation (Age-Tx), time on dialysis (Dial-Time), preemptive transplantation (Preemptive-Tx) and cause of renal failure classified according to the risk of disease recurrence (Recurrence-Risk). We used survival tree analysis to identify subgroups with similar 1- and 5-years graft survival and fitted Cox models to test the association between pre-transplant factors, subgroups and graft outcome.

Results: For 1-year graft survival 4 subgroups of patients were identified according to Age-Tx, Recurrence-Risk and Dial-Time. The Cox analysis revealed Preemptive-Tx (HR = 0.55, 95%CI 0.42-0.71) and Age-TX<3.9 years (2.31, 1.66-3.21) to be associated with 1 year graft failure. For the 5 years graft survival 6 subgroups were identified using Recurrence-Risk, Dial-Time and Age-Tx. The survival analysis showed that the subgroups with (i)Preemptive-Tx (0.76, 0.62-0.94); (ii)High Recurrence-Risk (2.06,1.75-2.42); (iii)short-term dialysis (<3.5 yrs) and young age (<3.5 yrs) (2.15,1.62-2.85); (iv)long-term dialysis (≥3.5 yrs) and adolescent age (Age-Tx>12.8 yrs) (2.49,1.88-3.30) were all significantly associated with 5 years graft prognosis compared to pre-emptive transplantations with Low/No Recurrence-Risk.

Conclusions: Non pre-emptive transplantation and diseases with a high risk of disease-recurrence as well as long-term dialysis in combination with adolescent age were associated with a worse renal graft outcome. The identification of these subgroups points out how interactions between factors play an important role in predicting renal graft prognosis. Additional analyses will include more graft-related factors like donor type and age.

OP50 - Association of HLA-DR7 with the development of a symptomatic Epstein-Barr virus (EBV) infection in paediatric renal transplant recipients

BRITTA HÖCKER[1], HENRI-JACQUES DELECLUSE[2], STEPHAN BÖHM[3], HELMUT FICKENSCHER[3], UTA KÜSTERS[3], PAUL SCHNITZLER[3], MARTIN POHL[4], ULRIKE JOHN[5], MARKUS J. KEMPER[6], HENRY FEHRENBACH[7], MARIANNE WIGGER[8], MARTIN HOLDER[9], MONIKA SCHRÖDER[10], REINHARD FENEBERG[1], SABINE KÖPF-SHAKIB[1], CANER SÜSAL[11], BURKHARD TÖNSHOFF[1]

[1]*UNIVERSITY CHILDREN'S HOSPITAL HEIDELBERG*

[2]*GERMAN CANCER RESEARCH CENTER, DIVISION OF PATHOGENESIS OF VIRUS ASSOCIATED TUMORS*

[3]*DEPARTMENT OF INFECTIOUS DISEASES, VIROLOGY, UNIVERSITY HOSPITAL OF HEIDELBERG*

[4]*UNIVERSITY CHILDREN'S HOSPITAL FREIBURG*

[5]*UNIVERSITY CHILDREN'S HOSPITAL JENA*

[6]*UNIVERSITY CHILDREN'S HOSPITAL HAMBURG*

[7]*CHILDREN'S HOSPITAL MEMMINGEN*

[8]*UNIVERSITY CHILDREN'S HOSPITAL ROSTOCK*

[9]*OLGA CHILDREN'S HOSPITAL STUTTGART*

[10]*CLEMENTINE CHILDREN'S HOSPITAL FRANKFURT*

[11]*DEPARTMENT OF TRANSPLANTATION IMMUNOLOGY, UNIVERSITY OF HEIDELBERG*

Introduction: So far, it is unclear why some patients exhibit pronounced acute clinical EBV-related symptoms during post-transplant EBV infection, whilst others remain asymptomatic despite a high, persistent EBV viral load. A genetic predisposition is likely.
Material and methods: In the framework of a prospective, multicentre trial among 106 paediatric kidney allograft recipients (aged 11.1±5.9 years), we therefore analysed the prevalence of HLA class I and II alleles and a potential association of HLA alleles with the development of a symptomatic EBV infection (defined as flu-like symptoms or infectious mononucleosis) in the first year post-transplant.
Results: Patients expressing HLA-DR7 bore a significantly increased risk of developing a symptomatic EBV infection (univariate regression analysis: OR 4.77; 95 %-CI 1.60 14.2; p=0.005). In a multivariate model, risk factors included HLA-DR7 expression (OR 5.65; 95 %-CI 1.26 25.3; p= 0.024), EBV high-risk (D+/R-) serostatus (OR 7.07; 95 %-CI 1.01 49.6; p=0.049) and overall immunosuppressive load (semiquantitative "Vasudev" score[1]) (OR 1.53; 95 %-CI 1.18 1.99; p=0.002). The prevalence of the HLA-DR7 allele amounted to 25 %. Having a comparable EBV risk constellation, HLA-DR7-positive patients developed significantly (p=0.005) more often a symptomatic EBV infection than HLA-DR7-negative recipients (9/14 (64 %) vs. 8/41 (20 %)). Asymptomatic patients with a high EBV viral load tended (p=0.095) to express HLA-DR7 less frequently than symptomatic patients with a high EBV viral load (3/17 (18 %) vs. 6/11 (55 %)).
Conclusions: Paediatric renal transplant recipients expressing HLA-DR7 develop significantly more often a symptomatic EBV infection than HLA-DR7-negative patients, possibly as a consequence of a pronounced anti-EBV immune response which, in the long run, may protect against PTLD. Indeed, HLA-DR7 induces an efficient T helper cell reaction through presentation of EBNA1 epitopes on antigen-presenting cells[2] and is known to be a protective factor against the development of PTLD[3]. [1] Vasudev B. et al., Kidney Int 2005 [2] Krüger S et al., J Immunother 2003 [3] Subklewe M et al., Transplantation 2006

OP51 - The Prevalence Of De Novo Food Allergy In Paediatric Renal Transplant Recipients

CHARLOTTE L DAVIES[1], CLAUDIA GORE[2], ROBERT J BOYLE[2], STEPHEN D MARKS[3]
[1]*UNIVERSITY COLLEGE LONDON MEDICAL SCHOOL*
[2]*DEPARTMENT OF PAEDIATRICS, IMPERIAL COLLEGE LONDON, UK*
[3]*DEPARTMENT OF PAEDIATRIC NEPHROLOGY, GREAT ORMOND STREET HOSPITAL FOR CHILDREN NHS TRUST AND UCL INSTITUTE OF CHILD HEALTH, LONDON, ENGLAND, UK*

Introduction: Food allergy affects 6 % of children and causes 85 % of childhood anaphylaxis. Anaphylaxis hospitalisation rates multiplied sevenfold between 1990–2000 in England. New-onset food allergy after liver, cardiac and intestinal transplantation has been reported but it is unknown if it is increased in paediatric renal transplant recipients (RTR).
Material and methods: We investigated whether de-novo allergy development occurred in RTR, using three questionnaires regarding general health, food allergy and atopy, by patient and/or parent interview. We obtained blood samples from children under 18 years who had undergone renal transplantation, from our single centre and analysed for eosinophilia, total-IgE, and cow's milk, egg and peanut-specific IgE. Questionnaire and IgE results were presented to a blinded allergist to determine allergic status.
Results: Seventy (60 % male) children aged 30–207 (median 161) months and 0–161 (median 37) months post-renal transplantation were included of whom the primary renal disease was non-immunologically based (62 % CAKUT). Eleven (16 %) RTR were sensitised to at least one food (cow's milk [6], egg [9], peanut [7]) and eight (11 %) were clinically 'allergic'. Total-IgE results ranged 1.0-2872.0 (median 16.5 kUIgE/L) for this cohort. Eosinophil counts ranged 0.0-1.07 (median 0.14 x109/L). Nine (13 %) participants reported food allergy symptoms by questionnaire. Six (9 %) reported parental history of food allergy. There was a significantly low breastfeeding rate (61 %) and duration, range 0–26 (median 0) weeks, in RTR. There was a significant difference in gestation, range 24–43 (median 40) weeks (p=0.05), and birthweight, range 0.7-5.7 (median 3.2) kilograms (p=0.03), between sensitised and non-sensitised children.
Conclusions: Food allergy prevalence in paediatric RTR was not increased to the general population (rates of 6-22 %) with no evidence of allergy being passively transferred from donor to recipient. There was no association with recipient-specific factors, such as immunological cause of renal disease, post-transplantation immunosuppression (as tacrolimus has been implicated) or degree of renal function.

OP52 - SUCCESSFUL ABO-INCOMPATIBLE KIDNEY TRANSPLANTATION IN CHILDREN

SCHAEFER BETTI[1], TOENSHOFF BURKHARD[1], GOMBOS PETRA[2], GOLRIZ MOHAMMAD[3], SCHMIDT JAN[4], MORATH CHRISTIAN[5], WUEHL ELKE[1], SCHAEFER FRANZ[1], SCHMITT CLAUS PETER[1]
[1]*CENTER FOR PEDIATRIC AND ADOLESCENT MEDICINE, UNIVERSITY OF HEIDELBERG, GERMANY*

[2]DEPARTMENT OF TRANSPLANTATION IMMUNOLOGY, INSTITUTE OF IMMUNOLOGY, UNIVERSITY OF HEIDELBERG, GERMANY
[3]DEPARTMENT OF GENERAL, VISCERAL, AND TRANSPLANTATION SURGERY, UNIVERSITY OF HEIDELBERG, GERMANY
[4]GENERAL AND VISCERAL SURGERY, KLINIK IM PARK, ZÜRICH, SWITZERLAND
[5]DEPARTMENT OF INTERNAL MEDICINE, DIVISION OF NEPHROLOGY, UNIVERSITY OF HEIDELBERG, GERMANY

Introduction: ABO-incompatibility precluded one third of living donation kidney transplantation or required intensified preconditioning protocols yielding variably success rates. The recently introduced combination of immunoadsorption (IA) and rituximab pretreatment demonstrated similar outcome rates for ABO-incompatible kidney transplantation (ABOi-Tx) as for ABO-compatible Tx in adults, experience in children is scant.
Material and methods: Three patients (1.9, 18.2, 19.7 years) underwent ABOi-Tx in our centre. A single dose of rituximab (375 mg/m2) was administered 24, 1 and 44 days preoperatively. Immunosuppressive regimen further comprised tacrolimus, mycophenolate mofetil, methylprednisolone and basiliximab; immunoglobulin G was infused at the day of ABOi-Tx.
Results: IA was performed 6, 10 and 11 times using Globaffin®, Immunosorba® and Glycosorb® columns, respectively, according to the preoperative isoagglutinine titers. Mean aPPT was 33±11 pre and 61±27 s post IA, INR 1.06±0.1 and 1.95±1.4, fibrinogen 4.6±1.7 and 1.7±0.6 mg/dl ($p<0.05$), respectively. Isoagglutinine titer were <1:4 post-IA and 1:8 or less at the day of Tx. All three patients achieved normal renal function within 2, 4 and 6 postoperative days. Major diffuse postoperative bleeding occurred in two of the three patients. Both patients required blood transfusion, one patient a surgical revision 4 hours after Tx, despite preoperative anticoagulation during IA with citrate only. One pyelonephritis associated increase in isoagglutinine titer to 1:128 and biopsy-proven acute humoral rejection (Banff type II, postoperative day 9) could adequately be treated by a single plasma exchange and four methylprednisolone pulses. Two subsequent pyelonephritis episodes were not associated with an increase in isoagglutinine titers. 18, 8 and 23 months after ABOi-Tx, serum creatinine is 0.4, 1.8 and 1 mg/dl, respectively.
Conclusions: ABOi-Tx can successfully be performed in pediatric patients with quadruple immunosuppression, rituximab and IA. Caution is mandatory regarding bleeding complications, most likely developing due to unspecific binding of coagulation factors during repeated IA.

OP53 - THE EFFECT OF CALCINEURIN-INHIBITION ON THE RENAL RENIN-ANGIOTENSIN SYSTEM. A NEW PLACE FOR RENIN EXCRETION.

AGNES PROKAI[1], LEONORA HIMER[1], ADAM VANNAY[1], KATALIN KIS-PETIK[1], NORA BERTA[1], ANNA KOSIK[1], ANDREA FEKETE[1], JANOS PETI-PETERDI[2], MIKLOS KELLERMAYER[1], TIVADAR TULASSAY[1], ATTILA J. SZABO[1]
[1]SEMMELWEIS UNIVERSITY
[2]UNIVERSITY OF SOUTHERN CALIFORNIA

Introduction: Tacrolimus (Tac) and Cyclosporin A (CyA) are two great potential immunosupprssants which are essential therapeutic solutions of the prevention of the allograft rejection and the long-term immunosuppression, however, it is well known and deservs special attention that both of them posses nephrotoxic potential.
Material and methods: Three week old, male C57 black 6 mice (n=15) were divided into three groups: control mice (C), treated with 0.075 mg/kg/day of Tac twice a day (Tac) or 2 mg/kg/day of CyA (CyA). After three weeks of administratration serum creatinin was measured, then the renin contant in the collecting duct (CD) and juxtaglomerular apparatus were evaluated applying FACS and multi-foton microscopy. The contraction of the vessels was assessed and the consequent fibrosis was determined by Masson staining.
Results: Serum creatinin was significantly elevated in the Tac and CyA groups. Both the JGA and CD renin content increased four time higher following the administration with calcineurin inhibitors, which was further supported by multi-foton microscopy, the renin granulation increased remarkably in both localizations. As a result of the local activation vasoconstriction was in present in both treated groups and as early as the third week of the treatment with immunosuppressants fiborotic islands were found in the kidney.
Conclusions: In summary, our studies revealed that calcineurin inhibitors possess nephrotoxic effect on the kidney parenchyma, which could be the consequence of the enhanced renin activity not only in JGA but in the collecting duct segment as well. Therefore, the inhibition of renin-angiotensin system could be beneficial in prevention of nephrotoxic effect of the calcineurin inhibitrors. However, further studies are needed to reveal what kind of inhibitors and in which combination could provide the most efficient treatment? REG_KM_09-1-2009-0016 BAROSS, REG_KM_09-1-2009-0016, TÁMOP-4.2.1.B-09/1/KMR, TÁMOP-4.2.2/B-10/1-2010-0013, SE-MTA Lendulet LP2001-008/2011

OP54 - Conversion from twice-daily (Prograf®) to once-daily (Advagraf®) tacrolimus formulation in stable pediatric kidney transplant recipients: a comparative pharmacokinetic study

LAPEYRAQUE ANNE-LAURE[1], KASSIR NASTYA[2], CLERMONT MARIE-JOSE[1], KRAJINOVIC MAJA[1], THEORET YVES[1], LITALIEN CATHERINE[1], PHAN VERONIQUE[1]
[1]*CHU SAINTE JUSTINE, UNIVERSITE DE MONTREAL*
[2]*UNIVERSITE DE MONTREAL*

Introduction: Compliance to immunosuppressive therapy is critical to prevent organ rejection. Advagraf® is an extended release formulation of tacrolimus (Tac) which may offer better adherence. In this study, the Tac pharmacokinetic (PK) parameters were evaluated in pediatric kidney transplant patients during the conversion from Prograf® to Advagraf®.

Material and methods: Stable patients transplanted for at least 6 months were converted from Prograf® to Advagraf® on a mg:mg daily dose. All patients underwent 2 steady-state 24 hours PK profiles (14 concentration-time points), the second one at least 2 weeks after the switch. Tacrolimus blood concentrations were determined by HPLC MS-MS. CYP3A5 genotype was assessed for each patient and correlated to PK parameters.

Results: Thirty-eight PK profiles from 19 patients (12 males) aged between 7.0 and 18.9 years were obtained at a median post-transplantation time of 43.7 months (9.5-128.5). Median Tac daily dose was 0.11 mg/kg (0.06-0.19). After the conversion from Prograf® to Advagraf® on a mg:mg daily dose, mean C0 and Cmin were consistently decreased, particularly in patients with CYP3A5 *3/*3 genotype. No statistically significant difference was observed for mean Cmax between the two formulations in this population. Time to maximum concentration (Tmax) was delayed with Advagraf®, consistent with its prolonged-release characteristics. Despite statistically significant difference in AUCs, the ratio of the least square means for AUC0-24 h was 90.8 % with 90 % CI limits between 80 % to 125 % (85.3 % to 96.7 % in the present study), which is the most commonly accepted definition of bioequivalence.

Conclusions: The steady state tacrolimus exposure of once daily tacrolimus formulation (Advagraf®) is equivalent to Prograf® twice a day after a mg:mg conversion in stable pediatric kidney transplant recipients. Because of the decrease in mean C0 and Cmin observed after the conversion to Advagraf®, patients must only be switched from one tacrolimus formulation to another under the control of tac therapeutic drug monitoring.

OP55 - Copper deficiency in cystinosis patients

MARTINE BESOUW[1], JERRY SCHNEIDER[3], FRANCESCO EMMA[4], MIRIAN JANSSEN[5], ELISABETH CORNELISSEN[6], MARCELLA GRECCO[4], FLEMMING SKOVBY[8], FRANÇOIS NOBILI[7], LAMBERTUS VAN DEN HEUVEL[2], ELENA LEVTCHENKO[1]
[1]*DEPT OF PEDIATRIC NEPHROLOGY, UNIVERSITY HOSPITALS LEUVEN, BELGIUM*
[2]*LABORATORY OF PEDIATRICS, CATHOLIC UNIVERSITY LEUVEN, BELGIUM*
[3]*DEPT OF PEDIATRICS, UNIVERSITY OF CALIFORNIA, SAN DIEGO, UNITED STATES OF AMERICA*
[4]*DEPT OF NEPHROLOGY & UROLOGY, BAMBINO GESù CHILDREN'S HOSPITAL AND RESEARCH INSTITUTE, ROME, ITALY*
[5]*DEPARTMENT OF INTERNAL MEDICINE, RADBOUD UNIVERSITY MEDICAL CENTRE, NIJMEGEN, THE NETHERLANDS*
[6]*DEPT OF PEDIATRIC NEPHROLOGY, RADBOUD UNIVERSITY NIJMEGEN MEDICAL CENTRE, THE NETHERLANDS*
[7]*DEPT OF PEDIATRIC NEPHROLOGY, UNIVERSITY HOSPITAL BESANÇON, BESANÇON, FRANCE*
[8]*DEPT OF CLINICAL GENETICS, JULIANE MARIE CENTRE, COPENHAGEN UNIVERSITY HOSPITAL, COPENHAGEN, DENMARK*

Introduction: Cystinosis is an autosomal recessive disorder, marked by intralysosomal cystine accumulation in various tissues, causing renal Fanconi syndrome (FS). The disease is treated by the administration of cysteamine which slows down the deterioration of renal function. Recently, 8 cystinosis patients were reported to suffer from skin lesions and some from severe bone and muscular weakness, caused by cysteamine. One patient died from cerebral ischemia. Electron microscopy of skin biopsies showed “cauliflower” collagen fibres, which could be caused by decreased collagen cross-linking. Since the formation of a stable collagen matrix requires collagen cross-linking we hypothesized that cysteamine might interfere with this process in analogy to D-penicillamine. Furthermore, since the generation of aldehydes required for cross-linking is catalyzed by the enzyme lysyl oxidase, which needs copper as a co-factor, we measured serum copper and ceruloplasmin levels and urinary copper excretion in cystinosis patients, since copper deficiency might contribute to cysteamine toxicity.

Material and methods: 35 cystinosis patients were included: 22 with FS (including 6 with cysteamine toxicity), 11 were transplanted, 1 was on hemodialysis after graft failure and 1 had ocular cystinosis. Serum copper and ceruloplasmin levels were measured and urine copper/creatinine ratio was determined.

Results: Mean+SD serum copper and ceruloplasmin levels were significantly lower in patients with cysteamine toxicity (63+7 vs 98+27 μg/dL and 0.20+0.02 vs 0.31+0.08 g/L respectively; $p<0.01$), urinary copper excretion was significantly increased in patients with FS (169+75 vs 35+20 μg/g; $p<0.01$).
Conclusions: Increased urinary copper excretion can cause copper deficiency in cystinosis patients with FS. This in turn might decrease lysyl oxidase activity leading to decreased aldehyde formation. Subsequent administration of cysteamine can block the remaining aldehydes, further diminishing collagen cross-linking. This mechanism can be responsible for cysteamine toxicity in cystinosis patients, therefore, copper suppletion might prevent cysteamine toxicity.

OP56 - Successful treatment with Tolvaptan in a 5-year-old girl with congenital SIADH

E A MARLIES CORNELISSEN[1], HEDI CLAAHSEN[2], ERNIE BONGERS[3], STEPHANIE NATSCH[4]
[1]*PED. NEPHROLOGY, RADBOUD UNIVERSITY NIJMEGEN MEDICAL CENTRE, NETHERLANDS*
[2]*PED. ENDOCRINOLOGY, RADBOUD UNIVERSITY NIJMEGEN MEDICAL CENTRE, NETHERLANDS*
[3]*GENETICS, RADBOUD UNIVERSITY NIJMEGEN MEDICAL CENTRE, NETHERLANDS*
[4]*PHARMACY, RADBOUD UNIVERSITY NIJMEGEN MEDICAL CENTRE, NETHERLANDS*

Introduction: The syndrome of inappropriate ADH secretion (SIADH) is among the most common cause of chronic hyponatremia in adult patients. In these patients selective vasopressin-2–receptor (V2R) antagonists can be used for long term treatment and recently an oral form, Tolvaptan, was introduced. In childhood, SIADH is mostly transient as after neurosurgery or other neurological conditions. Fluid restriction usually prevents development of acute hyponatriemia. Here, we describe a 5-year-old girl with severe chronic hyponatremia due to SIADH of unknown pathogenesis. She was successfully treated with Tolvaptan.
Material and methods: Case report
Results: The girl was adopted from China. She had a severe cleft palate but seemed to be otherwise healthy although further information was lacking. One week after arrival to the Netherlands she was admitted to a hospital because of convulsions. Further investigations revealed severe hyponatriemia (Na 121 mmol/l). Adrenal insufficiency and renal pathology was ruled out. Fluid restriction up to a daily fluid intake of 75 ml resulted in normalization of serum sodium values. With a daily fluid intake of 500 ml she developed severe hyponatremia (125 mmol/l) with persistent detectable vasopressin concentrations, high urinary sodium excretion and normal plasma renin levels. Therefore, the diagnosis chronic idiopathic SIADH was made. Mutations in vasopressin V2 receptor (AVPR2 gene) were ruled out. Because of the very low fluid intake resulting in inappropriate feeding and growth we started treatment with Tolvaptan 7 mg/day (0.7 mg/kg/day). Directly after the first dose, there was a significant decrease in urinary osmolarity with an increase in diuresis allowing normalization of fluid intake to about 1200 ml daily with normalizing sodium levels (133 – 136 mmol/l). After a treatment period of now 1 year Tolvaptan is well tolerated without detectable side effects.
Conclusions: Tolvaptan is a succesfull treatment option in children with congenital SIADH.

OP57 - QT and JT dispersion and cardiac performance in patients with Bartter's and Gitelman's disease

DUYGU OVUNC HACIHAMDIOGLU[1], KURSAT FIDANCI[3], NESRIN BESBAS[2], FAYSAL GOK[1], REZAN TOPALOGLU[2]
[1]*GULHANE MILITARY MEDICAL ACADEMY MEDICINE SCHOOL PEDIATRIC NEPHROLOGY DEPARTMENT*
[2]*HACETTEPE UNIVERSITY MEDICINE FACULTY PEDIATRIC NEPHROLOGY DEPARTMENT*
[3]*GULHANE MILITARY MEDICAL ACADEMY MEDICINE SCHOOL PEDIATRIC CARDIOLOGY DEPARTMENT*

Introduction: Left ventricular dysfunction, QT prolongation, and reduction of cardiac index leading to arrhythmias and sudden cardiac death have been reported in Bartter's (BS) and Gitelman's Syndrome (GS). QT dispersion (QTd) and JT dispersion (JTd) is simple noninvasive arrhythmogenic marker that can be used to assess homogeneity of cardiac repolarization and which has not been studied in pediatric BS/GS patients before. We aimed to assessed QTd and JTd and their relation with systolic and diastolic function of the LV in a group of children with BS/GS.
Material and methods: Nine BS/1GS patients (4 M and 6 F median age 9.7 years) and 20 (10 M, 10 F median 8 years) controls were investigated at rest. RR, QT intervals, corrected QT (QTc), QTd, corrected QTd (QTcd), JT, corrected JT (JTc), JTd, corrected JTd (JTdc) were measured with standard 12-lead electrocardiography (ECG) and two-dimensional, M-mode, pulsed-wave and color flow Doppler echocardiographic examinations were performed by a cardiologist who was blinded to the patients and controls. Left ventricular (LV) systolic performance was estimated from fractional shortening, LV output, Left ventricle mass, LV mass index (LVMI), LV geometry and LV myocardial performance index (LVMPI) was calculated.
Results: Patients and controls did not significantly differ with respect to female to male ratio, plasma potassium, plasma total magnesium, and plasma ionized calcium. QTd and JTd were significantly prolonged in patients with BS/

GS compare to controls p=0.014 and p=0.003 respectively. BS/GS patients had normal echocardiographic examination and baseline myocardial performance indexes.

Conclusions: Increases in QTd and JTd during the asymptomatic and normokalemic period may be risk factors for the development of cardiac complications during and after conditions predisposed to arrhythmias. The identification and recognition of other possible triggering mechanisms is extremely important in these patients and suggests the need for a systematic cardiac screening and management protocol for an effective prevention.

OP58 - EFFECTS OF TREATMENT OF KIDNEY STONE DISEASE IN CHILDREN BELOW 4 YEARS OF AGE

BOCHNIEWSKA VIOLETTA[1], JUNG ANNA[1], KALICKI BOLESLAW[1], JURKIEWICZ BEATA[1], LITWIN MIECZYSLAW[1]

[1]*DEPARTMENT OF PEDIATRIC, NEPHROLOGY AND ALLERGOLOGY, MILITARY MEDICAL INSTITUTE, WARSAW, POLAND*

[2]*DEPARTMENT OF SURGERY, PEDIATRIC HOSPITAL, DZIEKANOW LESNY, WARSAW, POLAND*

[3]*DEPARTMENT OF NEPHROLOGY & ARTERIAL HYPERTENSION, THE CHILDREN'S MEMORIAL HEALTH INSTITUTE, WARSAW, POLAND*

Introduction: The management of urinary stone disease has changed in the past decades. Modern technology and miniaturization of equipment contributed to the development of minimally invasive surgical techniques of treatment of urolithiasis in younger children.

Material and methods: The aim: retrospective analysis of results of treatment of urolithiasis in 106 children in age below 4 years.

Results: Results: 20/106 children (18,87 %) were treated non-invasively. The therapy was successful in 12/20 (60 %) children. 86/106 (81,13 %) pts were treated with invasive methods: ESWL was performed in 76/86 (88,37 %), open surgery in 17/86 (19,77 %), URSL in 11/86 (12,79 %) pts. Good results of treatment were achieved in: 62/76 (81,58 %) of children who underwent ESWL, 13/17 (76,47 %) of surgically treated children, 10/11 (90,91 %) of children who underwent URSL. 6 pts treated with ESWL require additional procedures: 4 URSL, 2 open surgery. In patients who underwent ESWL the most frequently observed complication was urinary retention (20/76 pts - 26,32 %). Adverse events after ESWL were transient (haematuria, pyuria, proteinuria, urinary tract infection, "stone bite", abdominal pain). In 2 patients who underwent URSL displacement of the stone from the ureter to the renal pelvis was observed (ESWL was performed). In 4 patients a DJ catheter was placed.

Conclusions: Conclusions: Use of minimally invasive methods (ESWL, URSL) even in children below 4 years of age is effective and safe and minimizes the need to perform open surgery.

OP59 - Proteinuria in Young Adults with Antenatal Bartter-Syndrome

GÜNTER KLAUS[1], MYRA MISDHAYINI[1], SIEGFRIED WALDEGGER[2], HORST SCHWEER[2], BERNHARD WATZER[2]

[1]*PEDIATRIC NEPHROLOGY, KFH AND UNIVERSITY OF MARBURG*

[2]*UNIVERSITY OF MARBURG*

Introduction: Patients with antenatal Bartter-Syndrome (aBS) have excessive renal electrolyte loss with hypokalemia, hypochloremic alkalosis, and depending on the type of disease hypercalciuria. Treatment consists of electrolyte supplements and COX-inhibitors from birth on. Previously we could show histological renal changes compatible with a Low-Sodium-Low-Potassium-Nephropathy (Reinalter et al, 2001). Clinically, a low grade proteinuria was observed in single patients. Therefore renal function was evaluated in young adult pts with aBS Patients: 13 adolescents and young adults with aBS, aged 21.2 (16–29) years. Molecular diagnosis revealed mutations in NKCC2 (n=6), ROMK (n=3), ClCKb (n=4) and were all continously treated with COX-inhibitors.

Material and methods: CCR, protein-und elektrolyte-excretion (in-patient setting), 24 h-ABDM, monofrequent bioelectric impedance (mBIA).

Results: Average excretion of Na 153±75.1 mmol/d, Cl 185.5±90.6 mmol/d. FENa correlated with systolic day blood pressure SDS (r=0,46, p=0.015). Total body water determined by mBIA was reduced in proportion to pt size (BMI 22.8±5.02 kg/m2, Z-score body water −1.56±0.88, fat-free mass −1.6±0.77). CCR was 83.1±30.5 ml/min/1,73 m², 6 pts had a CCR<90, 3 pts<50 ml/min/1.73 m2. Proteinuria was found in 10/13 pts (Alb/Crea 333±337 mg/g), 5 with tubular protein pattern. CCR correlated negatively with proteinuria (r=−0.4, p<0.01). 4 pts had increased NGAL excretion. Renin, Aldosterone and PGE2-excretion were elevated. Two pts had increased blood pressure on 24 h-ABDM.

Conclusions: More than 2/3 of pts with aBS (10/13) had mild proteinuria after ~21 years of disease and treatment. Reduced renal function was found in 10/13 pts (with COX-inhibitor). These results point to long-term risk of renal damage in pts with aBS.

OP60 - Nephropathic cystinosis in developed versus developing countries: a series of 213 patients

AURELIA BERTHOLET-THOMAS[1], VELIBOR TASIC[2], BRUNO RANCHIN[1], JULIEN BERTHILLER[3], PIERRE COCHAT[1]

[1]*CENTRE DE RéFéRENCE DES MALADIES RéNALES RARES «NéPHROGONES» AND EPICIME HOSPICES CIVILS DE LYON AND UNIVERSITé CLAUDE-BERNARD LYON 1, LYON, FRANCE*

[2]*DEPARTMENT OF PEDIATRIC NEPHROLOGY, UNIVERSITY CHILDREN'S HOSPITAL, 1000 SKOPJE, MACEDONIA*

[3]*INSERM, CIC201, EPICIME, RIPPS, CNRS UMR 5558 FRANCE; CHU LYON, HOP L PRADEL, SERVICE DE PHARMACOLOGIE CLINIQUE, UNIVERSITé. PôLE INFORMATION MéDICALE EVALUATION RECHERCHE, HOSPICES CIVILS DE LYON ET UNIVERSITé DE LYON, LYON, FRANCE*

Introduction: Nephropathic cystinosis is a rare inherited metabolic disorder characterized by intralysosomal cystine accumulation leading to renal Fanconi syndrome, progressive renal failure and extra-renal manifestations. The prognosis strongly relies on early adherence to cysteamine treatment together with conservative measures. Developing countries (DiC) experience many difficulties in patients' management with very few published data. The aim of the study was to assess challenges in the management of nephropathic cystinosis in DiC compared to developed ones (DeC) in term of growth, treatment and renal outcomes.

Material and methods: A questionnaire including demographic data, growth parameters, renal evolution and treatment, has been sent to about 65 pediatric nephrology units over 35 countries between April 2010 and May 2011. The study finally included 213 patients: 109 from DiC and 104 from DeC.

Results: DiC patients were a little older at diagnosis (1.5 vs. 1.3 yrs, p=0.04). Growth profile was dramatically different between DiC and DeC groups. 35 % of DiC could deliver cysteamine treatment to 53.8 % of their patients. In DiC, intra-leukocyte cystine assessment was only available in selected cases for diagnosis but never for treatment monitoring. A small part of DiC patients received conservative treatment such as indomethacin, human recombinant growth hormone or tube feeding. More patients reached end-stage renal disease in DiC patients: 53.2 % vs. 37.9 % within a shorter time: 8 yrs vs. 10 yrs. DiC median renal survival was 2-time less than for DeC: 6.3 yrs vs. 12.7 yrs, and only 3.75 yrs for untreated DiC patients.

Conclusions: In conclusion, there are unacceptable discrepancies between DiC and DeC in the management of patients with nephropathic cystinosis, since patients from DiC are treated like patients from DeC 30 years ago!

OP61 - EFFECT OF EXTENDED PREDNISOLONE TREATMENT FROM THREE TO SIX MONTHS, WITH EQUAL CUMULATIVE DOSES, ON CHILDHOOD NEPHROTIC SYNDROME: A NATION-WIDE, RANDOMISED CONTROLLED TRIAL

NYNKE TEENINGA[1], JOANA E. KIST-VAN HOLTHE[2], NIENSKE VAN RIJSWIJK[1], NIENKE I. DE MOS[3], WIM C.J. HOP[4], JACK F.M. WETZELS[5], ALBERT J. VAN DER HEIJDEN[1], JEROEN NAUTA[1]

[1]*ERASMUS MC UNIVERSITY MEDICAL CENTER – SOPHIA CHILDREN'S HOSPITAL, ROTTERDAM, THE NETHERLANDS*

[2]*VU UNIVERSITY MEDICAL CENTER, AMSTERDAM*

[3]*LEIDEN UNIVERSITY MEDICAL CENTRE LEIDEN*

[4]*ERASMUS MC UNIVERSITY MEDICAL CENTER, ROTTERDAM*

[5]*RADBOUD UNIVERSITY NIJMEGEN MEDICAL CENTER, NIJMEGEN*

Introduction: The relapse rate in children with nephrotic syndrome (NS) is high. A Cochrane meta-analysis suggests that prolonged prednisolone treatment for the initial episode of childhood nephrotic syndrome reduces the risk of relapse. Whether this results from increased duration of treatment or from higher cumulative dose remains unclear. We therefore compared the efficacy of our standard three month prednisolone regimen with a six month regimen, using equal cumulative doses.

Material and methods: A randomized, placebo-controlled, parallel-group trial was carried out in 69 hospitals in the Netherlands. Children aged nine months to 17 years presenting with NS without underlying disease were randomly assigned to either three months prednisolone followed by three months placebo or six months prednisolone, with equal cumulative doses (≈3360 mg/m2). Allocation concealment was pharmacy controlled. Participants, healthcare providers, and outcome assessors were blinded to group assignment. Primary outcome was frequently relapsing nephrotic syndrome (FRNS). This trial is registered at the Dutch National Trial Register, number NTR255.

Results: Between February 2005 and January 2010, 150 patients were randomly assigned to three months (n=74) or six months (n=76) prednisolone. 126 children that indeed started study medication (62 in the three month group and 64 in the six month group) were included in the analysis. Median follow up was 47 months (12–60). FRNS was found in 31/62 (50 %) children in the three month group, compared with 38/64 (59 %) in the six month group (hazard ratio 0.90 [95 % CI 0.56-1.45]; p=0.66). The incidences of a first relapse, steroid dependence, and adverse effects were similar in both groups.

Conclusions: Extending initial prednisolone treatment from three to six months without increasing cumulative dose does

not benefit clinical outcome in children with NS. Previous findings indicating that longer treatment regimens lead to better outcome may have resulted from increased cumulative dose rather than prolonged treatment duration.

OP62 - Protective effects of everolimus on puromycin-induced cytoskeletal alterations in human podocytes are mediated by RhoA-signalling

STEFANIE JERUSCHKE[1], ANJA BÜSCHER[1], MOIN SALEEM[2], PETER HOYER[1], JUN OH[3], PERIHAN NALBANT[4], STEFANIE WEBER[1]
[1]*PEDIATRIC NEPHROLOGY, PEDIATRICS II, UNIVERSITY OF DUISBURG-ESSEN, ESSEN, GERMANY*
[2]*CHILDREN'S RENAL UNIT, BRISTOL ROYAL HOSPITAL FOR CHILDREN, UNIVERSITY OF BRISTOL, BRISTOL, UK*
[3]*DEPARTMENT OF PEDIATRIC NEPHROLOGY, UNIVERSITY MEDICAL CENTER HAMBURG-EPPENDORF, HAMBURG, GERMANY*
[4]*CENTER FOR MEDICAL BIOTECHNOLOGY, MOLECULAR CELL BIOLOGY, UNIVERSITY OF DUISBURG-ESSEN, ESSEN, GERMANY*

Introduction: Podocytes are highly differentiated cells that play an important role in maintaining glomerular filtration barrier integrity. Proper organization of the actin cytoskeleton is essential for normal structure and function of podocytes. Based on studies with the immunosuppressant cyclosporine A, recovery of the actin cytoskeleton emerges as key for antiproteinuric effects in addition to the primarily known immunosuppressive functions. Thus, the antiproteinuric effects of the mTOR inhibitor everolimus (EV), a potent immunosuppressant used in renal therapy, might similarly involve the recovery of the actin cytoskeleton.
Material and methods: In this study, potential actin-related effects of EV were investigated in a puromycin (PAN) in vitro model of differentiated human podocytes. Cells were treated for 48 h with EV, PAN or in combination and cell morphology, actin structures, cell migration as well as adhesion and apoptosis were analyzed.
Results: EV substantially recovered PAN-induced cellular defects such as increased apoptosis, decreased adhesion and enhanced migration. These protective effects were associated with restored cell size and the recurrence of central actin stress fibers, both key features of proper podocyte morphology. Biochemical studies revealed that activity of the Rho GTPase RhoA and Myosin-light-chain (MLC), both regulators of actin stress fibers, was substantially increased by EV. This increase of MLC phosphorylation and the actin stress fiber recurrence was abolished by inhibition of the RhoA effector Rho-associated protein kinase (ROCK) using Y-27632, substantiating that the RhoA-ROCK-MLC pathway is the mediator of EV induced stress fiber reorganization.
Conclusions: Together, our data establish a novel role for the mTOR inhibitor EV in podocyte cytoskeletal remodelling in the context of the PAN injury model. We show that EV induces the recovery of cell morphology and adhesion, both key aspects of proper podocyte function. Thus, the cytoprotective activity of EV might involve multiple, independent pathways controlling the cytoskeletal reorganization as well as the previously shown immunosuppressive effects.

OP63 - Therapeutic drug monitoring of mycophenolate mofetil in children with steroid-dependent idiopathic nephrotic syndrome

JEROME HARAMBAT[1], AYMERIC DALLOCCHIO[2], VINCENT GUIGONIS[3], LYDIA ICHAY[4], LUCIE BESSENAY[5], FRANÇOISE BROUX[6], ARNAUD GARNIER[2], BRIGITTE LLANAS[1], DENIS MORIN[4], FRANCK SAINT-MARCOUX[3], STEPHANE DECRAMER[2]
[1]*BORDEAUX UNIVERSITY HOSPITAL, FRANCE*
[2]*TOULOUSE UNIVERSITY HOSPITAL, FRANCE*
[3]*LIMOGES UNIVERSITY HOSPITAL, FRANCE*
[4]*MONTPELLIER UNIVERSITY HOSPITAL, FRANCE*
[5]*CLERMONT-FERRAND UNIVERSITY HOSPITAL, FRANCE*
[6]*ROUEN UNIVERSITY HOSPITAL, FRANCE*

Introduction: Therapeutic drug monitoring of mycophenolate mofetil (MMF) can improve clinical outcome in organ transplantation and systemic lupus erythematosus but data is scare in idiopathic nephrotic syndrome. The aim of this study was to investigate whether mycophenolic acid (MPA) phamacokinetics is associated with disease control in childhood steroid-dependent nephrotic syndrome (SDNS).
Material and methods: This is a retrospective multicentric study of SDNS children treated with MMF±steroids. Area under the concentration time curve (AUC) of MPA was determined in all children based on sampling times at 20, 60 and 180 min post-dose using Bayesian estimation. The association between a threshold value of AUC and the relapse rate under MMF was assessed using a negative binomial model.
Results: Data of 90 patients (46 boys) including 134 MPA AUC were analyzed. Median age at diagnosis was 3.6 years and MMF was introduced at a median time of 2 years after disease onset. A total of 89 episodes of relapses were recorded (median follow-up 2.2 years). AUC MPA determination resulted in individual dose adaptation in 48 cases (36 %). The overall relapse rate under MMF decreased from

1 episode in 19 patient-months to 1 episode 31 patient-months after the first MPA AUC (p<0.01). The proportion of patients without relapse was significantly greater in AUC levels of >45 h.mg/l (82 % vs. 52 % in AUC <45). In a multivariable negative binomial model including sex, age at disease onset, number of previous immunosuppressive treatments and age at start of MMF, a level of AUC >45 h.mg/l was significantly associated with a lower relapse rate (RR 0.64; IC95% 0.49-0.91; p=0.01).

Conclusions: Our study suggests that therapeutic drug monitoring leading to individualized dosing may improve the efficacy of MMF in SDNS. A MPA AUC value greater than 45 h.mg/l should be considered in childhood idiopathic nephrotic syndrome.

OP64 - Efficacy and Safety of Rituximab in Difficult Steroid Resistant & Dependent Nephrotic Syndrome

ADITI SINHA, DIVYA BHATIA, ASHIMA GULATI, AMIT DINDA, PANKAJ HARI, ARVIND BAGGA
ALL INDIA INSTITUTE OF MEDICAL SCEINCES, NEW DELHI

Introduction: Rituximab (RTX) is promising therapy for patients with difficult steroid resistant (SRNS) & steroid dependent nephrotic syndrome (SDNS). We report its efficacy in 108 patients treated during 2005–11.

Material and methods: Patients with SRNS with failure or toxicity to calcineurin inhibitors (CNI), and difficult SDNS with or without prior resistance, received 2–4 doses of RTX (375 mg/sq.m/week). Response in SRNS was described as complete (CR) or partial remission (PR). For SDNS, relapse-free duration and relapses/6-months were calculated.

Results: STEROID RESISTANT NS: 44 patients (26 initial resistance; MCD 17, FSGS 27) received RTX at 9.3±4.4 yr. At 1.8±1.3 months, 16 (36.4 %) showed CR/PR. At 15±14 months, 6 patients each had sustained remission & steroid sensitive relapses; 4 had subsequent non-response. Favorable response was associated with MCD (P<0.028), late resistance (P<0.04) and prior response to CNI (P=0.001). PRIOR STEROID RESISTANCE: 24 patients, currently showing steroid dependence & CNI toxicity or failure received RTX at 12±5 yr. Therapy resulted in median (IQR) relapse-free duration of 10 (7–15) months; 75 %, 26 % and 5 % had remission at 6, 12 and 24-months respectively. On follow-up, 17 % had sustained remission, 30 % infrequent relapses & 48 % frequent relapses. STEROID DEPENDENT NS: 40 patients, 13±3 yr-old, failing multiple therapies, were administered RTX. Relapse-free duration was 21 (19–37) months; 80 %, 76 % and 27 % had remission at 12, 18 and 24-months respectively. Therapy resulted in reduced relapses (mean difference 1.9 episodes/6-months; P<0.001); 50 % had sustained remission. Twelve patients were redosed, with remission for 13 (9–14) months. Five patients had minor adverse effects (rash 3, throat pain 1, chills 1).

Conclusions: Rituximab induced remission in one-third patients with refractory SRNS; minimal change disease, late resistance and prior response to CNI predicted favorable response. Although steroid-free remission was 80 % at 1-yr in patients with SDNS, results were less satisfactory where steroid resistance had preceded steroid dependence.

OP65 - Response to Intensified Immunosuppressive Therapy Predicts Long-Term Prognosis in Steroid Resistant Nephrotic Syndrome (SRNS)

AGNES TRAUTMANN[1], FATIH OZALTIN[2], MONICA BODRIA[3], ALI ANARAT[4], BASSAM SAEED[5], MARTA AZOCAR[6], JUTTA GELLERMANN[7], DOROTA DROZDZ[8], RADOVAN BOGDANOVIC[9], RAFAEL KRMAR[10], ANETTE MELK[11], HELENA JARDIM[12], BRUNO RANCHIN[13], NIKOLETA PRINTZA[14], AUGUSTINA JANKAUSKIENE[15], FRANZ SCHAEFER[1]
[1]*PEDIATRIC NEPHROLOGY, UNIVERSITY CHILDREN´S HOSPITAL, HEIDELBERG, GERMANY*
[2]*PEDIATRIC NEPHROLOGY, HACETTEPE UNIVERSITY CHILDREN´S HOSPITAL, ANKARA, TURKEY*
[3]*INSTITUTO GIANNINA GASLINI, GENOVA, ITALY*
[4]*PEDIATRIC NEPHROLOGY, CUKUROVA UNIVERSITY CHILDRENS´S HOSPITAL, ADANA, TURKEY*
[5]*PEDIATRIC NEPHROLOGY, CHILDREN´S HOSPITAL DAMASCUS, SYRIA*
[6]*PEDIATRIC NEPHROLOGY, LUIS CALVO MACKENA CHILDREN´S HOSPITAL, SANTIAGO DE CHILE*
[7]*PEDIATRIC NEPHROLOGY, CHARITE UNIVERSITY CHILDREN´S HOSPITAL, BERLIN, GERMANY*
[8]*PEDIATRIC NEPHROLOGY, JAGIELLONEN UNIVERSITY CHILDRENS´S HOSPITAL, KRAKOW, POLAND*
[9]*PEDIATRIC NEPHROLOGY, CHILDREN´S HOSPITAL, BELGRADE, SERBIA*
[10]*PEDIATRIC NEPHROLOGY, KAROLINSKA UNIVERSITY CHILDREN´S HOSPITAL, STOCKHOLM, SWEDEN*
[11]*PEDIATRIC NEPHROLOGY, UNIVERSITY CHILDREN´S HOSPITAL, HANNOVER, GERMANY*
[12]*PEDIATRIC NEPHROLOGY, CHILDREN´S HOSPITAL, PORTO, PORTUGAL*
[13]*PEDIATRIC NEPHROLOGY, UNIVERSITY CHILDREN´S HOSPITAL, LYON, FRANCE*
[14]*PEDIATRIC NEPHROLOGY, ARISTOTELES UNIVERSITY CHILDREN´S HOSPITAL, THESSALONIKI, GREECE*
[15]*PEDIATRIC NEPHROLOGY, UNIVERSITY CHILDREN´S HOSPITAL, VILNIUS, LITHUANIAN*

Introduction: To evaluate the response to different pharmacologic treatment protocols and to identify predictors for long-term course of renal function in SRNS.

Material and methods: The PodoNet Registry collects clinical and genetical data of children with SRNS. Out of 1407 children from 64 centers in 24 countries, genetic study results are available from 1013, and family history from 974 children. Detailed longitudinal proteinuria and medication data allowing to classify responsiveness to intensified immunosuppression has been collected from 592 children. Response was based on defined criteria regarding proteinuria and serum albumin. Kaplan-Meier renal survival analysis was performed depending on initial response to immunosuppression and genetic diagnosis.
Results: 165 of 592 children (28 %) achieved complete and 72 (12 %) partial remission when treated with calcineurin inhibitors, MMF or both, whereas 349 (60 %) were multidrug resistant. 83 of 348 multidrug-resistant cases had a genetic disorder, 33 patients familial disease. Treatment with CNI-based protocols yielded complete or partial remission in 294 of 565 (64 %), CNI and MMF combined in 48 of 75 (64 %), MMF monotherapy in 31 of 85 (37 %), rituximab in 9 of 29 (31 %), steroid pulse therapies in 32 of 346 (9 %) and cyclophosphamide in 16 of 174 (9 %) treated patients. Monotherapy with RAS inhibitors was effective in 51 of 169 (30 %). In children achieving complete or partial remission on treatment, renal survival was 98 %/92 %, 95 %/78 % and 95 %/78 % at 5, 10 and 15 years respectively, as compared to 63 %, 36 % and 21 % in multidrug resistant cases. Renal survival in the latter group was similar to that seen in children with genetic/familial disease (70 %, 47 % and 29 %).
Conclusions: This PodoNet registry analysis showed a favourable long-term prognosis for patients responding to initial intensified immunosupression. Multidrug resistance is associated with a similarly poor long-term outcome as the identification of an underlying genetic disorder. In conclusion, the response to initial immunosuppressive therapy is as predictive as the identification of a genetic diagnosis for long-term outcome in SRNS.

OP66 - Advantages and disadvantages of rituximab versus oral immunosuppression for high degree steroid dependent nephrotic syndrome (SDNS) – an anonymous patient survey

IULIA STOICA, JUSTINE LANNEAU, AURéLIEN GALERNE, EKATERINA YUDINTSEVA, ELENA TUDORACHE, TIM ULINSKI
PEDIATRIC NEPHROLOGY UNIT, TROUSSEAU HOSPITAL, APHP, PARIS

Introduction: Rituximab (RTX) has become a promising strategy for high degree steroid and calcineurin inhibitor dependent idiopathic nephrotic syndrome. RTX seems to have at least equal efficacy for remission maintenance when compared to oral anticalcineurin inhibitor treatment. Both oral immunosuppressive treatment and RTX have specific advantages and disadvantages for the patients and their families.
Material and methods: We evaluated prospectively both treatment strategies in 15 patients between 10 and 18 years who were on oral immunosuppressive treatment (outpatient follow up every two to three months) and who were switched to RTX treatment with an 18-month B cell depletion period using repeated RTX infusions and monthly CD19 monitoring. The patients completed an anonymous questionnaire with potential advantages and disadvantages of oral immunosuppression and RTX treatment. At the time of the survey the patients had completed at least 12 months of oral immunosuppression and 12 months of RTX induced B cell depletion.
Results: The relapse number between both treatment periods was 0.8 and 0.6 respectively ($p>0.05$). 12/15 patients preferred RTX treatment to oral immunosuppression. The main reasons were: “Not afraid to forget oral treatment” (13/15); “don’t need my parents to manage my treatment at home” (11/15). “I feel free at home and I don’t think about my disease” (12/15). RTX disadvantages were: “too many outpatient visits for blood sampling” (6/15). I don’t feel well during the RTX infusion (2/15). Advantages of oral immunosuppression were not mentioned. Main disadvantages were “fear to forget” (13/15) and “I feel different from the others because I have to take pills twice daily”.
Conclusions: Adherence to longterm oral medication is difficult to achieve. In the studied pre/adolescents the wish to “feel free” and “to be like the others” seem to be the main reasons why RTX is the preferred treatment option for 80 % of high degree SDNS patients.

OP67 - ANEMIA MANAGEMENT IN CHILDREN RECEIVING CHRONIC PERITONEAL DIALYSIS

DAGMARA BORZYCH-DUZALKA[1], YELDA BILGINER[2], LARS PAPE[3], MUSTAFA BAK[4], LESLEY REES[5], AGNIESZKA URZYKOWSKA[6], SEVINC EMRE[7], NIKOLETA PRINTZA[8], DAFINA KUZMANOVSKA[9], EVA SIMKOVA[10], DIRK MÜLLER-WIEFEL[11], KAI RONNHOLM[12], ENRICO VERRINA[13], SEVGI MIR[14], JW GROOTHOFF[15], MICHEL FISCHBACH[16], GIOVANNA LEOZAPPA[17], ZOFIA WAWER[18], ENRICO VIDAL[19], BRADLEY WARADY[20], FRANZ SCHAEFER[21]
[1]*MEDICAL UNIVERSITY OF GDAńSK, POLAND*
[2]*HACETTEPE UNIVERSITY, IZMIR, TURKEY*
[3]*MEDIZINISCHE HOCHSCHULE, HANNOVER, GERMANY*
[4]*DR.BEHCET UZ CHILDREN RESEARCH AND EDUCATION HOSPITAL, IZMIR, TURKEY*
[5]*GREAT ORMOND STREET HOSPITAL FOR CHILDREN NHS TRUST, LONDON, UNITED KINGDOM*

[6]CHILDREN'S MEMORIAL HOSPITAL, WARSAW, POLAND
[7]ISTANBUL UNIVERSITY, ISTANBUL, TURKEY
[8]ARISTOTLES UNIVERSITY, THESSALONIKI, GREECE
[9]PEDIATRIC CLINIC, NEPHROLOGY UNIT, SKOPJE, MACEDONIA
[10]DUBAI HOSPITAL, DUBAI, UNITED ARAB EMIRATES
[11]KFH CENTER FOR CHILDREN AND ADOLESCENTS, HAMBURG, GERMANY
[12]HUCH HOSPITAL FOR CHILDREN AND ADOLESCENTS, HELSINKI, FINLAND
[13]G. GASLINI INSTITUTE, GENOVA, ITALY
[14]EGE UNIVERSITY FACULTY OF MEDICINE, IZMIR, TURKEY
[15]ACADEMIC MEDICAL CENTER, AMSTERDAM, THE NETHERLANDS
[16]CHILDREN'S DIALYSIS CENTER, STRASSBOURG, FRANCE
[17]DIP. NEFROLOGIA-UROLOGIA, UNITà DI DIALISI, ROMA, ITALY
[18]PUBLIC PAEDIATRIC TEACHING HOSPITAL, WARSAW, POLAND
[19]PEDIATRIC NEPHROLOGY, DIALYSIS AND TRANSPLANT UNIT, PADOVA, ITALY
[20]CHILDREN'S MERCY HOSPITAL, KANSAS CITY, USA
[21]CENTER FOR PEDIATRICS AND ADOLESCENT MEDICINE, HEIDELBERG, GERMANY

Introduction: Whereas anemia correction targets have recently been revised based on trial evidence for adult patients with chronic kidney disease, little information exists regarding the efficacy, modifiers and outcomes of anemia management in children.
Material and methods: We assessed practices, effectors and outcomes of pediatric anemia management in 1,411 pediatric PD patients followed prospectively in 30 countries.
Results: Sub-target hemoglobin (<10/9.5 g/dl in children older/younger than 2 years) was noted in 25 % of patients with significant regional variation (highest hemoglobin in North America and Europe, lowest in Asia and Turkey) and associated with low urine output, low serum albumin, high PTH, high ferritin, and the use of bio-incompatible PD fluid. Erythropoesis stimulating agents (ESAs) were administered in 92 % of patients, without efficacy differences related to ESA type or dosing interval. The weekly ESA dose was inversely correlated with age when scaled to weight, but age-independent when normalized to body surface area. ESA sensitivity was positively associated with residual diuresis and serum albumin, and inversely with serum PTH and ferritin. The prevalence of hypertension and left ventricular hypertrophy increased with the degree of anemia. Patient survival was positively associated with achieved hemoglobin and serum albumin, and inversely with ESA dose.
Conclusions: Anemia control in children receiving chronic PD shows major regional variation. ESA requirements are independent of age when dose is scaled to body surface area. ESA resistance is associated with indicators of inflammation, fluid retention and hyperparathyroidism. Anemia and high ESA dose requirements independently predict the risk of death on dialysis.

OP68 - PERITONEAL BIOPSY STUDY IN CHILDREN WITH CKD 5D AND HEALTHY CONTROLS

SCHAEFER BETTI[1], MACHER-GOEPPINGER STEPHAN[2], FISCHBACH MICHEL[3], ZALOSZYC ARIANE[3], BAYAZIT AYSUN K.[4], SALLAY PETER[5], TESTA SARA[6], AOUN BILAL[7], CERKAUSKIENE RIMANTE[8], NOBILI FRANCOIS[9], PFEIFLE VIKTORIA[10], HOLLAND-CUNZ STEFAN[10], SCHAEFER FRANZ[1], SCHMITT CLAUS PETER[1]
[1]CENTER FOR PEDIATRIC AND ADOLESCENT MEDICINE, UNIVERSITY OF HEIDELBERG, GERMANY
[2]DEPARTMENT OF PATHOLOGY, UNIVERSITY OF HEIDELBERG, GERMANY
[3]NEPHROLOGY DIALYSIS TRANSPLANTATION CHILDREN'S UNIT, UNIVERSITY HOSPITAL HAUTEPIERRE, STRASBOURG, FRANCE
[4]DEPARTMENT OF PAEDIATRIC NEPHROLOGY, SCHOOL OF MEDICINE, CUKUROVA UNIVERSITY, ADANA, TURKEY
[5]FIRST DEPARTMENT OF PEDIATRICS, SEMMELWEIS UNIVERSITY, BUDAPEST, HUNGARY
[6]PEDIATRIC NEPHROLOGY AND DIALYSIS UNIT, FONDAZIONE IRCCS CA' GRANDA OSPEDALE MAGGIORE POLICLINICO, MILAN, ITALY
[7]DEPARTMENT OF GENERAL PEDIATRICS, RAFIC HARIRI UNIVERSITY HOSPITAL, BEIRUT, LEBANON
[8]UNIVERSITY CHILDREN'S HOSPITAL, VILNIUS UNIVERSITY, VILNIUS, LITHUANIA
[9]HOSPITAL SAINT JACQUES, BESANCON, FRANCE
[10]PEDIATRIC SURGERY, UNIVERSITY OF HEIDELBERG, GERMANY

Introduction: The peritoneal membrane undergoes substantial alterations in adults on conventional PD. The effects of biocompatible solutions are unknown. Pediatric data have not yet been obtained, even though children are particularly suitable, since at PD onset they are largely devoid of tissue damage.
Material and methods: We initiated an international pediatric PD biopsy study for standardized tissue sampling from the parietal peritoneum and omentum. Until now specimens were obtained from 24 non-uremic controls (0.2-16.4 years), undergoing elective surgery for diseases unrelated to the peritoneum, and 33 children

on PD (0.7-20.1 years), of which 80 % were on biocompatible fluids.

Results: An intact CK5/6 positive mesothelial cell layer was demonstrated in 83 % of the biopsies obtained in controls, with calretinine staining being negative in some of the young children. In the latter submesothelial fat was absent, mean submesothelial compact zone reached down to the muscle fascia and was 272 (150–500) μm and thus thicker than reported in adults. Capillary density decreased with age and was 29.7 (21.7-53) in children below 6, 22.8 (12.8-50.8) below 12 years and 16.4 (11–25.6) capillaries /mm2 in adolescents. Omental vessel wall/lumen ratio appeared higher as compared to adults. In children on PD the mesothelial cell layer was preserved in 24 % of the biopsies only, submesothelial zone thickness was similar as in controls. PD increased capillary density in all age groups from [40.6 (8.1-43.2) at onset of PD and 64.8 (30.2-89) capillaries/mm2 after 30 (22–40) months on PD]. Microvessel morphology was unaltered. Activated fibroblasts and CD45/68 positive, inflammatory cells were detected in 47 % of the PD children. Biopsy related complications were not observed.

Conclusions: PD membrane biopsy sampling is feasible in infants and children. Our first findings in non uremic children suggest substantial differences in peritoneal morphology and vascularisation as compared to adults. Even with biocompatible PD solutions substantial peritoneal alterations develop.

OP69 - Sudden Blindness in Children on Chronic Peritoneal Dialysis: report of five cases

DI ZAZZO GIACOMO[1], DE GALASSO LARA[1], GUZZO ISABELLA[1], VALERIANI MASSIMILIANO[2], LEOZAPPA GIOVANNA[1], PERUZZI LICIA[3], PICCA STEFANO[1]
[1]*DEPARTMENT OF NEPHROLOGY AND UROLOGY, DIVISION OF NEPHROLOGY AND DIALYSIS, BAMBINO GESù CHILDREN'S HOSPITAL, ROME, ITALY*
[2]*DIVISION OF NEUROLOGY, BAMBINO GESù CHILDREN'S HOSPITAL, ROME, ITALY*
[3]*NEPHROLOGY DIALYSIS AND TRANSPLANTATION, REGINA MARGHERITA CHILDREN'S HOSPITAL, TURIN, ITALY*

Introduction: Anterior ischemic optic neuropathy (AION) is characterized by infarction of the optic nerve head due to hypoperfusion of the posterior ciliary arteries. It can occur in adult patients on chronic dialysis. In children, AION is associated with the use of peritoneal dialysis and low BP values. We present five cases from two Italian Pediatric Dialysis Units on nocturnal continuous cycling peritoneal dialysis (CCPD) who developed AION.

Material and methods: Patients were identified in the Italian Registry of Pediatric Dialysis.

Results: Four patients were young (5–35 months), one had 10 years of age. All were hypotensive and showed bilateral disc swelling with or without hemorrhages. In one patient, caudate nucleus (CN) abnormalities, hyperintensive in T2 related images, were found at MR. Treatment consisted in steroid administration and temporary PD withdrawal with dry body weight increase. Three showed partial monolateral vision recovery, two remained bilaterally blind with optic atrophy (follow up: 2–11 months).

Conclusions: Hypotension is confirmed to be a common finding in children on CCPD showing AION. In these children, the risk of hypotension is amplified by ultrafiltration, nocturnal physiologic BP nadir and possible autonomic dysfunction. The role of vascular calcification in AION genesis has been suggested in adult patients. In our series, highest pre-blindness PTH values (1559 and 643 pg/ml) were found in the two patients with definite loss of vision. A possible role of early calcification for AION occurrence in children on CCPD cannot be excluded. Interestingly, one patient in this series showed CN lesions indistinguishable from those found in a 3-yr-old patient on CCPD in our Unit without AION (not reported). Given the anatomic similarities of posterior ciliary and lenticular arteries (small, perforating, terminal), a common hemodynamic mechanism could explain this coincidence. In children on CCPD, AION could be the "tip of the iceberg" of a larger vascular damage of CNS.

OP70 - THE UK EXPERIENCE OF CHRONIC DIALYSIS IN INFANTS AND CHILDREN UNDER TWO YEARS OF AGE: A POST MILLENNIUM PERSPECTIVE ON BEHALF OF THE BRITISH ASSOCIATION FOR PAEDIATRIC NEPHROLOGY

HELEN E JONES[1], JOANNA C CLOTHIER[2], ANNA CASULA[3], MANISH D SINHA[2], SALLY A HULTON[4], CAROL INWARD[5]
[1]*GREAT ORMOND STREET HOSPITAL FOR CHILDREN, LONDON*
[2]*EVELINA CHILDREN'S HOSPITAL, LONDON*
[3]*UK RENAL REGISTRY*
[4]*BIRMINGHAM CHILDREN'S HOSPITAL*
[5]*BRISTOL ROYAL HOSPITAL FOR CHILDREN*

Introduction: To audit the current UK management of infants and children commenced on chronic dialysis when under two years of age.

Material and methods: Retrospective chart and UK Renal Registry audit over a five-year period ending 31st December 2009 of all infants and children commenced on chronic dialysis under two years of age. Outcome data collected until 31st December 2010. Data presented as median (range).

Results: 102 patients identified. Incidence 13.0 and prevalence 20.1 cases per million age related UK population. Of prevalent cases 66 % were male, 66 % white, 48/102 antenatally diagnosed. Primary renal diagnoses were congenital structural anomalies(55 %) and congenital/infantile nephroses(16 %). 31 infants commenced dialyisis under 1 month of age, median age at start of dialysis 5.9 months with weight 6 (1.1-12.4)Kg. 70/102(69 %) had co-morbidities. The commonest starting modality was peritoneal dialysis(PD) (79 %) with complications of hernias±hydroceles in 40 patients (80 % male)(n=99), peritonitis rate of 1 episode per 10.3 patient months with catheter replacement rate of 1 per 8.3 patients months. 46 % required a period on haemodialysis (HD). Duration of admission to effectively establish PD was 50(1–289) nights. 21 % started on HD with 55 % spending some time on PD. HD line infection rate was 1 per 9 patient months, HD catheter change 1 per 3.8 patient months. The proportion of dialysis duration spent as an inpatient for the cohort overall until transplantation, death or until 31/12/2010 was 18 % (n=100) and for those now transplanted 15 % (n=52). Outcome: 53 transplanted (32 living donor at weight 12(9.8-17.8)Kg, dialysis duration 20.7(6.6-51) months; 21 deceased donor, dialysis duration 29(13.7-60.4)months), 3 discontinued dialysis (function improved, 1 transplanted 16 months later), 27 continue on dialysis, 19 deaths (68 % had severe co-morbidities).

Conclusions: Dialysing infants and small children is challenging. This is the first complete national audit of outcome in this group and identifies important issues to address before improved outcome is anticipated.

OP71 - PERITONITIS INCIDENCE AND RISK FACTORS IN CHILDREN UNDERGOING CHRONIC PERITONEAL DIALYSIS (PD). A GLOBAL STUDY OF THE INTERNATIONAL PEDIATRIC PD NETWORK (IPPN)

DAGMARA BORZYCH-DUZALKA[1], VIMAL CHADHA[2], ANJA SANDER[3], NEJAT AKSU[4], LALE SEVER[5], ANJA BUESCHER[6], ALAN WATSON[7], MARIA SZCZEPANSKA[8], DOROTA DROZDZ[9], SARA TESTA[10], KAREL VONDRAK[11], ATTILA SZABO[12], KOEN VAN HOECK[13], BRUNO RANCHIN[14], GEMA ARICETA[15], GUNTER KLAUS[16], REYNER LOZA MUNARRIZ[18], BRADLEY WARADY[2], FRANZ SCHAEFER[19]

[1]*MEDICAL UNIVERSITY OF GDAńSK, POLAND*
[2]*CHILDREN'S MERCY HOSPITAL, KANSAS CITY, USA*
[3]*INSTITUT FÜR MEDIZINISCHE BIOMETRIE UND INFORMATIK, HEIDELBERG, GERMANY*
[4]*TEPECIK TEACHING AND RESEARCH HOSPITAL, IZMIR, TURKEY*
[5]*CERRAHPASA SCHOOL OF MEDICINE, INSTANBUL, TURKEY*
[6]*UNIVERSITäTS-KINDERKLINIK ESSEN, GERMANY*
[7]*CHILDREN & YOUNG PEOPLE'S KIDNEY UNIT, NOTTINGHAM, UNITED KINGDOM*
[8]*DIALYSIS DIVISION FOR CHILDREN, DPT. OF PEDIATRICS, ZABRZE, POLAND*
[9]*DIALYSIS UNIT UNIVERSITY CHILDREN'S HOSPITAL, KRAKOW, POLAND*
[10]*FONDAZIONE OSPEDALE MAGGIORE POLICLINICO, MILANO, ITALY*
[11]*UNIVERSITY HOSPITAL MOTOL, PRAGUE, CZECH REPUBLIC*
[12]*SEMMELWEIS UNIVERSITY, BUDAPEST, HUNGARY*
[13]*UNIVERSITY HOSPITAL ANTWERP, EDEGEM, BELGIUM*
[14]*SERVICE DE NéPHROLOGIE PéDIATRIQUE, HôPITAL FEMME MERE ENFANT, LYON, FRANCE*
[15]*HOSPITAL DE CRUCES, BARACALDO, SPAIN*
[16]*UNIVERSITäTSKLINIKUM GIESSEN UND MARBURG, GERMANY*
[17]*CENTER FOR PEDIATRICS AND ADOLESCENT MEDICINE, HEIDELBERG, GERMANY*
[18]*CAYETANO HEREDIA HOSPITAL, LIMA, PERU*
[19]*CENTER FOR PEDIATRICS AND ADOLESCENT MEDICINE, HEIDELBERG, GERMANY*

Introduction: Peritonitis is still the most common cause of PD technique failure in children. Its prevention is key to the long-term preservation of peritonea membrane function. The IPPN is a global consortium of pediatric dialysis centers collecting detailed prospective information on practices and outcomes in children undergoing chronic PD.

Material and methods: Between 2007 and 2012 1076 peritonitis episodes in 575 children were reported to the IPPN registry. Incidence analysis was limited to 776 episodes that occurred between the initial and last patient update. A multivariate risk factor analysis utilizing all available longitudinal information was performed by using generalized linear modeling.

Results: The global peritonitis incidence decreased over time, from 0.49 episodes per year in 2007 to 0.35 episodes per year in 2011, and varied regionally being highest in North America (1:26.9 pt months) and lowest in Asia (1:58.7 pt months). 66 % of episodes were culture positive (thereof 2/3 gram positive, 1/3 gram negative). Fungal episodes accounted for less than 3 % of episodes, and 5 % of reported episodes were relapses. The underlying cause of non-fungal primary peritonitis episodes was unknown in 59 % cases; identifiable causes included exit site/tunnel infection (9 %), touch contamination (7 %), and catheter leakage (4 %). Patients who experienced at least one peritonitis tended to be younger ($p<0.01$) and were on dialysis longer ($p<0.001$). Independent risk factors for infection included low serum albumin ($p<0.0001$) and the need to

use nutritional supplements ($p<0.01$), the presence of ostomies ($p<0.05$) and the use of an older cycler generation ($p<0.001$). Use of ß-octenidine for exit site care was independently associated with a lower peritonitis risk ($p<0.0001$).
Conclusions: The risk of PD-associated peritonitis continues to decrease, albeit with major regional variability. Young children continue to be at greater risk of peritonitis. Malnutrition/inflammation, the presence of ostomies and the choice of PD technologies appear to impact on individual peritonitis risk.

OP72 - ENCAPSULATING PERITONEAL SCLEROSIS IN PEDIATRIC PERITONEAL DIALYSIS PATIENTS: THE EXPERIENCE OF THE ITALIAN REGISTRY OF PEDIATRIC CHRONIC DIALYSIS

ENRICO VIDAL, ALBERTO EDEFONTI, ROBERTO CHIMENZ, BRUNO GIANOGLIO, GIOVANNA LEOZAPPA, SILVIO MARINGHINI, FRANCESCA MENCARELLI, CARMINE PECORARO, FLORA PUTEO, SARA TESTA, ROSSELLA CANNAVò, ENRICO VERRINA
ITALIAN REGISTRY OF PEDIATRIC CHRONIC DIALYSIS

Introduction: Encapsulating peritoneal sclerosis (EPS) is a rare but serious complication of chronic peritoneal dialysis (CPD). Despite the growing attention that EPS has received during the last 10 years, its causes and pathogenesis are not yet fully understood, and such clinical issues as its epidemiology, diagnosis and treatment still need clarification. EPS incidence in adult CPD patients varied from 0.7 to 1.7 %, while few data are available among children on CPD. The aim of this study was to describe the incidence and characteristics of EPS in a large pediatric CPD patient population (Italian Registry of Pediatric Chronic Dialysis - IRPCD).
Material and methods: We retrospectively reviewed files of patients starting CPD at <16 yrs of age, recorded from Jan 1986 to Dec 2011 by the IRPCD.
Results: Over a 25-yr period, 712 patients aged 16 yrs or less at the start of chronic dialysis (median age 6.4 yrs, range 0.1-16) were treated with PD in 18 Dialysis Centres. The median duration of first CPD cycle was 17.7 months (range 1–198), and 42 patients (5.8 %) were treated for more than 5 yrs. A diagnosis of EPS was made in 13 patients (1.8 %), on the basis of recurrent bowel obstruction and peritoneal thickening with calcification at the abdominal CT. Diagnosis was confirmed by both the macroscopic findings and the histological picture. Median age was 6.8 yrs (0.7-15.2) at the start of CPD and 16.1 yrs (6.5-20.4) at EPS diagnosis. All EPS cases had received CPD for longer than 5 yrs. In 7 out of 13 patients the primary renal disease (PRD) was represented by primary glomerulopathy, namely FSGS (5) and congenital nephrotic syndrome (2); the incidence of EPS in the FSGS patients of our series was 10.2 %, while it was only 1.2 % among the patients with other forms of PRD. The 13 EPS patients had received at least one cycle of therapy with beta-adrenergic blocking agents, and had been treated with hypertonic dialysis solutions. Peritonitis incidence (1:26.8 CPD-months) was lower than from that of the whole patient group (1:21.9; $p<0.05$), whereas it was similar if infants were excluded from the analysis (1:28.3). All EPS patients were shifted to HD and were treated with corticosteroids. Five patients died after a median period on HD of 15.6 months (0.25-24.5), 3 were transplanted, and 5 were still on HD at the end of the study period.
Conclusions: EPS incidence in our patients was similar to that reported in the only available multicenter-based pediatric report (Hoshii S, et al. Perit Dial Int 2002), and was associated with a high risk of mortality, even after the transfer of patients to HD. Previous papers described overall 19 pediatric patients with EPS, 30 % of whom affected by FSGS (38 % in our series): therefore, it may be speculated if molecules involved in kidney fibrosis could play a role in the mechanisms by which mesothelial cells undergo epithelial-to-mesenchymal transition during and after the course of PD.

POSTER PRESENTATIONS

P1 - Two-year follow-up and management of Mild Isolated Antenatal Hydronephrosis

PAULA MATOS[1], TERESA COSTA[1], ARTUR ALEGRIA[1], CALDAS AFONSO[2], HELENA PINTO[2], FILIPA LIMA[2], CLARA GOMES[3], JOSé ESTEVES[4], MARGARIDA ABRANCHES[5]
[1]*CENTRO HOSPITALAR DO PORTO*
[2]*HOSPITAL S JOãO*
[3]*HOSPITAL PEDIáTRICO DE COIMBRA*
[4]*HOSPITAL STA MARIA*
[5]*HOSPITAL PEDIáTRICO D. ESTEFANIA*

Introduction: Objectives: Assessment of the outcome of infants with isolated hydronephrosis, detected prenatally, observed in 5 Pediatric Nephrology referral centres.
Material and methods: Retrospective study with review of clinical cases of children born between January 2005 and December 2006, with mild isolated hydronephrosis (MIAHN) (antero-posterior pelvic diameter of 5–14 mm) at the third trimester of gestation. Children with APPD≥ 10 mm, in the first postnatal US or during follow-up, underwent voiding cystourethrography (VCUG) and/or renogram with MAG 3. All had a follow-up time of 24 months.
Results: We examined a total of 726 cases, with predominance of males in a 2.3:1 ratio; 330 had bilateral pathology with a total of 1070 Renal Units (RU) affected; 562 fetuses

had MIAHN. From those 562 children with MIAHN, 36 % (192) had a first normal postnatal ultrasound; in 62 % (352) the degree of hydronephrosis has stabilized; only in 2 % (13) occurred an aggravation of hydronephrosis After 24 months of follow-up, in 91 % of the cases no associated significantly pathology was identified; hydronephrosis regressed completely, partially or persisted. In 6 % (33) was diagnosed VUR, with cortical lesions in 42 % (14); when comparing the severity of postnatal hydronephrosis with the degree of VUR, and with the presence of lesions in DMSA, no correlation was found with statistical significance (p=0,24). Fifteen children (3 %) required surgical intervention for pelvi-ureteric stenosis, obstructive megaureter, PUV or height grade reflux); the hydronephrosis progression to values>15 mm had strong correlation with the need for surgery (p<0,0001)

Conclusions: Almost all infants with prenatal diagnosis of MISHN have a good outcome, with stabilization of the degree of hydonephrosis. However, 15 children presented aggravation and need for surgery. These children with MISHN should be supervised by serial ultrasound and further examinations in case of aggravation of the degree of hydronephrosis or emergence of urinary infection.

P2 - CYSTIC VARIANT OF WILMS TUMOR PRESENTING WITH URETERAL EXTENSION

CENGIZ ZEYBEK, MUKERREM SAFALI, VURAL KESIK, SÜLEYMAN KALMAN, FAYSAL GÖK
GULHANE MILITARY MEDICAL ACADEMY ANKARA TURKEY

Introduction: Wilms' tumor, also known as nephroblastoma (NB), is a complex mixed embryonal neoplasm of the kidney composed of three elements : blastema, epithelia and stroma . The tumor is usually solid but rarely predominantly cystic . Although invasion of renal collecting system is common, extension down into the ureter is not.

Material and methods: A 17-month-old boy was referred to our hospital because of intermittent clotted mass in his urine and then gross hematuria that persists 2–3 days.

Results: Ultrasound and MRI showed left cystic renal mass measuring 9 x 7 x 10 cm which had thick irregular septas with solid components. But cystic nephroma (CN) and cystic partially differantiated nephroblastoma (CPDN) distinction could not be made with magnetic rezonans imaging studies. Renal trucut biopsy was performed but limited amount of mass tissue has been obtained, probabaly due to cystic component, so distinction between NB, CN and CPDN has not been made properly. Radical nephroureterectomy was performed. Macroscopic examination of specimen showed a rounded and sharply demarcated tumoral mass with 11 x 10 x 9 cm in size. It was mostly cystic and contain limited solid areas. Lumen was filled with tumoral tissue in the proximal part of the ureter. Microscopically, the solid areas of the tumor showed triphasic pattern, composed of blastemal,epithelial (tubular structures) and differantiated stromal elements. Ureteral opening filled with necrotic tumoral extension but ureteral invasion has not been demonstrated. Tumor was diagnosed as cystic Wilms' tumor histopathologically. Postoperative chemotherapy was started with vincristine and dactinomisin for stage 2 disease.

Conclusions: Ureteral extension of Wilms' tumor is rare. None of Wilms' tumor patients that reported ureteral extension, ureteral invasion has not been found like our patient . In addition, Wilms' tumor should be considered in the differential diagnosis of multilocular cystic lesions of the kidney especially in older children.

P3 - LONG-TERM RISKS OF CHILDREN WITH UNILATERAL RENAL AGENESIS AND MULTICYSTIC DYSPLASTIC KIDNEY

NATASA MARCUN VARDA
UNIVERSITY MEDICAL CENTRE MARIBOR, DEPARTMENT OF PAEDIATRICS, LJUBLJANSKA 5, 2000 MARIBOR, SLOVENIA

Introduction: Unilateral renal agenesis (URA) and multicystic dysplastic kidney (MDK) are quite common renal congenital anomalies. Children with both anomalies function as having only a single kidney. Follow-up of these children once a year has been proposed because of possible long-term risks. The aim of our study was to found out the proportion of associated renal anomalies and possible long-term problems e. g. proteinuria and hypertension of our children with URA and MDK.

Material and methods: 43 children, 30 with URA and 13 with MDK, have been included in our study. Medical documentation was reviewed and urinalysis, serum creatinine, microalbuminuria, blood pressure measurement and renal ultrasound performed.

Results: Mean age of the included children was 10.6± 7.5 years. There were 28 boys (65 %) and 15 girls (35 %). All children with MDK and only 40 % of children with URA were diagnosed in the neonatal period. In 10 children (23.3 %) associated renal anomalies were diagnosed. Only 2 children had problems with urinary tract infections. In 6 children (13.9 %) microalbuminuria was detected and in 9 of them (20.9 %) hypertension was diagnosed. In 2 children with important associated anomalies of the contralateral kidney reduced renal function was noticed. In 2 children with MDK nephrectomy has been performed because of complications. In 5 children (11.6 %) antihypertensive treatment was initiated.

Conclusions: Both URA and MDK are mostly uncomplicated renal anomalies. However, associated renal anomalies

and long-term risks are possible, necessitating regular follow-up and sometimes treatment of these children.

P4 - Urine cytokine profiles in unilateral congenital hydronephrosis.

KATARZYNA TARANTA-JANUSZ, ANNA WASILEWSKA, MARLENA WASZKIEWICZ-STOJDA, PIOTR PROTAS, RENATA FIŁONOWICZ
MEDICAL UNIVERSITY OF BIAŁYSTOK, DEPARTMENT OF PEDIATRICS AND NEPHROLOGY

Introduction: Congenital obstructive nephropathy is the leading cause of chronic renal disease in children. Rapid diagnosis and initiation of the treatment are vital to preserve function and/ or to slow down renal injury. We aimed to evaluate possible clinical application of urinary MCP-1, OPN, and RANTES as useful non - invasive markers in children with congenital hydronephrosis (HN) caused by ureteropelvic junction obstruction (UPJO).
Material and methods: The study cohort consisted of 15 children with severe HN who required surgery (median age 1.03 years) and two control groups (control group 1: 21 patients with mild, non-obstructive HN; control group 2: 19 healthy children). All of the children had normal renal function. Urinary (u) concentrations of MCP-1, OPN and RANTES were performed using immunoenzymatic ELISA commercial kits and was expressed in ng/ mg cr.
Results: Increased levels of MCP-1, OPN and RANTES were found in children with HN in comparison to control 1 and 2 ($p<0.01$). There was no correlation with serum creatinine level, age of patients and GFR. Receiver operator characteristic analyses revealed good diagnostic profile only for uMCP-1 in identifying children with abnormal DRF (<40 %) among study and control 1 groups (area under the curve (AUC) 0.862), and in detecting kidney injury in all examined children (AUC - 0.704).
Conclusions: Urinary MCP-1 seemed to be promising non - invasive parameter for the early detection of obstruction. Additional studies with larger number of patients are required to confirm a potential application of uMCP-1 as a promising parameter for early identification of kidney obstruction.

P5 - CELLULAR MECHANISMS OF THE KIDNEY PATHOLOGY FORMATION

VALENTINA LUCHANINOVA, TATIANA POGODAEVA, VALENTINA KAREDINA
VLADIVOSTOK STATE MEDICAL UNIVERSITY, RUSSIA

Introduction: Basophils and mast cells are the various models of cell differentiation, in spite on some common phenotypic features.

Material and methods: As an object for the study of mast cell (MC) divisions were used samples of renal capsule, parenchyma, tissue in the area of the gate, obtained from 6 fetuses and 10 dead infants. Basophils (B) were studied in 18 neonatal blood samples. The main group consisted of fetuses and newborns from mothers with kidney disease (16 samples), control group - from healthy women (18 samples). B. were determined after staining the suspension of mononuclear blood cells to specific antigens CD34 and CD117. To identify MC, the method of coloring Leffler used.
Results: The average content of CD 117, 34 positive basophils in blood was revealed: the main group 73,52±2,49 % and the control - 3,14±0,78 %. $p<0,001$. Mast cells in the samples of the control group fetuses were found small groups with large granules in the cells. Evaluation of MC populations of the main group fetuses identified high of its activity. The most numerous of mast cells was encountered in samples of the gate (from 2,33±0,58 to 13,67±1,15 a stillborn fetuses and infants who have lived less than a day, and from 6,0±1,0 to 23,67±4,04 in infants who have lived more than a day). Defined statistical significance of differences in the performance of the MC in the gate and renal parenchyma samples, regardless of life expectancy ($P<0,001$).
Conclusions: Obviously, the pathology of the mother effects on the activity both: tissues mast cells and blood basophils. Granulocytes of blood and labrocytes of tissue - a unified system of regulation that determines the development of kidney pathology.

P6 - RENAL SURVIVAL IN CHILDREN WITH A SOLITARY FUNCTIONING KIDNEY – THE KIMONO-STUDY

WESTLAND RIK[1], KURVERS ROEL AJ[2], VAN WIJK JOANNA AE[1], SCHREUDER MICHIEL F[2]
[1]*DEPARTMENT OF PEDIATRIC NEPHROLOGY, VU UNIVERSITY MEDICAL CENTER, AMSTERDAM, THE NETHERLANDS.*
[2]*DEPARTMENT OF PEDIATRIC NEPHROLOGY, RADBOUD UNIVERSITY NIJMEGEN MEDICAL CENTRE, NIJMEGEN, THE NETHERLANDS*

Introduction: Background. The hyperfiltration hypothesis implicates that children with a solitary functioning kidney (SFK) are at risk to develop hypertension, (micro)albuminuria and, eventually, chronic kidney disease. THE KIMONO-STUDY (=KIdney of MONOfunctional Origin) aims to determine the presenting age of renal injury in children with an SFK.
Material and methods: 407 patients were evaluated on symptoms of renal injury during follow-up. We defined renal injury as hypertension and/or (micro)albuminuria and/or an impaired glomerular filtration rate and/or the use

of renoprotective medication. Patients were subdivided in congenital or acquired SFK groups to study the differences between SFK-types. Ipsilateral renal anomalies (CAKUT) were noted as a discriminative risk factor for renal damage. Renal survival was analyzed using Kaplan-Meier-analysis.
Results: Renal injury was found in 37 % of all children, with a higher incidence in acquired SFK patients (P=0.002). The risk of renal injury increased by age (odds ratio [OR] 1.07; P<0.001) and by the presence of CAKUT (OR 1.91; P<0.01). Children in the highest quartile of renal length were less likely to develop renal injury (OR 0.90; P<0.05). Survival analyses showed an overall median survival time of 14.8 (95 % confidence interval 13.7 - 16.0) years. Renal survival was independent from SFK-type but deteriorated when ipsilateral CAKUT was present.
Conclusions: THE KIMONO-STUDY demonstrates that a large proportion of children with an SFK develop symptoms of renal injury over childhood. This shows the applicability of the hyperfiltration hypothesis in humans and emphasizes the need for clinical follow-up in all children with an SFK starting at birth.

P7 - The assessment of thiol status in children with neurogenic bladder due to myelomeningocele.
AGATA KORZENIECKA-KOZERSKA, EDYTA TENDERENDA, ANNA WASILEWSKA
DEPARTMENT OF PAEDIATRICS AND NEPHROLOGY

Introduction: Oxidative stress can cause tissue damage in many diseases both children and adults. Oxidative status depends on the balance between total oxygen radical absorbance capacity and anticoxidants as a compensatory reaction of the body. It is considered that oxidative status can play an important role in pathogenesis in dysfunction of urinary in neurogenic bladder. The aim of this study was to measure antioxidant (thiol status) in patients with neurogenic bladder and to correlate it to parameters of bladder function.
Material and methods: The investigation was conducted on two groups of children. The first group constituted of 41 children with neurogenic bladder due to myelomeningocele (MMC). The second group consisted of 20 healthy children with no abnormalities in urinary and nervous systems. The antioxidant status were assessed based on the enzyme immunoassay of thiol (ELISA) and compared to the urodynamic outcomes and to the healthy control.
Results: The median value of urinary protein thiol level was significantly lower in NB patients than in healthy control. We found the statistically significant differences in urinary protein thiol level between patients with and without overactivity and between catheterized and non catheterized patients.
Conclusions: This study demonstrates that antioxidant status in patients with neurogenic bladder decreased and the level of thiol status was dependent on the grade of bladder hyperactivity Oxidative stress may be involved in the pathogenesis of bladder dysfunction related to neurogenic damage.

P8 - Dysplastic fetal kidneys have disturbed cell proliferation, apoptosis and primary cilia formation
KATARINA VUKOJEVIC[1], MERICA GLAVINA DURDOV[2], MARIJAN SARAGA[3], MIRNA SARAGA-BABIC[1]
[1]*DEPARTMENT OF ANATOMY, HISTOLOGY AND EMBRYOLOGY, SCHOOL OF MEDICINE, UNIVERSITY OF SPLIT, SPLIT, CROATIA*
[2]*DEPARTMENT OF PATHOLOGY, UNIVERSITY HOSPITAL IN SPLIT, SPLIT, CROATIA*
[3]*DEPARTMENT OF PAEDIATRICS, UNIVERSITY HOSPITAL IN SPLIT, SPLIT, CROATIA*

Introduction: Development of human kidneys requires a fine balance between processes of cell proliferation and apoptosis, which are partly controlled by signaling of the primary cilia. Dysplastic kidneys are developmental disorders associated with poorly differentiated nephrons, perturbed cell turnover and maturation, and are responsible for chronic renal failure.
Material and methods: Mid-gestational normal and dysplastic human kidneys were histologically analyzed using fluorescent immunohistochemical staining to Ki-67 proliferation marker, TUNEL and caspase-3 apoptotic marker, and α-tubulin for detection of primary cilia. Proliferating cells were counted in normal and dysplastic kidneys, and their proliferation index was compared and analyzed by the Kruskal-Wallis and Dunn's pos thoc test. Probability values of P<0.05 were regarded as significant.
Results: In normal fetal kidneys, nephron cells contained 11.31 % of proliferating cells, while interstitium contained only 2.2 %. In dysplastic kidneys, proliferating cells contributed to 19.36 % of poorly developed nephrons and to 6.9 % of cells in interstitium. Dysplastic kidneys had a significantly higher proliferation index than normal fetal tissue. Different forms of dysplastic nephrons showed unequal proliferation activity, with occasional "knots" of hyperproliferation. Apoptotic cells were found both in the nephrons and interstitium of dysplastic kidneys, and were more abundant than in normal fetal kidneys. Depending on the degree of differentiation, in dysplastic nephrons primary cilia were completely missing or were irregular. In areas of nephrons without proliferation activity, the primary cilia were more numerous, long and branching in comparison to those in normal mid-gestational kidneys.
Conclusions: Dysplastic fetal kidneys displayed increase in proliferation and apoptotic activity in comparison to normal fetal kidneys. Depending on the degree of disturbed

nephrogenesis, primary cilia formation was altered as well. We propose that in addition to disturbed proliferation and apoptosis, secondary changes in primary cilia also contribute to false cells signaling in dysplastic kidneys.

P9 - RETROSPECTIVE ANALYSIS DATA OF RENAL CORTICAL SCINTIGRAPHY IN ALBANIAN CHILDREN WITH VESICO-URETERAL REFLUX

DIAMANT SHTIZA[1], ENKELEJDA SHKURTI[2], SOKOL BUBA[3], MAKSIM BASHO[4], IRENA PALLOSHI[5]
[1]*DEPARTMENT OF PEDIATRICS, SERVICE OF NEPHROLOGY, UHC "MOTHER TEREZA" TIRANA, ALBANIA*
[2]*LECTURER OF STATISTICS, FACULTY OF NURSING, TIRANA, ALBANIA*
[3]*DEPARTMENT OF PEDIATRICS, SERVICE OF SURGERY, UHC "MOTHER TEREZA" TIRANA, ALBANIA*
[4]*DEPARTMENT OF PEDIATRICS, SERVICE OF IMAGING, UHC "MOTHER TEREZA" TIRANA, ALBANIA*
[5]*DEPARTMENT OF PEDIATRICS, CLINIC HOSPITAL OF ELBASAN, ALBANIA*

Introduction: Renal cortical scintigraphy with 99mTc-DMSA actually is the most important examination in the evidence of parenchyma damage due to pyelonephritis. The aim was evaluation of correlation between vesicoureteral reflux degrees diagnosed through voiding cystourethrogram and alteration in renal cortical scintigraphy.
Material and methods: During 3 years period, were diagnosed through voiding cystourethrogram 153 children with VUR. Age from 1 – 36 months, ratio F:M=1,55:1. Was considered normal, uniform capture of 99mTc-DMSA; was considered as a scar the zone with low capture of 99mTc-DMSA, this zone was unique or multiple.
Results: Were found 33 right VUR, 31 left VUR and 89 bilateral VUR, total of 242 reflux unit. We founded that 49 children were in the age group 0–1 year, 104 from 1–3 years. According to the VUR degree were found 45 reflux units of first degree; 104 of second degree; 54 of third degree; 30 of fourth degree; and 9 of fifth degree. 50 % were habitant of Tirana, 50 % were habitant of the other region of Albania. In 62,5 % of cases were found scar, in 47,2 % of them were found scar multiple, only 15,2 % had one scar, and 37,5 % were without scar. First degree of VUR: 7 % without scar, second and third degree 33 % with scar and 20 without scar, fourth degree 15 with scar and 2 without scar, fifth degree 7 scintigraphy all with scar multiple.
Conclusions: We didn't found any scar only in the first degree of VUR, but the fifth degree show always multiple scars. In the 3 to 5 degree were found focal and multiple scars in more than 50 % of cases. We recommend that renal cortical scintigraphy with DMSA is very important to be accomplished in all children who suffered with VUR from 3 to 5 degree and in all the children that have a acute pyelonephritis in the first year of life.

P10 - ANTIBIOTIC PROPHYLAXIS IN HIGH DEGREE VESICOURETERAL REFLUX. PROSPECTIVE, RANDOMIZED AND MULTICENTRIC STUDY. PRELIMINARY RESULTS

MAR ESPINO[1], RAMON ARESES[2], CARMEN GARCIA MESEGUER[3], ANTONIA PEÑA[3], MARTA MELGOSA[3], MARTA RUPEREZ[1], MERCEDES MITJAVILLA[4], JOSE CARMELO ALBILLOS[1]
[1]*HOSPITAL FUNDACION ALCORCON. NEFROLOGIA PEDIATRICA. MADRID*
[2]*HOSPITAL DONOSTIA. NEFROLOGIA PEDIATRICA. SAN SEBASTIAN*
[3]*HOSPITAL INFANTIL LA PAZ. NEFROLOGIA PEDIATRICA. MADRID*
[4]*HOSPITAL FUNDACION ALCORCON. MEDICINA NUCLEAR*
[5]*HOSPITAL INFANTA SOFIA. SERVICIO RADIODIAGNOSTICO. MADRID.*

Introduction: Prophylactic treatment (PT) has been demonstrated no useful to avoid recurrent pyelonephritis and new renal scars in vesicoureteral reflux (VUR) of low degree. There are several studies in VUR of high degree with inconclusive results in awaiting the end of multicenter clinical trials. We try to demonstrate that in VUR of high degree (grade III to V according International Vesicoureteral Reflux Classification) the incidence of new renal scars and PN with PT is not lower than with follow-up and early treatment of each urinary tract infection episode.
Material and methods: Design: prospective, randomized and multicentric study. Patients: those with primary vesicoureteral reflux (VUR) grade III to V recruited in Hospitals with Pediatric renal Units. They were randomized to treatment with PT or not. Image studies (voiding cystourethrography, renal scan, ultrasonography) will be collected and examined by a second blind specialist. Patients with the second episode of PN were removed of the study. We analyzed new renal scar, PN, lower urinary tract infection, asymptomatic bacteriuria, germen, antibiotics sensibility, renal function parameters and vesicoureteral reflux evolution. Also we described the problems of the recruitment and the follow-up of the study. Economical support: Institute Carlos III. Spanish Health Ministry-EC07/90847. Nº EUDRACT:2007-006253-60
Results: We included 28 patients (7 were lost or removed in following), 13 with VUR grade III (4 prenatal diagnosis and 9 after pyelonephritis) and 8 with VUR grade IV or V. 9 patients received PT and 12 were randomized no treatment.

During the follow-up 10 patients had PN (7 without PT and 3 with PT) and 11 patients had not PN (5 without PT and 6 with PT). We did not find statistical difference with X2 test. No new scar was found in the follow-up, however length of scar increased and also differential renal function in renal scan decreased en 3 patients. After one new episode of pyelonephritis, at least 3 patients request to give up the study. Patients removed from the study because of 2 episode of pyelonephritis presented more episodes.

Conclusions: In our study, there is no evidence of effectiveness of prophylactic treatment to avoid pyelonephritis and no new renal scar was detected. Some patients are more likely to have recurrent pyelonephritis regardless of treatment choice.

P11 - HEPATOCYTE NUCLEAR FACTOR-1β (HNF-1β) MUTATIONS PREVALENCE IN RENAL PATHOLOGY

ZARAUZA SANTOVEÑA ALEJANDRO[1], MARTA MELGOSA HIJOSA[1], OLGA ZURITA MUÑOZ[2], CARMEN GARCIA MESEGUER[1], ANTONIA PEÑA CARRION[1], LAURA ESPINOSA ROMAN[1], MERCEDES NAVARRO TORRES[1], ANGEL CAMPOS BARROS[2]

[1]*PEDIATRIC NEPHROLOGY SERVICE. HOSPITAL LA PAZ. MADRID.*

[2]*INSTITUTO DE GENéTICA MéDICA Y MOLECULAR (INGEMM), IDIPAZ, UAM, HOSPITAL LA PAZ, Y CIBER DE ENFERMEDADES RARAS (U753), ISCIII, MADRID.*

Introduction: HNF-1β mutations, initially linked to renal cysts and diabetes syndrome (MIM 137920), have also been associated with kidney malformations. The purpose of this study is two fold: estimate mutation prevalence in children with developmental renal pathology and describe their phenotype.

Material and methods: During one year all children diagnosed with unilateral multicystic renal dysplasia (MRD), unilateral renal agenesis (RA), glomerulocystic kidney disease (GKD),horseshoe kidney (HK), renal hypoplasia (RH), non-specific bilateral cystic renal disease (CD) or non-specific renal hyperechogenity (RHE) were studied. HNF-1β mutations were detected with HRM and MLPA.; demographic, clinical and analytical data were also recorded.

Results: In all, 58 children (28 φ/ 30 δ) were diagnosed with MRD (16 patients (pts)); RA (8 pts); GKD(1 pt); HK (1 pt); RH (6 pts); CRD(17pts) and RHE (9 pts) . Mutations (M+) were detected in 6 children (10.3 %): 5 complete hemizygote deletions and 1 previously described heterozygous sense inversion mutation in p.S148L. The M+primary diseases were 3 CD, 1 MRD,1 RHE and 1 triad syndrome RH. No statistically significant differences were found for diabetes, tumor or kidney malformations familial history or of hypertension prevalence or hepatopathy. No patient developed diabetes. Magnesium supplementation was needed in 2/6 M+(33,3 %) versus 5/52 M - (9,6 %) patients. Urinary magnesium excretion was significantly higher in M+than in M – patients (4.16 vs 8.35 %); no hypouricemia was found. 3/6 M+patients had chronic renal disease (CRD) vs 25 % of M - ; the p.S148L mutation boy showed the most severe phenotype with advanced hepatopathy and CRD stage 4.

Conclusions: HNF-1β gen mutations were found in 10,3 % of our population, a lower incidence than previously reported. M+pts showed higher urinary magnesium excretion than M- pts but no hypouricemia was observed. Clinical presentation was varied. The prognostic implication of these mutations is still unknown.

P12 - PHENOTYPE AND OUTCOME IN HNF-1β GENE MUTATION

MARINA MUñOZ, ANDRES RICO, JOSE MARIA VALLE, ALVARO MADRID, SARA CHOCRON, ENRIQUE LARA, RAMON VILALTA, JL NIETO

HOSPITAL UNIVERSITARI VALL D'HEBRON

Introduction: Hepatocitary nuclear factor-1β (HFN-1β) encoded by TCF2 gene, regulates specific gene expression in various tissues such as kidney, liver and pancreas islets and is involved in the embryonic development of these organs. Mutations of HFN-1β cause maturity-onset diabetes of the young type 5 (MODY5) and kidney anomalies including agenesis, hypoplasia, dysplasia and cysts. Asymptimatic transaminitis, neonatal cholestasis, hyperuricemia and hypomagnesemia are part of the extrarenal manifestations.

Material and methods: We performed a retrospective review of all our patients affected by HFN-1β mutation. Form of presentation and phenotype features were analyzed.

Results: Mutation of HFN-1β was found in five patients with large predominance in males (80 %). Renal manifestation was variable, from prenatal diagnosis of multicystic kidney dysplasia (40 %) to finding of renal dysfunction or ultrasound abnormalities in diabetic patients (60 %). Renal dysplasia with or without cyst was found in all cases. Renal function was normal in three cases, and the others developed renal failure, one of them is in end stage. Both affectation of kidney and pancreas was found in 80 % of cases. MODY5 appeared in 80 % of patients and was diagnosed during teenage. Liver involvement was 40 % and was presented as an asymptomatic transaminitis. Mild hypomagnesemia appeared in two patients.

Conclusions: Mutations of HFN-1β are a diagnose factor but the genotype-phenotype correlation is very difficult to be detected. However, as a result of this review, it has been possible to classify these patients into two groups, who

have an important deterioration of the renal function with an early diagnose, and those who have a normal renal function and often were diagnosed of early onset diabetes during adolescence. Renal and pancreas involvement appears in most of the cases. Mutations of HFN-1β, even uncommon, constitute an entity which should be considered in cases of congenital cystic abnormalities of the kidney.

P13 - Frequency of renal anomalies in asymptomatic relatives of the patients with CAKUT

BURCU BULUM ÖZTÜRK[1], ASLI KAVAZ[1], BIRSIN ÖZÇAKAR[1], EVREN ÜSTÜNER[2], EBRU DÜŞÜNCELI[2], DUYGU DUMAN[3], MESIHA EKIM[1], SUAT FITÖZ[2], MUSTAFA TEKIN[3], FATOŞ YALÇINKAYA[1]
[1]*ANKARA UNIVERSITY SCHOOL OF MEDICINE, PEDIATRIC NEPHROLOGY, ANKARA, TURKEY*
[2]*ANKARA UNIVERSITY SCHOOL OF MEDICINE, PEDIATRIC RADIOLOGY, ANKARA, TURKEY*
[3]*ANKARA UNIVERSITY SCHOOL OF MEDICINE, PEDIATRIC GENETICS, ANKARA, TURKEY*

Introduction: Congenital anomalies of the kidney and urinary tract (CAKUT) occur in 1 in 500 births and are a major cause of morbidity in children. Most cases of CAKUT are sporadic and limited to the urinary tract but some of them are syndromic or associated with positive family history. Aim of this study is to determine the frequency of renal anomalies in asymptomatic relatives of the patients with CAKUT.
Material and methods: A total of 149 patients with CAKUT (78 girls, 71 boys) who have been followed-up in our center were enrolled the study. Thorough history of consanguineuos marriage, family history of any renal diseases and dialysis therapy were inquired and renal ultrasonography could be performed to 270 first-degree relatives of 100 patients with CAKUT.
Results: The mean ages of the patients at diagnosis and at the time of the study were 3.4±3.1 and 6.9±4.6 years, respectively. Thirty-four (%23) patients were diagnosed antenatally. Vesicoureteral reflux was the most frequent abnormality (n=52), followed by renal hypoplasia/dysplasia (n=28), ureteropelvic junction obstruction (n=19), posterior urathral valve (n=11) and multicystic dysplastic kidney, horseshoe kidneys, ectopic kidney (each=7) and the other abnormalities (n=18). There was consanguinity between parents in 25 % of the patients. 104 individuals in 70 (47 %) families had known kidney or urinary tract diseases and 41 patients were on dialysis therapy or had renal transplantation. A total of 66 renal abnormalities were established in 60 of 270 first-degree relatives who were unaware of the abnormalities before. The same abnormality in more than one patient was detected in 15 families, 5 of which had consanguinity.
Conclusions: This study indicates once more that familial clustering is common and genetic mechanisms are very important in the pathogenesis of sporadic CAKUT. Consanguinity marriage can also play a role in familial clustering. Identification of the new disease causing genes will provide further insights into the knowledge of the kidney and urinary tract development.

P14 - Endoscopic treatment of vesicoureteral reflux with Deflux- a single Croatian center experience

DANICA BATINIC[1], DANKO MILOSEVIC[1], MARIJA TOPALOVIC-GRKOVIC[2], LJILJANA NIZIC[1], KRISTINA VRLJICAK[1], MIRJANA POROPAT[3], MAJA LEMAC[1]
[1]*UNIVERSITY HOSPITAL CENTER ZAGREB, DEPARTMENT OF PEDIATRIC NEPHROLOGY*
[2]*UNIVERSITY HOSPTAL CENTER ZAGREB, DEPARTMENT OF ANESTESIOLOGY AND INTESIVE CARE*
[3]*UNIVERSITY HOSPITAL CENTER ZAGREB, DEPARTMENT OF NUCLEAR MEDICINE*

Introduction: Vesicoureteral reflux (VUR) is a common condition that may lead to renal damage and end-staged renal failure. Traditionally, treatment options are long term prophylactic antibiotics or ureterocystoneostomy. Recently, promising results of endoscopic treatment by a subureteral injection of dextranomer/hyaluronic acid copolymer (Deflux) were demonstrated.
Material and methods: Medical records of 41 patients (7 boys and 34 girls) who received Deflux injections for treatment of VUR from 2004 to 2011 were reviewed for oucome. All the patients were followed up with voiding cystourethrography at 6 months after the procedure.
Results: The mean age at the tretment was 6 years and 6 months (range, 3 years and 6 months to 9 years and 8 months). A total of 32 patients (78.1 %) had unilateral VUR and 9 patients (21.9 %) had bilateral VUR, comprising 50 treated renal units. Overall cure rate was 78.0 % (39/50). Among the 50 renal units treated, 60.0 % (30/50) were cured with a single injection, and a second and third injection raised the cure rate to 76.0 % (38/50) and 78.0 % (39/50), respectively. Resolution of VUR, defined as grade, was seen in 1/1 (100.0 %), 17/20 (85.0 %), 20/27 (74.0 %) and 1/2 (50.0 %) ureters from grade I do IV respectively. No procedure-related complications were seen.
Conclusions: Endoscopic treatment with Deflux is an effective and safe treatment for VUR. In our study, it demonstrated a cure rate of 78.0 % of renal units. With this promising success rate, we could recommend the use of endoscopic Delux injection as the first line treatment for

children with VUR. Further experience and increased use of Deflux may improve our cure rate.

P15 - COPY NUMBER VARIATION ANALYSIS IN MACEDONIAN CHILDREN WITH RENAL HYPODYSPLASIA AND AGENESIS

NADICA RISTOSKA-BOJKOVSKA[1], VLADIMIR J LOZANOVSKI[1], ZORAN GUCEV[1], ALI GHARAVI[2], SIMONE SANNA-CHERCHI[2], VELIBOR TASIC[1]
[1]*UNIVERSITY CHILDREN'S HOSPITAL, MEDICAL SCHOOL, SKOPJE, MACEDONIA*
[2]*DIVISION OF NEPHROLOGY, COLUMBIA UNIVERSITY, NEW YORK, USA*

Introduction: There is evidence that chromosomal imbalances such as microdeletions and duplications may be associated with congenital anomalies of the kidneys and urinary tract. Here we present clinical-genetic correlations from 86 Macedonian patients (subset from a large multi-center study) with renal hypodysplasia/agenesis (RHD) subjected to high-resolution copy number variations (CNVs) analysis.
Material and methods: Genome-wide search for CNVs was conducted with the Illumina 610-Quad arrays in 86 Macedonian children with syndromic or isolated RHD.
Results: Eight submicroscopic structural variants diagnostic for known human syndromes were found in eight children (9.3 %). These syndromes were not recognized clinically or by standard karyotyping. While only the 1p22.2-31.1 deletion was found in two independent patients, the other seven were unique, and included the 1q43-44 deletion, the 3pter-p25 deletion, the 7q36 deletion, the 16p11.2 distal deletion, the 17q deletion responsible for the renal cysts and diabetes syndrome, the 20p partial trisomy, and the chromosome X duplication at the region for the mental retardation with panhypopituitarism syndrome. One child had two known syndromes, indicating high mutational burden for this patient. Among the extra-renal manifestations, facial dysmorphy, epilepsy, and developmental delay were present in three children, Hirschprung's disease and ventricular septal defect in one each. Milder phenotypes such as inguinal hernia and cryptorchism were found in two and one patient, respectively. The average age at clinical diagnosis was 2.8 years; the age at molecular diagnosis was 6.2 years.
Conclusions: Molecular diagnosis of RHD, impossible by clinical grounds, can be achieved by CNV analysis in ~10 % of the patients. Because a significant fraction of patients develop extra-renal manifestations that are often clinically apparent later in life, while renal malformations can be diagnosed in-utero, pre-natal CNV analysis can significantly improve genetic counseling and risk stratification for serious developmental abnormalities such as mental retardation at a stage when interventions can be done.

P16 - The incidence of kidney anomalies among Bulgarian Children

ANELIA BOUEVA, SVETLANA MARINOVA, POLINA MITEVA, DIMITER ROUSSINOV, GALIA ZLATANOVA, MARIA GAYDAROVA, TATIANA TSANOVA, TONKA LISICHKOVA, STANISLAV STEFANOV, SNEGANA GANEVA
MEDICAL UNIVERSITY, SOFIA, BULGARIA

Introduction: Objectives: In a Bulgarian screening study performed between 2010 and 2012, 4011 healthy children were included. The aim was to estimate the prevalence of kidney anomalies.
Material and methods: Methods: The children included in the screening study were aged 1 to 17 years, almost equally distributed in gender. Urine samples were taken, blood pressure and BMI were measured and US of the kidney was performed.
Results: Results: We found that the prevalence of previously unrecognized kidney anomalies was 2.8 %. The children population of Bulgaria was 1 200 000 at that time. It means that 33 600 children are presumed to have "hidden" anomalies.
Conclusions: Conclusion: We suggest a screening US study to be done routinely among healthy children in the first years of their life.

P17 - RENAL DYSPLASIA IN BARDET-BIEDL SYNDROME

VELIBOR TASIC[1], LIDVANA SPAHIU[2], NADICA RISTOSKA-BOJKOVSKA[1], ALEKSANDRA JANCEVSKA[1], VLADIMIR J LOZANOVSKI[1], ZORAN GUCEV[1]
[1]*UNIVERSITY CHILDREN'S HOSPITAL, SKOPJE, MACEDONIA*
[2]*PEDIATRIC CLINIC, UNIVERSITY CLINICAL CENTER, PRISHTINE, KOSOVO*

Introduction: Bardet-Biedl syndrome (BBS) is a multisystem genetic disorder characterized with central obesity, pigmentary retinopathy, polydactyly, mental retardation, and hypogenitalism. Renal abnormalities have been recognized as a cardinal feature of the disease with serious prognostic implication. The aim of this study was to analyze the renal status in children with BBS and to implement appropriate interventions in those with progressive course.
Material and methods: The diagnosis of BBS was established on the basis of criteria proposed by Beales et al. (J Med Genet 1999). Imaging of the kidneys and urinary tract was performed with ultrasound study, Tc99mDMSA scan and cystographic study. Twenty four hour urine collections were obtained for estimation of proteinuria and creatinine

clearance. Blood pressure was monitored at clinical visits or as 24-hour ambulatory monitoring.
Results: There were 4 children (3 males, 1 female) aged 5, 6, 13 and 14 years. Three children displayed abnormal kidney ultrasound and Tc99mDMSA scan resembling dysplastic kidney(s). Two of them had overt proteinuria (glomerulo-tubular pattern). Three children had normal blood pressure and glomerular filtration rate (GFR): 107, 145 and 95 ml/min/1.73 m2, and the fourth had hypertension and progressive worsening of the GFR at 65 ml/min/1.73 m2.
Conclusions: Children with BBS should undergo imaging studies of the kidneys and urinary tract at initial work up; in those with renal dysplasia proteinuria, GFR and blood pressure should be regularly monitored to slow down progression to terminal renal failure.

P18 - The Evaluation of Various Sonographic Parameters for Prediction of Vesicoureteral Reflux

SEVINC EMRE, ALEV KADIOGLU, ALEV YILMAZ, ZEYNEP YURUK YILDIRIM, ILMAY BILGE, AYSEGUL SUCU, AYDAN SIRIN
ISTANBUL UNIVERSITY ISTANBUL MEDICAL FACULTY PEDIATRIC NEPHROLOGY DEPARTMENT

Introduction: Vesicoureteral reflux (VUR) is one of the major urologic problems in children which may lead to recurrent urinary tract infection (UTI) and reflux nephropathy. Various sonographic parameters have been reported to indicate VUR in children. The aim of the study was to evaluate these parameters for prediction of vesicoureteral reflux in children.
Material and methods: Fifty seven patients had been investigated by voiding cystourethrography because of recurrent urinary tract infection (33 female, 24 male; mean age: 5.7± 3.8 years) were enrolled in the study. Sixty nine renal units with VUR were compared with 43 renal units without VUR regarding kidney size, renal volume, parenchymal width, parenchymal echogenity, corticomedullary differentiation, deformity of the kidney outline, renal pelvic dilation according to hydronephrosis grading system of Society for Fetal Urology and antero-posterior pelvic diameter, renal calyceal dilation, distal ureteral diameter, fluctuating renal pelvis, ureteric jet Doppler waveform, reverse flow to ureter detected by colour-flow Doppler.
Results: Among parameters evaluated, antero-posterior pelvic diameter and distal ureteral diameter were significantly higher in the renal units with VUR ($p=0.022$ and 0.001, respectively). There was no significant difference between the two groups regarding the other parameters ($p>0.05$).
Conclusions: Our findings confirmed that none of the US findings is spesific for VUR. Ureteric jet Doppler waveform, reverse flow to ureter detected by colour-flow Doppler suggested to be associated with VUR by some authors was not found to be related to VUR in our study. However, the children with renal pelvic or distal ureteric dilation were more likely to have VUR.

P19 - Identification of new genes involved in renal hypodysplasia

JEANPIERRE CéCILE[1], PARISOT MELANIE[2], NITSCHKE PATRICK[2], HEIDET LAURENCE[2], SAUNIER SOPHIE[1], MARTINOVIC JELENA[3], BLANCHET PATRICIA[4], ANTIGNAC CORINNE[1], SALOMON RéMI[1]
[1]*INSERM U983, FACULTé PARIS DESCARTES*
[2]*HOPITAL NECKER, APHP, FONDATION IMAGINE*
[3]*UNITé DE FOETOPATHOLOGIE, LABORATOIRE CERBA, ST OUEN L'AUMôNE ET UNITé DE FOETOPATHOLOGIE, APHP, HôPITAL ANTOINE BéCLèRE; CLAMART*
[4]*SERVICE DE GéNéTIQUE ET DE FOETOPATHOLOGIE, HôPITAL ARNAUD DE VILLENEUVE, MONTPELLIER*

Introduction: Renal hypodysplasia (RHD) is an heterogeneous condition encompassing a spectrum of kidney development defects that are responsible for pediatric end-stage renal failure and mortality. Dominant mutations in PAX2, EYA1, SIX1 and HNF1B, four transcription factor genes with a crucial role during kidney development, have been identified in syndromic forms of RHD. However, there is clear evidence that other genes involved in isolated and syndromic RHD remain to be identified. Moreover, examination of families highly suggests that not only dominant but also recessive causes of non-syndromic RHD exist.
Material and methods: Exome sequencing of 5 fetuses belonging to independent consanguinous families was performed using the 50 Mb Agilent SureSelect assay and a SOLiD4 sequencer.
Results: This allowed us to identify mutations in 3 genes never reported as mutated in RHD patients: a one-base pair deletion in FGF20 and a splicing mutation in ITGA8 in fetuses with bilateral renal agenesis and a missense variation, predicted as damaging by Polyphen2, in ITGA3 in a fetus with multicystic dysplasia. Segregation of the mutations with the kidney development defect in the families, expression profile of the genes in fetal kidney and renal phenotype of mice models support the role of these genes in RHD.
Conclusions: Fonctional studies are in progress to formally demonstrate the effect of the mutations in nephrogenesis.

P20 - DOES THE DEGREE OF ANTENATAL HYDRONEPHROSIS CAN BE A PROGNOSTIC MARKER ?

SEÇİL CONKAR, VÜSET MAMMADOV, NİDA DİNÇEL, SEVGİ MİR
EGE UNIVERSITY PEDIATRIC NEPHROLOGY

Introduction: Antenatal hydronephrosis (ANH) is the most common urological pathology during fetal life and detected in 1–3 % of all pregnancies. Hydronephrosis does not always mean obstruction.The aim of follow up of newborns with AHN is to diagnose serious urinary tract anomalies earlier and limit the detailed exams.In this study, we aimed to explain if there is a relation between the degree of AHN and prognosis.
Material and methods: In the study,Urinary ultrasound (US) results of 42 patients on the postnatal 1-3rd and 7-10th days, 1st month, 1st and 2nd years were noted rectospectively,besides the antenatally results.
Results: There were 35 unilateral and 7 bilateral hydronephrotic kidneys.21(42 %) were regressed by postnatal 13 months. Regressed kidneys were in grade 1(66 %) and 2 (34 %) while there weren't any regression in grade 3 and 4 HN.At the end of 2 years, there were 25 hydronephrotic kidneys (21UPS, 1UVS, 3 VUR,3were extrarenal pelvis).17/21 UPS were non-obstructive.4 had were gone to surgery,with varying degrees(1–4),on the 1st,6th,11th months and 2.5 years.From these 4, one operated on 6th months, without renal damage.The other 3(6 %) high graded hydronephrosis and paranchymal thinness on the 1st, 3rd days of ultrasonographic evaluation, are still in follow as grade 1 CRD. One UVS patient,hadn't operated or parachymal damage.All VUR's were unilateral (grade 2,3 and 5), resolved in 24 months.Patients with grade 5 and 3 reflux were AHN with the degree of 1 and 3,respectively.
Conclusions: Fourthy two percentage of patients with AHN, completely resolves at the age of 2 years.Surgical incidence is found as 8.6 %, in the high grades. It should be in mind that, paranchymal loss in postnatal period and high grade AHN have to be followed more crossly.

P21 - Congenital and aquired solitary kidney in children

GABRIEL KOLVEK, LUDMILA PODRACKA
SAFARIK UNIVERSITY

Introduction: Long-term prognosis of children with a solitary kidney (SK) is controversial. Findings in adult kidney donors are not entirely reassuring for children whose life expectancy is likely to exceed periods of follow-up of donors. The aim of this study was to evaluate microalbuminuria, blood pressure and estimated glomerular filtration rate over the followed period.
Material and methods: 27 children (16 boys) with SK were evaluated, 8 with unilateral agenesis (UNA; mean age 14.2±8.8; average follow-up 4.4±3.1), 19 after nephrectomy (NX; mean age 17.8±5.1; average follow-up 7.1±4.5). The diagnosis of the congenital SK was established on the basis of an ultrasound examination confirmed by a nuclear scan with technetium traced dimercaptosuccinyl acid. Microalbuminuria, blood pressure and serum creatinine (Jaffé method) were recorded from the medical files on each follow-up. The glomerular filtration rate (eGFR) was estimated using the Schwartz formula corrected for age and gender. Changes of variables were followed in time and compared between both groups.
Results: Microalbuminuria was rising significantly with follow-up time in both groups (UNA $r=0.657$, $p<0.01$; NX $r=0.349$, $p<0.01$). Hypertension was more common in patients after NX, but the difference did not reach the statistical significance (n.s.; 12.5 % vs. 31.6 %). No significant changes of eGFR were present during the follow-up within both groups (UNA $r=0.262$, $p<0.10$; NX $r=0.143$, p=n.s.).
Conclusions: Microalbuminuria is rising with follow-up time in children with solitary kidney. Hypertension occured more commonly in children after NX. Overall, no significant changes of eGFR were present, but some individuals with poorer prognosis were identified within both groups. Further prospective studies are needed to elucidate the long-term prognosis of children with solitary kidney due to either UNA or NX.

P22 - Remission and recurrence free 1 year follow up in a patient with onset of factor H antibody associated atypical HUS under induction therapy with Plasmapheresis and introduction of maintenance therapy with i.v. IgG and MMF

SARUNAS RUDAITIS[1], JOHANNES HOFER[2], JONAS SURKUS[3], THERESE JUNGRAITHMAYR[2], BIRUTE PUNDZIENE[1]
[1]*DEPARTMENT OF CHILDREN'S DISEASES, HOSPITAL OF LITHUANIAN UNIVERSITY OF HEALTH SCIENCES KAUNAS CLINICS, KAUNAS, LITHUANIA*
[2]*DEPARTMENT OF PEDIATRICS I, MEDICAL UNIVERSITY INNSBRUCK, AUSTRIA*
[3]*NEPHROLOGY DEPARTMENT, MEDICAL ACADEMY, LITHUANIAN UNIVERSITY OF HEALTH SCIENCES, KAUNAS, LITHUANIA*

Introduction: Factor H antibodies (FH Ab) develop in 6-10 % of aHUS patients. The role of FH Ab in disease onset, progression and treatment is of critical interest for physicians and patients dealing with this unsolved problem. At present, evidence based therapy recommendations for this group of patients are missing. Many patients develop end stage renal disease and recurrence rates within the first year are up to 70 %.
Material and methods: A 15 year old girl was addmited to the hospital because of weakness, vommiting anddecreasing amount of urine. 6 days ago she had otitis. On examination slight oedema and normal blood pressure. Laboratory analysis showed anemia (Hb - 71 g/l), thrombocytopaenia

(55x10 9/l), elevated serum creatinin concentration (1219 μmol/l), high LDH (2612 U/l), low haptoglobin (86 mg/l) and low C3 (0,38 g/l) levels. Hemodialysis (n= 8) and plasmapheresis (regime as recommended in Guidlines of The European Paediatric Study Group for HUS) were started within 24 hours after addmition to the hospital. After 18 plasmapheresis sessions total remission (normalization of hematologic parameters and renal function) was obtained. 17 day later plasmapheresis sessions had to be started again because of hematologic relapse: Hb – 57 g/l, thrombocytes – 87x10 9/l, haptoglobin – 29 mg/l, C3 – 0,48 g/l, LDH – 418 U/l, serum creatinin concentration – 95 μmol/l (total number of plasmapheresis – 36). At that time FH Ab associated aHUS was diagnosed and after remission maintanance therapy (3 months after the onset) with i.v. IgG 2 g/kg body weight (days 0, 21, 41) and Mycophenolate mofetil (started on day 2; 600 mg/m² twice a day) was introduced.

Results: 12 months after onset of the disease the patient is on hematological and renal remission. The FH Ab Titers are in the low range (Titer cut off <100 AU/ml; low range <500 AU/ml). Despite normal C3 levels the measurement of the terminal complement complex in plasma reveals ongoing slight complement activation.

Conclusions: Early start and aggressive plasmapheresis, followed by maintance therapy with IgG and MMF seems to be a good therapeutic option in aHUS associated Fh Ab aHUS.

P23 - Investigating Bardet Biedl syndrome: identification and modelling of a novel mutation in BBS5

CHARLES VAN LENNEP, MOHAMED AL-HAMED, ROSLYN SIMMS, JOHN SAYER
NEWCASTLE UNIVERSITY

Introduction: Bardet Biedl syndrome (BBS) is an autosomal recessive disorder and is considered a ciliopathy. It is primarily characterised by renal abnormalities (cystic dysplasia), rod-cone dystrophy, post-axial polydactyly, learning difficulties, obesity and male hypogonadism. To date there are 15 genes implicated (BBS1-15) in this syndrome, with a homozygous mutation at one locus being sufficient to cause the phenotype.

Material and methods: In a consanguineous family with 3 children exhibiting a BBS phenotype, we aimed to identify the underlying gene defect. We performed homozygosity mapping and direct sequencing of known BBS genes within regions of homozygosity. We established an animal model of BBS using zebrafish to recapitulate the BBS phenotype. Using injection of a morpholino oligonucleotide targeted towards the translation site of BBS5, we created morphant embryos. These were phenotyped using light and fluorescent microscopy.

Results: The 3 affected siblings showed homozygosity at the BBS5 locus on chromosome 2. Using direct sequencing, we found a novel frameshift mutation c.967insT (p.A323CfsX55) in exon 12 of BBS5. BBS5 morphant zebrafish recapitulated some of the clinical features including structural cardiac abnormalities (with situs inversus), tail abnormalities and pronephric duct dilatation with evidence of renal dysfunction.

Conclusions: We describe a family with clinical features of BBS, together with a novel mutation in BBS5. Modelling of this disease in zebrafish mimics the human disease phenotype.

P24 - DEPA-HUS in Chinese brothers presenting with recurrent Haemolytic uraemic syndrome

ALISON L.T. MA, W.M. LAI, P.C. TONG, NIKO K.C. TSE
PAEDIATRIC NEPHROLOGY CENTRE, DEPARTMENT OF PAEDIATRICS AND ADOLESCENT MEDICINE, PRINCESS MARGARET HOSPITAL, HONG KONG

Introduction: DEAP-HUS (Deficiency of complement factor H-related plasma proteins and Autoantibody Positive form of Heamolytic ureamic Syndrome) represents a relatively new subtype of HUS. We report two Chinese brothers who suffer from this condition in Hong Kong.

Material and methods: Retrospective review of a first born 10-month old baby of non-consanguineous parents presented to a district hospital with influenza A with acute renal failure (oliguria and cr 500umol/l), microangiopathic haemolytic anaemia, thrombocytopenia (70x 109/l)), high lactate dehydrogenase of 2405u/l(209–513), and low serum C3 level 0.48 g/l (0.79-1.52) He was managed with haemodialysis and had full recovery of his kidney function in 2 weeks. 3 months later, he developed another episode of acute renal failure (cr 571unol/l) with roseola infantum. He improved with plasma infusion and haemodialysis but suffered from stage III chronic kidney disease then (cr 89umol/l). He remained well until 2 years later where he developed the third episode of acute renal failure with influenza B infection. He responded to plasma exchanges with gradual recovery of kidney function to his baseline. His younger brother also had the same presentation of acute renal failure with viral illness at 7 months of age who had full recovery of his kidney function after plasma exchanges and haemodialysis.

Results: DEAP-HUS work up was done in view of recurrent and familial form of HUS. ADAMTS level was normal. Anti-factor H antibody was tested positive in this patient (titre 450, normal <100) Heterozygous chromosomal deletions were found on complement factor H gene(CFH), Complement factor H-related(CFHR) 1 and CFHR 3 gene in the patient, his sibling and his

father who is asymptomatic. No mutations were found in factor H, factor I and MCP genes.
Conclusions: We report two brothers who develop DHEA-HUS. Clinicians should be alerted to children who present with recurrent and atypical HUS. The optimal therapy for prevention of the disease is yet to be defined.

P25 - PRE-EMPTIVE ECULIZUMAB TREATMENT TO PREVENT ATYPICAL HEMOLYTIC UREMIC SYNDROME RECURRENCE AFTER CADAVERIC KIDNEY TRANSPLANTATION

ROSANNA COPPO[1], ELENA BRESIN[2], ALESSANDRO AMORE[1], ROBERTO BONAUDO[1], ETTORE SABADINI[2], ROBERTA CAMILLA[1], RACHELE GALLO[1], LICIA PERUZZI[1], PIERO RUGGENENTI[2], GIUSEPPE REMUZZI[2]
[1]*NEPHROLOGY, DIALYSIS, TRANSPLANTATION, R. MARGHERITA HOSPITAL, TURIN, ITALY*
[2]*UNIT OF NEPHROLOGY AND DIALYSIS, AZIENDA OSPEDALIERA OSPEDALI RIUNITI DI BERGAMO, BERGAMO, ITALY*

Introduction: Outcome of atypical emolytic uremic syndrome (aHUS) is poor. Despite plasma therapy, 70-80 % of patients progress to ESRD and frequently relapse after transplant. Uncontrolled complement activation, often sustained by genetical abnormalities, is crucial in the pathogenesis. Liver-kidney transplantation restores bioavailability of liver-produced complement factors, but is burdened by unacceptable mortality. Humanized anti-C5 monoclonal antibody eculizumab offers a novel therapeutic option. We used it in a child with familial aHUS ensued at 6 months and a heterozygous loss of function mutation in complement factor H gene (3645 C>T). Benefits of eculizumab in recurrent aHUS after transplantation and prior to transplantation from a living donor have been reported. We describe a succesful case of aHUS treated with eculizumab before cadaveric kidney transplantation.
Material and methods: At 5 years of age, 6 months after immunization against Neisseria meningitidis, he was transplanted from deceased pediatric donor, after 1 plasma exchange and hemodialysis session. Eculizumab was infused intravenously immediately before transplant (600 mg), post-transplant on day 1 (300 mg) and day 7 (600 mg), and then every other week thereafter (300 mg). He was induced with low-dose thymoglobulin and basiliximab, and maintained on steroid, cyclosporine and mycophenolate mofetil.
Results: Graft function promptly recovered. Pre-transplant C5 circulating levels were normal (30–50 U/ml) and, just after the first eculizumab administration, dropped steadily below 5U/ml. Serum C3 and C4 levels, platelet count and all markers of hemolysis remained normal over follow-up. Three months after transplant, outcome was complicated by Burkholderia cepacia central venous catheter (CVC) colonization and sepsis, that recovered after CVC removal and treatment with meropenem. At 7 months post transplant, he is well without signs of hemolysis with serum creatinine of 0.5 mg/dl.
Conclusions: Pre-emptive eculizumab treatment safely prevented aHUS recurrence after kidney transplant in a child with factor H mutation. Continued eculizumab treatment may prevent complement and disease activation even throughout serious infectious complications.

P26 - OCULAR INVOLVEMENT IN A CHILD WITH FAMILIAL HYPOMAGNESEMIA WITH HYPERCALCIURIA AND NEPHROCALCINOSIS

BELDE KASAP[1], CANER ALPARSLAN[2], ALKAN BAL[2], MARTIN KONRAD[3], ÖNDER YAVAŞCAN[1], NEJAT AKSU[1]
[1]*İZMIR TEPECIK RESEARCH AND TRAINING HOSPITAL DEPARTMENT OF PEDIATRIC NEPHROLOGY, İZMIR, TÜRKIYE*
[2]*İZMIR TEPECIK RESEARCH AND TRAINING HOSPITAL DEPARTMENT OF PEDIATRICS, İZMIR, TÜRKIYE*
[3]*UNIVERSITY CHILDREN'S HOSPITAL, DEPARTMENT OF GENERAL PEDIATRICS, MUENSTER, GERMANY*

Introduction: In patients with nephrocalcinosis accompanied by hypomagnesemia, hypercalciuria, hyperuricemia, hypermagnesiuria, impaired GFR, and sometimes hypocitraturia, the most likely diagnosis is familial hypomagnesemia with hypercalciuria and nephrocalcinosis (FHHNC). The most common underlying genetic defect is a mutation in the CLDN16 gene encoding claudin 16, however, CLDN19 mutation is suggestive in case of additional ocular involvement.
Material and methods: Case Summary:
Results: A 6-year-old girl was admitted with polyuria and polydypsia, recurrent urinary tract infections, bilateral nephrolithiasis, and nephrocalcinosis. Her physical examination was normal. Laboratory findings revealed proteinuria, hypercalciuria, high urea, serum creatinine, uric acid, and parathyroid hormone levels, and low magnesium levels. The GFR calculated due to Schwartz formula was 69.6 ml/min/1.73 m2 and creatinine clearance calculated upon 24 hour collected urine was 60 mL/min/1.73 m2. Other laboratory findings were in normal range. The renal ultrasound revealed bilateral diffuse hyperechogenicity of the pyramids, typical for medullary nephrocalcinosis. Ophthalmologic examination revealed bilateral maculopathy characterized by sharply demarcated areas of depigmentation and atrophy in both macular areas and bilateral irregularity in retinal pigment epithelium. The suspected clinical

diagnosis was FHHNC and it was confirmed by the identification of a homozygous truncating mutation (W169X) in CLDN19.

Conclusions: FHHNC should be kept in mind while evaluating a child with medullary nephrocalcinosis, although it is a rare cause. Particularly a simple test, plasma magnesium level may lead us to the diagnosis. Additional opthalmologic findings should rise a high index of suspicion about CLDN 19 mutation rather than CLDN 16 mutation in patients with FHHNC.

P27 - Long diagnostic way in girl with hematuria

JOSEF GUT[1], PAVLINA PLEVOVA[2], JOSEF STEJSKAL[3]
[1]*DISTRICT HOSPITAL, CESKA LIPA*
[2]*DPTM. OF CLINICAL GENETICS, UNIVERSITY HOSPITAL OSTRAVA)*
[3]*DPTM. OF PATHOLOGY, UNIVERSITY HOSPITAL PRAGUE- MOTOL)*

Introduction: Glomerular thin membrane disease (also benign familial hematuria) is taken as a benign entity, but the clinical experience and new insights in molecular genetics background should be taken in account. Also patients must be followed up. Stepwise changes in urinalysis- findings of gross hematuria and proteinuria- are not typical for BFH and herald possible complications.

Material and methods: Case report: The 16 years old girl with family history (her grandmother died on chronic renal insuficiency- CHRI with biopsy-unproved diagnosis of diabetic nephropathy and her mother and younger brother have intermittent isolated hematuria with normal function and BP without deafness in family).In our patient since 4 years asymptomatic gross hematuria without proteinuria (coca-cola color) occurred nearly every morning. This symptom was verified during hospitalizations (2000–2005) with extensive examinations (USG, IVU, CT, MCUG, cystoscopy, C3, C4, ANA, anti DNA antibody, ANCA, cellular and humoral immunological examination). Glomerular erythrocytes with specific acanthocytes by phase microscopy repeatedly revealed . Three kidney biopsies (2000, 2003 and 2007) showed identical findings: "pure" thin basal membrane nephropathy (TBMN) and normal immunostaining for alfa 1(IV) and 5(IV). Since 2005 proteinuria 0.5-1.8 g/day (20-75 mg/m2/hour) occurred without changes in albumin and cholesterol levels. Currently her proteinuria under ACEI therapy is kept in range 0.5-1 g/day.

Results: Whole family was examined by new genetic method. Direct sekvenation of exon 25 of alfa5 (IV) gene proved missense mutation 1871 G>A (pGly 624Asp) in heterozygotic status in girl and her mother and in hemizygotic status in her brother .The mutation is registrated in HGMD Cardiff database as a pathogenic mutation for X linked Alport syndrome (XLAS).

Conclusions: Until recent decades, XLAS in female heterozygotes „carrier"was largely minimized, but these females have widely variable outcomes. Some affected females exhibiting normal urinalysis and function, while others develop CHRI and deafness (12 % of females demonstrate CHRI, which increase to 30-40 % after age 60 years).

P28 - Renal Manifestations in Children with Tuberous Sclerosis Complex

SE JIN PARK[1], KI SOO PAI[1], SUNG HWAN KIM[1], JAE IL SHIN[2], TAE-SUN HAA[3]
[1]*DEPARTMENT OF PEDIATRICS, AJOU UNIVERSITY SCHOOL OF MEDICINE, AJOU UNIVERSITY HOSPITAL, SUWON, KOREA*
[2]*DEPARTMENT OF PEDIATRICS, YONSEI UNIVERSITY COLLEGE OF MEDICINE, SEVERANCE CHILDREN'S HOSPITAL, SEOUL, KOREA*
[3]*DEPARTMENT OF PEDIATRICS, CHUNGBUK NATIONAL UNIVERSITY COLLEGE OF MEDICINE, CHEONGJU, KOREA*

Introduction: Several types of renal abnormalities may be seen in individuals with Tuberous sclerosis complex (TSC), including angiomyolipoma, renal cyst, and polycystic kidney disease. Care for an individual with TSC may require ongoing and different treatment for each renal disease depending on the manifestations they have. Here, we will address our experience on pediatric patients with TSC requiring evaluation and treatment for renal manifestations.

Material and methods: A retrospective analysis was made on 29 patients in whom TSC was diagnosed between 2001 and 2011 at three medical centers. All patients had clinical diagnoses of TSC as defined by the 1998 tuberous sclerosis complex consensus conference.

Results: The patients consisted of 19 boys and 10 girls with a mean age of 13.35±6.45 years (range 1 to 26 years). The renal disease associated with TSC included angiomyolipoma in 16 patients (55.1 %), renal simple cyst in one (3.4 %), nephrocalcinosis in one (3.4 %), and renal cell carcinoma in one patient (3.4 %). Eight patients (27.5 %) presented with normal kidney contours at abdominal ultrasonography. Perirenal hematoma from angiomyolipoma was detected in one patient (3.4 %). Transcatheter embolization was performed in four patients (13.7 %) with angiomyolipoma. Radical nephrectomy was done in two patients (6.9 %) due to renal cell carcinoma and recurrent angiomyolipoma after angioinfarction. One patient underwent renal replacement therapy due to chronic renal failure after nephrectomy.

Conclusions: In our review of 29 cases of TSC, renal manifestations are variously reported in 72.4 % of patients. Most angiomyolipomas associated with TSC were asymptomatic but increased steadily in size, although severe

hemorrhages were rare. Therefore, patients with TSC should be followed-up with abdominal ultrasonography or magnetic resonance imaging. Renal function should also be screened and evaluated periodically.

P29 - INCREASED RENAL ECHOGENICITY IN FETUS

Introduction: Introduction: Prenatal diagnosis of urinary tract abnormalities facilitates optimal postnatal care as well as prenatal surgical therapy indicated in rare cases. Furthermore it gives the parents the alternative to terminate the pregnancy in the most severe cases where very poor postnatal prognosis is expected. In a healthy fetus the echogenicity of kidneys and liver is similar. The prenatal increase of the renal echogenicity may be associated with many diseases. The aim of presentation is to provide an overview of the most frequent diagnosis that are associated with increased renal echogenicity and to report four cases: fetus with autosomal-dominant and autosomal-recessive polycystic kidney disease, with renal dysplasia of unknown etiology and fetus with a congenital erythropoietic porphyria.
Material and methods: 534 fetuses with a suspicion of urinary tract abnormality were examined in 2005–2011. A 6-MHz probe (Acuson S 2000, Aloka 5500) was used.
Results: 21 cases of the increased bilateral renal echogenicity were detected among 534 fetuses i.e. 3,9 %. Pathological findings were: 1. obstructive uropathy caused mostly by subvesical obstruction (9 cases)- 7 pregnancies were terminated artificially, one spontaneously, 1 child is alive and has a normal renal function. 2. transiently increased echogenicity of unknown etiology with a normal amniotic fluid volume (4 cases). 3. increased echogenicity without obstruction with a reduction of amniotic fluid volume (7 cases) – reasons were heterogenous e.g. autosomal- recessive polycystic kidney disease associated with death in the first day of life, cytomegaloviral infection and bilateral cystic dysplasia of unknown etiology (both pregnancies were terminated), congenital erythropoietic porphyria. 4. increased echogenicity without obstruction with an adequate amniotic fluid volume – autosomal – dominant polycystic kidney (1 case).
Conclusions: Increased renal echogenicity connected with decreased amniotic fluid volume has usually very poor prognosis. In the cases of normal amniotic fluid volume the determination of prognosis is very difficult, in some cases renal hyperechogenicity becomes normal postnatally.

P30 - IMMUNOHISTOCHEMICAL DIAGNOSIS OF ALPORT SYNDROME: THE FIRST EXPERIENCE IN THE REPUBLIC OF BELARUS

NATALIA TUR[2], EVGENIY CHERSTVY[1], ALEKSANDR SUKALO[1], TATIANA LETKOVSKAYA[1], VIKTORIA SAVOSH[1], IVAN SAKHARAU[1], SERGEY DEDIK[1]

[1]*BELARUSIAN STATE MEDICAL UNIVERSITY*
[2]*REPUBLIC CENTER FOR CHILDREN NEPHROLOGY AND RENAL REPLACEMENT THERAPY*

Introduction: Alport syndrome (AS) is a genetic disorder caused by defects in the genes encoding α3, α4, or α5 chains of collagen type IV. The earliest change in AS is thinning of the glomerular basement membrane (GBM), hence electron microscopy may not always be enough to differentiate AS from TBMD. Immunohistochemistry (IHC) should be performed in such cases. Objectives: Estimate the expression of α3 and α5 type IV collagen chains in renal glomeruli of hematuric patients and it's significance for hereditary nephritis diagnostics.
Material and methods: This study is based on renal biopsy specimens and clinical data from 16 patients of the Republic Center of Pediatric Nephrology, Minsk, Belarus. Patients had either family history of renal disease or presence of interstitial foam cells. IHC staining of specimens with antibodies to α3 and α5 chains of type IV collagen was performed.
Results: Light microscopy showed mesangial proliferation in 13 cases, FSGS in two cases and one child had membranoproliferative glomerulonephritis. In two cases complete absence of α3 and α5 chains expression was found, which is diagnostic for X-linked AS. Focal negative expression of α3 chain, combined with absence of α5 was found in 7 patients. Four patients had normal staining for α3 subunit with absence of α5 expression. Such pattern of collagen IV chains expression is typical for autosomal recessive AS. Electron microscopy data from all the patients revealed focal thickening, splitting of GBM with electron-dense deposits. In three other patients positive staining for α3 and α5 subunits, combined with normal electron microscopy data and uncomplicated family history allowed to rule out the diagnosis of AS.
Conclusions: The absence of α3 and α5 chains from the GBM is diagnostic of AS. Furthermore, renal expression of collagen IV chains allows to differentiate X-linked and autosomal recessive AS.

P31 - Membrano-proliferative glomerulonephritis (MPGN) of solitary kidney in an infant with congenital cystic adenomatoid malformation of the lung (CCAM)

TOMASZ JARMOLIńSKI[1], MARCIN ZANIEW[2], BOżENA JACHIMIAK[3], ELżBIETA URASIńSKA[4], GRAżYNA DAWID[5]

[1]*DEPT. OF PEDIATRICS, REGIONAL HOSPITAL, MIęDZYRZECZ, POLAND*
[2]*DISTRICT CHILDREN'S HOSPITAL, POZNAń, POLAND*
[3]*DEPT. OF PEDIATRIC NEPHROLOGY, DISTRICT HOSPITAL, GORZóW, POLAND*
[4]*DEPT. OF PATHOLOGY, POMERANIAN MEDICAL UNIVERSITY, SZCZECIN, POLAND*

[5]DEPT. OF PEDIATRIC CARDIOLOGY, POMERANIAN MEDICAL UNIVERSITY, SZCZECIN, POLAND

Introduction: CCAM is a rare pulmonary hamartomatous abnormality associated with other congenital malformations in up to 25 % of cases (abdominal wall abnormalities, kidney, central nervous system, gastrointestinal, cardiac and great vessels defects and sirenomelia). The aim of the study was to present unusual coincidence of CCAM, unilateral renal agenesis and glomerulonephritis.
Material and methods: This is a case report of 2-yr-old boy who at the age of 7 months was referred to pediatric nephrologist for evaluation of proteinuria, which had been observed since birth. The baby of nonconsanguineous parents was delivered by a 39-yr-old diabetic mother. Antenatally, a lung abnormality and renal agenesis were suspected. After birth, he presented with severe respiratory distress and cardiac failure. Chest CT showed picture of CCAM type II according to Stoker classification. Echocardiography and abdominal sonography revealed cardiomyopathy and left kidney agenesis respectively.
Results: On admission, urinary Pr/Cr ratio was 6 mg/dl/mg/dl, hypoproteinemia (48 g/l) with mild hypoalbuminemia (33 g/l) and hypocomplementemia (C3–77 mg/dl) were also found. Treatment with ACEI was started with moderate influence onto urinary protein excretion. At the age of 10 months, operative kidney biopsy was performed. Among 20 glomeruli seen in light microscopy, 2 were sclerosed and the rest showed lobularity with prominent mesangial proliferation and thickened double contoured vascular loops. Immunohistology revealed IgM and C1q mesangial deposits and electron microscopy showed mesangial and endothelial cells proliferation with subepithelial and subendothelial deposits and double-contoured basement membranes with segmental thickening. Glomerular changes corresponded with type III MPGN – kidney abnormality not described in CCAM till now. Taking into account genetic and/or immunological cause of glomerulopathy, treatment with cyclosporine A was started after completing immunizations. Proteinuria gradually disappeared and kidney function after 6 months of treatment was normal.
Conclusions: MPGN may appear in patients with CCAM. The nature of this coincidence is not clear and requires further studies.

P32 - THE EFFECTS OF ALDOSTERONE BLOCKADE ON PROTEINURIA AND URINARY TGF-beta1 IN PATIENTS WITH ALPORT SYNDROME

ANTONIO MASTRANGELO[1], MARISA GIANI[1], AMEDEA SILVIA TIRELLI[2], ROBERTA VILLA[1], HELMUT HOPFER[3], STEFANO TUROLO[2], GIUSEPPINA MARRA[1], ALBERTO EDEFONTI[1]

[1]PEDIATRIC NEPHROLOGY AND DIALYSIS UNIT, FONDAZIONE IRCCS CA' GRANDA OSPEDALE MAGGIORE POLICLINICO, MILAN, ITALY
[2]LABORATORY OF CLINICAL PATHOLOGY, FONDAZIONE IRCCS CA' GRANDA OSPEDALE MAGGIORE POLICLINICO, MILAN, ITALY
[3]INSTITUTE OF PATHOLOGY, UNIVERSITY HOSPITAL BASEL, BASEL, SWITZERLAND

Introduction: Alport Syndrome (AS) is a progressive hereditary glomerular disease characterized by hematuria, ocular abnormalities, sensorineural deafness and progressive renal failure. Recent data indicate a role for aldosterone in the worsening of proteinuria, by promoting fibrosis mediated by Transforming Growth Factor-beta1 (TGF-beta1) pathway. Spironolactone (SP) antagonizes the pro-fibrotic effect of aldosterone and reduces proteinuria in different renal diseases. Aim of our study was to evaluate the efficacy of SP in reducing proteinuria and urinary TGF-beta1 excretion in AS proteinuric patients with normal renal function.
Material and methods: Ten AS children, with normal renal function and persistent (>6 months) proteinuria (uPr/uCr ratio>1) were investigated. SP (25 mg once a day for 6 months) was added to the pre-existing therapy with ACE inhibitors (ACEI; 9 patients) and Angiotensin II receptor blockade (ARB; 1 patient). Proteinuria, renal function, serum protein and albumin, serum and urinary electrolytes and urinary TGF-beta1 were measured at least two times in the periods preceding and following the beginning of SP therapy. Plasma renin activity (PRA) and serum aldosterone were also measured.
Results: After the beginning of SP therapy we observed in all patients a significant decrease of proteinuria (from 1.77±0.8 to 0.86±0.6; $p<0.001$) and urinary TGF-beta1 (from 104±54 to 41±20 pg/mg creatinine; $p<0.01$), from the first 30 days of treatment and during the whole period of SP administration. PRA values did not change during the study period, while serum aldosterone increased from 105±72 pg/ml to 303±156 pg/ml ($p<0.001$). Side effects consisted of gynecomastia in one obese boy.
Conclusions: The addition of SP to a pre-existing treatment with ACEI and/or ARB contributed to a significant reduction in proteinuria. This effect was mediated by a decrease of TGF-beta1 and was not associated with major side effects

P33 - Variability in renal phenotype during HDR syndrome: a case-report with glomerular nephropathy

CHENOUARD ALEXIS[1], ISIDOR BERTRAND[1], ALLAIN LAUNAY EMMA[1], MOREAU ANNE[1], LE BIDEAU MARC[2], ROUSSEY KESLER GWENAELLE[1]

[1]NANTES UNIVERSITY HOSPITAL
[2]HOSPITAL OF SAINT NAZAIRE

Introduction: HDR syndrome (Hypoparathyroidism, sensorineural Deafness, Renal abnormalities) is a rare autosomal dominant disorder caused by mutations in the GATA-3 gene, a transcription factor coding for a protein involved in vertebrate embryonic development. So far, less than a hundred cases with significant renal involvement have been described.
Material and methods: We report on a patient suffering from HDR syndrome with glomerular nephropathy.
Results: A. was admitted to hospital at 17 months of age because of generalized seizures revealing severe hypocalcemia (1.23 mmo/L) related to a hypoparathyroidism. Magnesemia and renal function were normal as autoimmune tests. A screening for the 22q11 deletion was negative. At 3 years of age, a chronic renal failure (estimated glomerular filtration rate eGFR: 40 ml/mn/1.73 m2) was fortuitously detected, associated with hypercalciuria and nephrocalcinosis. A renal biopsy revealed a tubulointerstitial nephritis. Moreover, a delayed language development led to the diagnosis of severe bilateral sensorineural deafness. At 4 years of age, he developed a nephrotic syndrome with a bilateral interstitial pneumonia complicated by a transitory cardiac involvement. A renal biopsy revealed a segmental diffuse proliferative glomerulonephritis and persistent nephrocalcinosis. Considering the multisystemic organ involvement, a metabolic disease was suspected but all investigations were negative. At 13 years of age, HDR syndrome was confirmed by direct sequencing of the GATA-3 gene showed a de novo mutation. At 15 years of age, the eGFR is 50 ml/mn/1.73 m2 with a persistent glomerular proteinuria and tubular disorders.
Conclusions: To our knowledge, glomerulonephritis in HDR syndrome has never been reported. HDR in this patient was not initially diagnosed due to the appearance of a transitory cardiac involvement and atypical renal symptoms. Further studies of GATA-3 are needed to explore the involvement of this transcription factor.

P34 - POLYCISTIC KIDNEY DISEASE: A SINGLE CENTRE EXPERIENCE.

LAURA MASSELLA, GIACOMO DI ZAZZO, FRANCESCO EMMA
BAMBINO GESù CHILDREN'S HOSPITAL, IRCCS, ROME, ITALY

Introduction: Autosomal dominant polycystic kidney disease (ADPKD) and autosomal recessive polycystic kidney disease (ARPKD) are the two most frequent forms of cystic renal disorders. ARPKD is rare (1:20.000 live births) and is frequently symptomatic at birth; renal function often deteriorates during childhood; conversely, ADPKD is more frequent (1–2.5:1000 live births) and generally becomes symptomatic during adulthood, when it represents one of the first causes of ESRD. Herein, we report the evolution of patients with ADPKD and ARPKD followed in the Nephrology and Dialysis Unit of the Bambino Gesù Children's Hospital since 1990.
Material and methods: The cohort comprises 104 patients, including 89 ADPKD patients (mean age 10.1 years) and 15 ARPKD patients (mean age 3.9 years) (newborns that died following treatment withdrawal at birth were not included).
Results: The M:F ratio was 1.4:1 in ADPKD and 1:2 in ARPKD. At the last follow-up, 5 patients had died (4 ARPKD and 1 ADPKD). Chronic renal failure was present in 3.4 % of patients with ADPKD (3/88) and 63 % of ARPKD patients (7/11). Currently 1 patient remains on dialysis and 7 have been transplanted (3 ADPKD+4 ARPKD). Liver involvement was present in all ARPKD children; hepatic cysts were observed in 4/89 ADPKD patients. The incidence of hypertension in non-transplanted patients was 100 % in ARPKD and 20 % (17/86) in ADPKD.
Conclusions: Renal function can be compromised also in children with ADPKD, as previously reported; the prevalence of hypertension is significant in ADPKD, also during childhood. These results highlight the need to monitor ADPKD patients from early childhood to detect hypertension and to apply early measures aimed at preventing cardiovascular complications.

P35 - X-linked hypophosphatemic rickets and FGF-23: Cinacalcet vs Paricalcitol treatment.

RAMON VILALTA, SARA CHOCRON, ENRIQUE LARA, ALVARO MADRID, MARINA MUñOZ, JOSE NIETO
HOSPITAL VALL D'HEBRON,BARCELONA

Introduction: Background: Fibroblast growth factor 23 (FGF-23) is modulated by vitamine D metabolites, serum and dietary phosphate and possibly PTH. In hypophosphatemic rickets, phosphate is administered with adverse FGF-23 and PTH increase and a vicious circle is established. Cinacalcet or paricalcitol could minimize these effects.
Material and methods: Objective: To see variations in phosphorus metabolism, PTH and FGF-23 in two populations under low phosphorus dosage, native vitamine D and cinacalcet or paricalcitol. Patients and methods: X-linked hypophosphatemic rickets was genetically confirmed in all cases. Phosphorus was reduced to 30 mg/kg/day, and calcitriol was substituted by native vitamine D Group A: Paricalcitol treatment (2 patients) Group B: Cinacalcet treatment (4 patients) Controls (before treatment change, 2 weeks after and every 3 months for 1 year), included height, weight, RTP,TmP,FGF-23 and PTH.

Results: Results: -FGF-23 was reduced in both groups, more in Cinacalcet group. -Serum phosphorus incresead, more in Cinacalcet group.
Conclusions: Conclusions: -Both treatments (cinacalcet or paricalcitol) reached acceptable metabolic control. -The small number of patients puts a limit in these conclusions

P36 - Somatic mosaicism in Alport syndrome: New mutation in the COL4A5 gene

SONJA BEICHT[1], GERTRUD STROBL-WILDEMANN[2], SABINE RATH[1], HANNS-GEORG KLEIN[1], JULIA HOEFELE[1]
[1]*CENTER FOR HUMAN GENETICS AND LABORATORY MEDICINE DR. KLEIN & DR. ROST, MARTINSRIED, GERMANY*
[2]*HUMANGENETIK ULM MVZ, ULM, GERMANY*

Introduction: Alport syndrome (AS) is a hereditary progressive nephritis associated with mutations in COL4A3, COL4A4, and COL4A5. It is characterized by hematuria and proteinuria, sensorineural hearing loss and ocular changes. The nephritis frequently leads to end-stage renal disease. Mutations in the COL4A5 gene are responsible for X-linked Alport syndrome, which is the most common form.
Material and methods: Here we report a rare form of inheritance in a boy and his mother affected by Alport syndrome. The boy developed microhematuria at the age of one year. Hearing loss was diagnosed at 14 years of age. Furthermore, he developed proteinuria. His mother has also been affected by microhematuria and hearing loss since the age of 14 years. In addition, she suffers from myopia. Both have a serum creatinine within the normal range.
Results: DNA sequence analysis of the COL4A5 gene in the son revealed the novel hemizygote mutation c.2396-1 G>A at the splice acceptor site of intron 29 replacing 100 % of conserved guanine with adenine at position 1 of the splice acceptor site. This alteration most likely leads to aberrant splicing and a premature translational stop. The mother, who is carrier of this mutation, exhibits a mosaic pattern. The analysis of different tissues including mesoderm (leukocytes and urine sediments) and ectoderm (hair roots and oral mucosa) revealed a percentage of mutant cells between 12 % and 32 %.
Conclusions: Due to the fact that mesoderm and ectoderm are affected in the mother, we hypothesize that the mutation occurred early in embryonic development. Our findings indicate that particularly in female patients with clinical features of Alport syndrome, potential somatic mosaicism of the COL4A5 gene should be considered. Small somatic mosaics could be missed by Sanger sequencing, but can be reliably detected by NGS.

P37 - RENAL HISTOPATHOLOGICAL FINDINGS IN PATIENTS WITH 2,8-DIHYDROXYADENINURIA

VIDAR EDVARDSSON, SVERRIR HARDARSON, RUNOLFUR PALSSON
LANDSPITALI - THE NATIONAL UNIVERSITY HOSPITAL OF ICELAND

Introduction: Adenine phosphoribosyltransferase (APRT) deficiency is an autosomal recessive disorder of purine metabolism that leads to excessive urinary excretion of the poorly soluble 2,8-dihydroxyadenine (DHA). The most common clinical manifestations are recurrent radiolucent kidney stones and chronic kidney disease (CKD), frequently presenting in childhood. The aim of this study was to characterize the renal histopathological findings in affected patients, including the distribution of DHA crystal deposition.
Material and methods: Medical records of 32 Icelandic patients listed in the APRT Deficiency Registry of the Rare Kidney Stone Consortium were reviewed. Patients who had undergone kidney biopsy or nephrectomy were identified and the renal histology slides examined.
Results: Three patients had undergone kidney biopsy and one had nephrectomy performed. Patient 1 presented at 9 months of age with acute obstructive kidney injury due to bilateral stone impaction, requiring unilateral nephrectomy. Patient 2 was a 42 year old man with history of recurrent kidney stones since childhood and acute kidney injury (AKI) superimposed on advanced CKD. Patient 3 was a 42 year old woman with recurrent kidney stones and stage 4 CKD. Patient 4 was a 55 year old woman with severe AKI but no past history of stones. Variable degree of renal scarring, chronic interstitial inflammation and glomerulosclerosis was observed in the renal tissue specimens in all 4 cases. These changes were by far least pronounced in the young child. Extensive DHA crystal deposits were seen in the renal tissue in all cases, primarily located in the cortex, most commonly within tubular lumina. Examination under polarized light greatly facilitated the detection of renal crystals.
Conclusions: Renal pathological findings in patients with APRT deficiency include extensive DHA crystal deposits, primarily located in the renal cortex, significant tubulointerstitial scarring, inflammation and secondary glomerulosclerosis. These findings may be present from early childhood.

P38 - Severe, generalised and refractory cholestatic pruitus in an ARPKD child on PD successfully treated with naltrexone.

SøREN RITTIG[1], AKSEL LANGE[1], HENNING GROENBAEK[1], LOUISE WINDING[2], JOHAN POVLSEN[1]
[1]*AARHUS UNIVERSITY HOSPITAL*
[2]*LILLEBAELT HOSPITAL, KOLDING*

Introduction: Autosomal recessive polycystic kidney disease (ARPKD) is associated with early onset CKD, cholestatic liver disease, poor thrive, and in some patients a debilitating generalized pruritus.
Material and methods: Case: A child without familial history of kidney disease developed poor thrive and jaundice during the first months of life.
Results: Blood tests were consistent with cholestatic liver disease with bilirubin of 70 micromol/L, ALAT of 130 U/L, and gammaGT of 270 U/L. Plasma bile acids were markedly increased at130 micromol/L. Ultrasound showed bilaterally enlarged kidneys with poor parenchymal differentiation as well as marked hepatomegaly, hepatic fibrosis later confirmed by liver biopsy and abnormal portal venous flow. Genetic characterization is on-going. GFR was initially normal but decreased rapidly. The clinical picture was characterized by marked hypertension (> 99th percentile) and poor thrive (body weight app. -2.8 SD for age). Renal replacement therapy: Initiated on HD at the age of 18 months, but switched to PD due to lack of vascular access. Now successfully managed on APD (12 hours daily)with Baxter HomeChoice using a total of 6.5 L Physioneal, a dwell volume of 450 ml (= 900 ml/m2 BSA) and a tidal of 70 % giving a total of 20 cycles per night (32 min/cycle). Pruritus: Due to the congenital hepatic fibrosis, the child developed severe, generalised cholestatic pruritus refractory to treatment with oral antihistamines, topical steroids, rifampicin, and ursodiol. However, the child was successfully treated with the opioid antagonist, naltrexone 25 mg twice daily (app. 5 mg/kg/day)
Conclusions: Conclusions: 1) Despite very large kidneys, liver, and spleen, this child with ARPKD was successfully managed on APD. 2) Naltrexone may be an effective adjuvant in the management of cholestatic pruitus in children with ARPKD.

P39 - Mutation rate of NPHS2 and WT1 in Hungarian children with SRNS

ANDREA KERTI[1], RóZSA CSOHáNY[1], ESZTER JáVORSZKY[1], ATTILA J. SZABó[1], OTTó ÁRKOSSY[2], PéTER SALLAY[1], VINCENT MORINIéRE[3], VIRGINIA VEGA-WARNER[4], ORSOLYA LAKATOS[5], TAMáS SZABó[6], CORINNE ANTIGNAC[3], GYÖRGY REUSZ[1], KáLMáN TORY[1]
[1]*IST DEPARTMENT OF PEDIATRICS, SEMMELWEIS UNIVERSITY, BUDAPEST, HUNGARY*
[2]*FMC SZéPVÖLGYI DIALYSIS CENTRE, SZENT JáNOS HOSPITAL, NEPHROLOGY OUTPATIENT DEPT, BUDAPEST, HUNGARY*
[3]*INSERM U983, HôPITAL NECKER, PARIS, FRANCE*
[4]*DEPARTMENTS OF PEDIATRICS AND HUMAN GENETICS, UNIVERSITY OF MICHIGAN, ANN ARBOR, MICHIGAN, USA*
[5]*DEPARTMENT OF PEDIATRICS, UNIVERSITY OF PéCS, HUNGARY*
[6]*UNIVERSITY OF DEBRECEN, MEDICAL AND HEALTH SCIENCE CENTER, PEDIATRIC INSTITUTE, DEBRECEN, HUNGARY*

Introduction: The genetic form of steroid-resistant nephrotic syndrome (SRNS) is heterogeneous; more than 10 genes have already been identified. The most frequently mutated gene in isolated SRNS is NPHS2. Mutations of WT1 have been identified in girls with isolated SRNS and in boys with associated genital abnormalities.
Material and methods: Out of a cohort of 49 Hungarian unrelated patients with SRNS and/or nephrotic-range proteinuria, 40 patients were screened for NPHS2 and 20 children (11 girls) for WT1 mutations.
Results: NPHS2 and WT1 mutations were found in 11/40 and 2/20 patients, respectively. Five of the 11 patients with NPHS2 mutations were either homozygous or compound heterozygous for severe (truncating or p.R138Q) mutations. Two patients carried the p.V290M mutation either in homozygous state or in association to the p.R138Q mutation. While the 5 patients with severe mutations progressed to ESRD before the age of 10 years, the 2 patients carrying p.V290M mutation showed an extremely mild clinical course, none of them developed nephrotic syndrome below the age of 18 years. Four of the 11 patients with NPHS2 mutations were found to carry a single heterozygous mutation. Though the role of a second unidentified mutation cannot be excluded, their pathogenicity is questionable in two cases, as one of them reached complete remission after cyclosporine therapy and the second patient with associated hypospadias was also found to carry a heterozygous splice mutation in WT1 (c.1228+4 C>T), which can entirely explain his phenotype. The second boy with a WT1 missense mutation presented with Denys-Drash syndrome.
Conclusions: The mutation rate of NPHS2 and WT1 in Hungarian children corresponds to the European cohorts. We propose that besides the NPHS2 p.R229Q variant, the p.V290M mutation should also be screened in Eastern European patients with late-onset SRNS. Patients with SRNS may carry a single heterozygous NPHS2 mutation by chance.

P40 - CHILDHOOD PRESENTATION AND RENAL OUTCOME OF APRT DEFICIENCY (2,8-DIHYDROXYADENINURIA) IN ICELAND

VIDAR EDVARDSSON, INGER AGUSTSDOTTIR, RUNOLFUR PALSSON
LANDSPITALI – THE NATIONAL UNIVERSITY HOSPITAL OF ICELAND

Introduction: Adenine phosphoribosyltransferase (APRT) deficiency is a rare autosomal recessive error of adenine metabolism resulting in the renal excretion of large amounts of the poorly soluble 2,8-dihydroxyadenine (DHA). Reported childhood manifestations include radiolucent kidney stones, urinary tract infections and acute kidney injury. The aim of this study was to assess presenting features and long-term renal outcome in Icelandic patients who presented with the disease before 18 years of age.
Material and methods: Medical records of 32 Icelandic patients listed in the APRT Deficiency Registry of the Rare Kidney Stone Consortium were reviewed. Data are presented as median and range. This work is supported by NIH, the NIDDK and the ORD, grant number 1U54DK083908-01.
Results: Fifteen patients, 6 boys and 9 girls, presented or were diagnosed in childhood. Median age at presentation was 1.6 (0.2 to 17) years. Age at diagnosis, was 4.8 (0.6 to 42.3) years and was delayed in 12 patients for 2.9 (0.03 to 39.2) years. Reddish-brown diaper stain led to the diagnosis in 5 cases, 2 had renal colic, 2 kidney stones, 2 acute kidney injury and 1 had urinary tract infection. Two patients were discovered during family screening of index cases and urinary DHA crystals were an incidental finding in 2 cases. All patients were prescribed allopurinol treatment at the time of diagnosis. The disappearance of urinary DHA crystals was considered as an adequate treatment response. At latest follow-up, 13.2 (0.02-28.1) years following diagnosis, the median estimated glomerular filtration rate (eGFR) was 90.2 (14.1 to 146) ml/min/1.73 m2. In 3 patients the eGFR was less than 60 ml/min/1.73 m2.
Conclusions: Clinical features of APRT deficiency appear to vary greatly in childhood. A significant diagnostic delay occurred in the majority of cases and very likely contributed to the impairment of renal function observed in our patient sample.

P41 - Iatrogenic hypercalcemia: description of 4 cases

PAOLA POGGIO, VINICIO GOJ, LUCA BERNARDO, ELISABETTA SCURATI MANZONI
PEDIATRICS DIVISION FATEBENEFRATELLI HOSPITAL

Introduction: International literature seldom reports cases of iatrogenic hypercalcemia . We here report four cases of hypercalcemia occurred after taking vitamin D/Calcium and homeopathic dietary supplementation.
Material and methods: Descrioption of four cases
Results: 1. 14 month-old girl with a month 's history of vomiting. She had been given high dosages of a homeopathic remedy containing Calcium salts . On admission to hospital : serum calcium, phosphorus and alkaline phosphatase levels were 11,3- 6,9 mg/dl and 130 U/l respectively. After three weeks suspension: serum calcium-phosphorus 9,5-5 mg/dl and alkaline phosphatase 180 UI/l. 2. 5 year-old boy with acute pyelonephritis. He had been taking dietary supplements containing Vitamin D3 and calcium carbonate for six months plus calcium fortified water and chocolate. On admission to hospital serum calcium and alkaline phosphatase levels were 11,5 mg/dl and 129 U/l respectively, urine calcium/creatinine was 0,44. Ultrasounds revealed kidney and bladder gravel. After a months' suspension and adequate diet - hydration : serum calcium 9,8 mg/dl, alkaline phosphatase 180 UI/ and urine calcium/creatinine was 0,22 whilst ultrasounds revealed bladder gravel. 3. 5 month-old boy with hematuria. He had been given 900 UI/die of Colecalciferol since birth. Serum calcium was 11,5 mg/dl, vitamin D3 65 pg/ml, urine calcium/creatinine 0,75 . After 45 days suspension his labs showed serum calcium 10,5 mg/dl and urine calcium/creatinine 0,6. 4. 11 month-old boy asymptomatic. He had been given 2500 UI/die of 25(OH) vitamin D3 since birth. Serum calcium, phosphorus and alkaline phosphatase levels were 11,6 - 6 mg/dl and 276 U/l respectively, 25(OH) vitamin D3 was 64,3. ng/ml. After 14 days suspension, labs turned normal.
Conclusions: These cases underscore the need to be attentive to the possibility of hypercalcemia in patients treated with vitamin D/Calcium or homeopathic dietary supplements. Such supplements can be harmful and therefore must be adeguately prescribed when necessary.

P42 - A case of Sesame's syndrome with severe tubulopathy

LYDIA LICHTENBERGER[1], AUDREY VANRENTERGHEM[1], DJAMAL DJEDDI[1], ROSA VARGAS-POUSSOU[2], BERNARD BOUDAILLIEZ[1]
[1]*DEPARTMENT OF PEDIATRICS, AMIENS HOSPITAL, AMIENS 80054, FRANCE*
[2]*DEPARTMENT OF GENETICS EUROPEAN GEORGES POMPIDOU HOSPITAL PARIS FRANCE*

Introduction: The syndrome of EAST (epilepsy, ataxia, sensorineural deafness, tubulopathy) or SeSAME (seizures, sensorineural deafness, ataxia, mental retardation, electrolyte imbalance) is a rare recessive autosomal disease with mutations of KCNJ10 gene coding for potassium channel kir 4.1
Material and methods: We report the case of a 2-year-old girl born from consanguine parents with a syndrome of Sesame. Clinically, the patient presented at 6 months staturo-weight and psychomotor delay, hypokaliemia 2,2 mmol/l with hyperkaliuria, hypomagnesaemia, ataxia, nystagmus, axial hypotonia, epileptic seizures, sensorineural hearing loss
Results: This mutation was described in the literature, associated with a loss of canal kir 4.1 function in vitro

(Reichold M and al. PNAS on 2010). The potassium needs are increasing in the evolution at 24 meq / kg / day and the water at 200 ml / kg / hour because of the tubulopathy's aggravation.

Conclusions: The neurological prognosis is severe with an obstinacy of the crises in spite of anticonvulsant drugs. Nutrition and water are exclusively administered by the gastrostomy. The prognosis is difficult to expect because of few cases described in the literature

P43 - Urinary reference values for the management of children with urolithiasis and its relationship with a family history of stone forming

Mª CONCEPCIóN SAEZ DE BARROSO[1], Mª DOLORES RODRIGO[2], FELIX GRASES[1], GUILLEM FRONTERA[3], ANA MARIA GARCIA[4], CRISTINA GOMEZ[4], JAVIER LUMBRERAS[2], Mª CONCEPCION MIR[2]

[1]*LABORATORY OF RENAL LITHIASIS RESEARCH, UNIVERSITY OF BALEARS ISLANDS.*

[2]*PEDIATRIC NEPROLOGY DEPARTMENT. SON ESPASES HOSPITAL.PALMA DE MALLORCA.*

[3]*RESEARCH INSTITUTE. SON ESPASES HOSPITAL. PALMA DE MALLORCA*

[4]*LABORATORY DEPARTMENT. SON ESPASES HOSPITAL. PALMA DE MALLORCA.*

Introduction: Metabolic abnormalities are one of the most important ethiological factors contributing to the increased prevalence of renal lithiasis. For the correct diagnosis of these abnormalities, clinicians need reference values identifying the normal range for urine composition. However, relevant data in children are scarce due to the difficulty of performing proper urine collections at this age. Besides this, the role of the family history is often not taken into consideration.Objectives: To study the presence of urinary metabolic abnormalities in a sample of healthy school children, using cut-off points that are described in the literature.

Material and methods: Urine samples were obtained from 184 children (5–12 years): a spot sample collected in the afternoon, and a 12-h overnight collected sample. Concentration of calcium, phosphate, oxalate, uric acid, magnesium, citrate and creatinine was determined in all samples. The solute/creatinine and calcium/citrate ratios were calculated for the detection of metabolic abnormalities.

Results: Diagnosis of hypercalciuria is highly dependent on some conditions that concern sample collection, especially previous food intake. Calcium/creatinine and calcium/citrate ratios are higher in children with a family history of lithiasis. Hyperphosphaturia was detected in 90 % of the studied population. On the contrary, no children showed abnormal oxalate urinary values. Hypomagnesuria and hypocitraturia were mostly conditioned by the period of the day in which samples were collected. Moreover, regarding hypocitraturia, establishing a correct diagnosis is also hindered by the wide range of cut-off points that are reported in the literature

Conclusions: The reference values that are currently used to diagnose urinary metabolic abnormalities do not seem to be adequate for our children population in many cases. It might be of great importance to standardize some methodological issues of the studies that are conducted to describe these values in our geographical area. Moreover, the inclusion of children with a family history of lithiasis may affect the results of these studies

P44 - NOVEL DELETION IN HYPOTONIA-CYSTINURIA SYNDROME

HALIL İBRAHIM AYDIN[1], CENGIZ ZEYBEK[1], JOHN W CREEMERS[2], DUYGU ÖVÜNÇ HACIHAMDIOĞLU[1], SÜLEYMAN KALMAN[1], FAYSAL GÖK[1]

[1]*GULHANE MILITARY MEDICAL ACADEMY ANKARA TURKEY*

[2]*UNIVERSITY OF LEUVEN BELGIUM*

Introduction: Cystinuria type I can be associated with hypotonia-cystinuria syndrome (HCS;MIM 606407), 2p21 deletion syndrome and atypical HCS. HCS that is caused by microdeletions of SLC3A1 and PREPL on chromosome 2p21 presents with generalized hypotonia at birth, failure to thrive, growth retardation, cystinuria type I and inherited as autosomal recessive manner. We here report a novel deletion in a Turkish patient with hypotonia-cystinuria syndrome.

Material and methods: A 9 years old female patient born a consanguineous marriage.

Results: She was diagnosed as lysinuric protein intolerance by hypotonia, feed problems and urine amino acid analysis at the of 2 months and protein restriction and L-citruline therapy was started at another hospital. The patient was reevaluated at the age of 9 years because of the absence of hyperammonemia attacks even high protein intake, normal blood ferritin, lactate dehydrogenase levels and HCS was suspected. There is no sign of nephrolithiasis or urolithiasis. No hypocalcemia, no sign for respiratory chain deficiencies has been noticed. The plasma and Urine amino acid analysis revealed normal plasma and high urine levels of lysine, arginine, ornithine, cystine . The demonstration of a homozygous deletion in SLC3A1 and PREPL genes confirmed the diagnosis of HCS. The deletion extends from the intron between PPM1B and SLC3A1 to the intron between exon 2 and exon 1 of PREPL. All exons of SLC3A1 and all coding exons of PREPL are deleted. Her mother and father's plasma and urine amino acid analysis are normal.

Conclusions: This deletion has not been described before. The deletion extends from the intron between PPM1B and

SLC3A1 to the intron between exon 2 and exon 1 of PREPL. All exons of SLC3A1 and all coding exons of PREPL are deleted. The deletion is homozygous, both parents are carriers.

P45 - FGF23 levels in healthy children and the pediatric predialysis population: uniformity before implementation – a meta-analysis.

ABRAHAM YAEL[1], WESTLAND RIK[1], HEIJBOER ANNEMIEKE C[2], KOSTENSE PIET J[3], KET JOHANNES CF[4], VAN WIJK JOANNA AE[1]
[1]*DEPARTMENT OF PEDIATRIC NEPHROLOGY, VU UNIVERSITY MEDICAL CENTER, AMSTERDAM, THE NETHERLANDS.*
[2]*DEPARTMENT OF CLINICAL CHEMISTRY, VU UNIVERSITY MEDICAL CENTER, AMSTERDAM, THE NETHERLANDS*
[3]*DEPARTMENT OF EPIDEMIOLOGY AND BIOSTATISTICS, VU UNIVERSITY MEDICAL CENTER, AMSTERDAM, THE NETHERLANDS*
[4]*MEDICAL LIBRARY, UNIVERSITY LIBRARY, VU UNIVERSITY MEDICAL CENTER, AMSTERDAM, THE NETHERLANDS.*

Introduction: Fibroblast growth factor 23 (FGF23) has been measured repeatedly in healthy children and pediatric patients in their predialysis phase. However, reference range values and expected FGF23 values for different stages in chronic kidney disease are lacking. This study aims to explore the potential implementation of FGF23 as a renal marker for children.
Material and methods: A meta-analysis was performed to determine FGF23 reference range values in healthy children and evaluate FGF23 levels in the pediatric predialysis population. MEDLINE and EMBASE (from inception until November 2011) were searched without language restriction. Data was pooled and analysed using RevMan 5.1.
Results: Twenty studies, containing 704 healthy children and 509 pediatric predialysis patients, were included for review. For healthy children mean C-terminal FGF23 and intact FGF23 were 70.5 (standard deviation (SD) 32.7, reference range (RR) 16.8-124.1) RU/mL and 30.8 (SD 13.4, RR 8.8-82.9) pg/mL, respectively. Predialysis patients had a mean C-terminal FGF23 of 138.4 (SD 130.6) RU/mL and an intact FGF23 of 59.9 (SD 59.0) pg/mL. A large heterogeneity was found between studies, possibly due to a disorganized categorization in stages of chronic kidney disease, a wide variation in patient age, measurement of either C-terminal FGF23 or intact FGF23, medium of FGF23 measurement and missing data.
Conclusions: Pediatric studies about reference ranges in FGF23 are scarce and heterogeneous in design, methodology and included patients. In order to implement FGF23 in daily pediatric practice, more studies with uniformity in methodology will be of utmost importance.

P46 - Common treatment, rare complication

HITESH PRAJAPATI, ERIC FINLAY
LEEDS GENERAL INFIRMARY

Introduction: We report the case of an 8-year-old boy who has Mowat-Wilson syndrome. In keeping with the characteristics of the syndrome, our patient has dysmorphic features, developmental delay, Tetralogy of Fallot, Hirschsprung's disease and epilepsy. His epilepsy was managed with valproate and his Hirschsprung's disease had needed a subtotal colectomy and colostomy. He also had gastroesophageal reflux and was fed via a jejunal tube.
Material and methods: He presented with a 2 year history of reduced mobility, pain and poor weight gain. He was eventually found to have a femoral fracture. His radiograph showed gross osteopenia and skeletal survey demonstrated old rib and clavicular fractures. Further investigations demonstrated a raised alkaline phosphatase, low serum phosphate and calcium, proteinuria and glycosuria.
Results: It was felt that our patient had an acquired proximal tubulopathy, a rare complication of valproate treatment. He was started on enteral electrolyte supplements and the valproate substituted with levetiracetam. Our patient's course was complicated by status epilepticus and hypocalcaemic tetany. Enteral supplements were increased but the large jejunal solute load with a short colon, led to large stoma losses and acute kidney injury. Enteral input was suspended and changed to parenteral nutrition. Gradually his renal function normalised, mobility improved, he was seizure free and began to thrive.
Conclusions: In keeping with the few case reports in the literature, our patient's tubulopathy has resolved after stopping valproate. Our patient is now off all electrolyte supplementation with negative urinanalysis. His case demonstrates a rare complication of a common treatment and specifically the difficulties of managing a proximal tubulopathy after a long delay in reaching the diagnosis. Since identifying this case we have identified 3 other children with proximal tubular dysfunction all on valproate with gastrostomies. 1 child has made a complete recovery on weaning off valproate and the other two are in the weaning phase.

P48 - Major hypercalcemia revealing subcutaneous fat necrosis in a newborn

BOUCHIREB KARIM, CORBIERE CHRISTINE, BOYER OLIVIA, KRUG PAULINE, LESAGE FABRICE, SALOMON REMI
HOPITAL NECKER

Introduction: Subcutaneous fat necrosis (SFN) is a rare condition characterized by an acute transient hypodermatitis that develops within the first weeks of life. The main complication is hypercalcemia that is most often moderate. We report here a one- month-old girl with a severe hypercalcemia revealing a SFN. Her plasmatic calcium at diagnosis is one of the highest ever reported in this uncommon condition.
Material and methods: Observation: A four-week-old female newborn was seen at the emergency department for failure to thrive, constipation and vomiting. She was born after a caesarean section for a prolonged labor complicated by a meconium aspiration at a gestational age of 41 weeks. Apgar scores were 7 at 1 min and 9 at 5 min. At physical exam, the child was dehydrated and presented with disseminated firm non inflammatory subcutaneous nodules highly suggestive of SFN
Results: Laboratory testing showed a major hypercalcemia of 5.2 mmol/L, with 2.30 mmol/l of ionized calcium. She was treated with a single intravenous pamidronate infusion (0.5 mg/kg) associated to hyperhydration, furosemide (2 mg/kg/day) and prednisolone (2 mg/kg/day). Her milk was also changed to a very low calcium formula, and vitamin D supplements were stopped. Subsequently, calcemia normalized after 5 days and the medications were discontinued. The girl was discharged at day 10. Calcemia 1 week later was mildy increased (2.84 mmol/L). Laboratory studies performed at last follow-up at day 45 revealed the persistence of a mild hypercalcemia (2.77 mmol/L) while the child was still under low calcium formula and without Vitamin D supplements.
Conclusions: Patients with SFN should be closely monitored for hypercalcemia which can be severe. Bisphosphonate treatment should be considered in major or resistant hypercalcemia. A long term monitoring of blood calcium is recommended for 2–3 months. However, the prognosis is good in almost all cases

P49 - Hypocalcemia and seizures: a case of vitamin D-resistant rickets

BéATRICE ROLAND-GOSSELIN, ODILE BASMAISON, BRUNO RANCHIN, ANNE-LAURE LECLERC, ALEXANDRE BELOT, PIERRE COCHAT, JUSTINE BACCHETTA
HOSPICES CIVILS DE LYON AND UNIVERSITé DE LYON

Introduction: Infants with hypocalcaemia usually present with seizures whereas it is less common in older children and teenagers.
Material and methods: We report on a 29 month-old boy with a past of familial consanguinity and seizures beginning at the age of 6 months, arriving in France and presenting with alopecia, stridor and severe skeletal deformations/fractures, in association with a global developmental delay.
Results: He had been receiving valproate therapy since the age of 6 months, a cerebral scan having ruled out a central etiology for seizures; at that time, serum calcium and phosphorus had not been measured. At the time of evaluation, a severe hypocalcemia (1.3 mmol/L with normal circulating proteins) with almost normal 25OH vitamin D3 (70 ng/mL), high circulating 1–25 OH2 vitamin D3 (> 250 pmol/L), and low phosphate levels (0.9 mmol/L) were found, in association with a dramatic increase of both PTH (509 pg/L) and total alkaline phosphatase (ALP, 8960 IU/L). Radiological assessment found multiple fractures, diffuse osteopenia, gross deformations and delayed epiphyseal maturation. All these findings led to the diagnosis of vitamin D-resistant rickets (VDRR), with a likely mutation in the VDR gene (VDRR2). An oral management with calcium 0.1 mmol/kg and calcifediol 150 mcg/kg per day was initially initiated, but failed to correct both the clinical, biochemical and radiological abnormalities. Therefore nocturnal calcium infusions (2, then 3 and 4 mmol/kg per day) on a central catheter were begun, in association with both native and active vitamins D (100 000 IU of cholecalciferol weekly, and 1.5 mg/kg of alfacalcidol daily), and phosphate supplementation (3 mmol/kg per day). After four months, the clinical and radiological parameters have rapidly improved, notably with the beginning of walking and a better mineralization on plain radiographs; in contrast, the biological parameters slowly improved, with a total serum calcium remaining low (1.7 mmol/L) and high ALP levels (4000 IU/L).
Conclusions: Despite its side effects (two infections on the central catheter within the first two months), this intensive management dramatically improved the quality of life of the patient; with this case report, we highlight the interest of checking serum calcium and phosphate in children with growth retardation, seizures and/or unexplained bone deformations, and also discuss the main characteristics and the management of VDRR2, an orphan disease affecting less than 20 patients in France.

P50 - Are overweight and obese children at increased risk for urolithiasis ?

PRZEMYSLAW SIKORA[1], WITOLD KOLLATAJ[2], BEATA BIENIAS[1], MAREK MAJEWSKI[1], HALINA BORZECKA[1], ANNA WIECZORKIEWICZ-PLAZA[1], MALGORZATA ZAJACZKOWSKA[1]
[1]*DEPARTMENT OF PEDIATRIC NEPHROLOGY, MEDICAL UNIVERSITY OF LUBLIN, POLAND*
[2]*DEPARTMENT OF PEDIATRIC ENDOCRINOLOGY AND DIABETOLOGY, MEDICAL UNIVERSITY OF LUBLIN, POLAND*

Introduction: In adults, high body mass index (BMI) associated with urolithiasis (UL) has been reported in numerous studies. Since the prevalence of overweight (OW) and obesity (OB) in our patients with UL was much lower than that in Polish general pediatric population we decided to assess an association between high BMI and UL in children.
Material and methods: The study comprised 63 children aged 12.1+3.6 years with essential OW or OB without UL (group I) and 20 children aged 12.7+3.6 years with essential OW or OB and UL (group II). All analyzed stones contained calcium oxalate (CaOx). Controls consisted of 48 healthy, age- and gender-matched children with normal BMI. According to protocol, 24-hour urinary excretions of crystallization promoters [calcium (Ca), phosphate (P), oxalate (Ox), uric acid (UA)] and inhibitors [citrate (Cit), magnesium (Mg)] were determined and adjusted to body mass (BM), body surface area (BSA) and ideal body mass (IBM). In addition, relative urinary supersaturations (URSs) with CaOx, UA, apatite and brushite were calculated.
Results: When adjusted to BM or BSA, Ca, P, Ox, Cit and Mg excretions were significantly negatively correlated with BMI. If these parameters were adjusted to IBM, only Ca excretion showed weak negative correlation with BMI whereas UA excretion was significantly positively correlated with BMI. When adjusted to IBM, UA excretion was significantly higher and Ca excretion was significantly lower in group I than in controls and group II showed significantly higher Ca and Ox excretions as compared to group I. There were no significant differences between all groups in assessed URSs.
Conclusions: In children, OW and OB seem not to increase the risk of UL despite higher UA excretion. Children with OW or OB and UL and those with normal BMI and UL demonstrate similar metabolic pattern of UL. Available references for 24-hour urinary excretion of solutes are not appropriate for children with high BMI.

P51 - An adolescent girl with nephrocalcinosis, urolithiasis and left-sided hemihypertrophy- a case of medullary sponge kidney

PRZEMYSLAW SIKORA[1], AGNIESZKA BRODZISZ[2], PAWEL WIECZOREK[2], MAREK MAJEWSKI[1], BEATA BIENIAS[1], MALGORZATA ZAJACZKOWSKA[1]
[1]*DEPARTMENT OF PEDIATRIC NEPHROLOGY, MEDICAL UNIVERSITY OF LUBLIN, POLAND*
[2]*DEPARTMENT OF PEDIATRIC RADIOLOGY, MEDICAL UNIVERSITY OF LUBLIN, POLAND*

Introduction: Medullary sponge kidney (MSK) is a rare congenital abnormality characterized by cystic dilatation of the medullary collecting tubules. The disorder is often complicated by nephrocalcinosis, urolithiasis, tubular dysfunctions and urinary tract infection. MSK may be rarely associated with a variety of extrarenal, developmental anomalies including hemihypertrophy or Beckwith-Wiedemann syndrome but for the last decade such cases were not reported.
Material and methods: 17-year old girl was referred to our department for metabolic evaluation of nephrocalcinosis and urolithiasis which were incidentally detected by ultrasonography (US) performed due to abdominal pain.
Results: Medical history showed one episode of acute pyelonephritis at age of 6 years and renal colic at age of 14 years when small solitary renal stone within the pelvicalyceal system (P-CS) of the left kidney was found. Since infancy a leg length discrepancy was observed. The initial US demonstrated hyperechoic medulla and possibility of several small stones within the P-CSs of both kidneys. On physical examination signs of left-sided hemihypertrophy, as evidenced in lower limbs, feet, face and tongue were revealed. These findings justified a performance of further imaging studies- intravenous pyelography (IVP) and contrast computed tomography (CT) which revealed typical signs of MSK including calyceal "brush"- like appearance. Laboratory evaluation showed renal hypercalciuria, hypocitraturia, sterile leukocyturia and normal eGFR. The patient was successfully treated with thiazides and potassium citrate during 1-year follow-up. The treatment of one acute episode of urinary tract infection was also needed.
Conclusions: MSK should be always considered in the differential diagnosis of nephrocalcinosis. However, for specific diagnosis of MSK, potentially harmful radiologic studies as IVP and/or contrast CT are required. The presence of known associated extrarenal abnormalities may facilitate diagnostic decisions.

P52 - SUCCESSFUL TREATMENT OF EARLY RESPIRATORY DYSFUNCTION IN CYSTINOSIS BY NON INVASIVE POSITIVE PRESSURE VENTILATION

MOHAMED EL NAGGARI[1], IBTISAM EL NOUR[1], HUSSEIN AL KINDY[2], AAMIR AL SHAHRABALLY[2], ANAS ALWOGOUD ABDELMOGHETH[3]
[1]*SULTAN QABOOS UNIVERSITY HOSPITAL; PEDIATRIC NEPHROLOGY*
[2]*SQUH; PEDIATRIC PULMONOLOGY*
[3]*SQUH; PEDIATRIC INTENSIVE CARE*

Introduction: Cystinosis is a rare metabolic disorder characterized by lysosomal cystine accumulation leading to multi-organ damage, with kidneys being clinically first affected. Extra-renal symptoms of cystinosis, generally appears after the first decade. Respiratory insufficiency caused by overall respiratory muscle myopathy is a severely

invalidating and sometimes a life-threatening complication of cystinosis.

Material and methods: A 4 years old Omani girl, diagnosed as Infantile Nephropathic Cystinosis at age of 21 months. On initial presentation, she had signs and symptoms of Fanconi Syndrome with detection of pathognomonic corneal cystine crystals. Cysteamine was prescribed for her but the family had no compliance to medications and did not come for follow up for 2 years. The patient presented to the hospital at age of 4 years with severe failure to thrive (weight 6.1 kg <3rd %), pallor, metabolic acidosis, hypophosphatemia, hypokalemia, severe chest deformity with rachitic manifestations and bronchopneumonia with respiratory failure that needed admission to Pediatric Intensive Care Unit (PICU). During her 3 month stay in PICU; she was ventilated with two failed trail of extubated to Continuous Positive Airway Pressure. Challenges for failure of extubation were respiratory dysfunction due to muscle myopathy, electrolyte disturbance, chest deformity, feeding intolerance and infections. Multidisciplinary team was involved for starting Cysteamine gradually tell achieving good response, building up the weight (increased 3 kg) using total parental nutrition and high caloric formula through continuous Nasogastric tube feeding, correction of electrolyte, physiotherapy, play therapy and family support. We started use of CPAP first then shifted to continuous non-invasive positive pressure ventilation (NIPPV). Treatment was monitored clinically by observing respiratory distress, pattern of breathing, level of consciousness and biochemically using arterial blood gas observing respiratory acidosis and carbon dioxide retention. Gradual weaning was done tell reaching Nocturnal NIPVV then until complete stoppage of support.

Results: Patient discharged home with no ventilator support after 4 month of intensive rehabilitation, repeated counseling and family support. We continued on nutritional support by using feeding tube at home. Very close follow up for monitoring of the respiratory status which showed improvement of respiratory dysfunction and normal blood gas results.

Conclusions: Cysteamine is the only available treatment for cystinosis, allowing postponing the deterioration of renal function and the occurrence of extra-renal complications. Cysteamine can deplete cystine accumulation in muscles. When respiratory dysfunction establishes, no treatment options had been described so far. In this reported case, we used NIPPV for correction of hypoventilation and early respiratory dysfunction.

P53 - Pediatric Urolithiasis in Armenia: Major Changes over 2 Decades

ASHOT SARKISSIAN[1], ERNST LEUMANN[3], ALBRECHT HESSE[4], ARA BABLOYAN[2], NINA ARIKYANTS[2]

[1]*YEREVAN STATE MEDICAL UNIVERSITY*
[2]*ARABKIR JOINT MEDICAL CENTRE, YEREVAN, ARMENIA*
[3]*UNIVERSITY CHILDREN'S HOSPITAL, ZURICH, SWITZERLAND*
[4]*EXPERIMENTAL UROLOGY, UNIV. OF BONN, GERMANY*

Introduction: Pediatric urolithiasis, an important health problem in Armenia, is subject to overall living conditions. The aim of the study is to determine whether the changes of the social and economic conditions in Armenia – which were catastrophic in the 90-ies and have since normalized – have had on effect of pediatric urolithiasis.

Material and methods: We studied prospectively all 391 patients aged 1 month to 16 years admitted with urolithiasis from 1992 to 2011 at the Arabkir hospital (national referral center for pediatric nephrology). All calculi were examined by infrared spectroscopy. We compared the data obtained in two decades, 1992–2001 (period I) and 2002–2011 (period II), characterized by major changes in economy and social life in Armenia.

Results: The overall number of children with urolithiasis decreased by 46 %, whereas the distribution of gender and age has remained similar: There were 254 patients (69 % male, mean age 7.8±4.1) in period I versus 137 patients (64 % male, mean age 7.04±4.9) in period II. Period II is characterized, as compared to period I, by a higher proportion of (mostly metabolic) CaOx stones (73 % vs. 65 %) and by lower rates of infectious stones (primarily struvite, 11.7 % vs. 16 %) and of endemic stones (5.8 % vs. 7 %). Most striking is the strong decrease of the number of endemic primary bladder stones from 20 (8 %) to 3 (2 %, $p<0.001$).

Conclusions: In connection with the improved economic situation and better living conditions the incidence of pediatric urolithiasis has nearly halved, mainly as the result of a strong decrease of infectious stones and endemic renal stones and of the near disappearance of primary bladder stones. These changes are presumably the effect of a more balanced nutrition and of better management of pyelonephritis.

P54 - Metabolic features in children with urolithiasis in Elbasan/Albania

IRENA PALLOSHI[1], REZART XHEPA[2], DIAMANT SHTIZA[2], ANYLA BULO[1]

[1]*PAEDIATRIC DISEASE, NEPHROLOGIC DISEASE, HOSPITAL OF ELBASAN, ALBANIA*
[2]*PAEDIATRIC DISEASE, SERVICE OF NEPHROLOGY UNIVERSITY HOSPITAL CENTER OF TIRANA, ALBANIA*

Introduction: The presence of stones in the urinary tract is a significant medical and social problem. It is important to

study the influential factors in stone formation. Objective To study the metabolic abnormalities in the children with urolithiasis .To study the frequency, spread, determinant factors and composition of kidney stones in the children of Elbasan city in Albania.

Material and methods: In a prospective study during one year we studied 37 children (20 boys), aged 8±3DS; that presented with blood in urine, recurrent UTI, renal colic or with ultrasonography positive regarding kidney stones. We make laboratory analyses: microscopic and urine culture, pH, complete blood count, renal function, 24 hour urine collection (2 measures) for magnesium, sodium, uric acid, potassium, calcium, citrate, oxalate and phosphate. Demographic features, diet, liquid consumption were recorded.

Results: The incidence of kidney stones in children of Elbasan is 0,4 ‰. Twelve of children live in the city and the others in rural area; 37.8 % have positive familial history for renal calculi; male/female ratio is1.17:1 We found pelvic stones in 89.1 % of cases, ureter stones in 8.3 % and bladder stones in 2.7 %. We studied the stones with infrared spectroscopy; we found cystine stones in 14 %, uric acid 14 %, struvite 14 %, calcium phosphate 14 %, calcium dehydrate 14 %, calcium monohydrate 28 %. Ca/Cr ratio in 24 hours urine is 2.008 and Na/K ratio is 11.049

Conclusions: Kidney stones are predominant in rural areas. The predisposed factors of kidney stones are low fluid intake and high dietary intake of protein and sodium consummating (pickles and junk). The calcic lithiase is dominant (58 %)

P55 - Urinary lithogenic risk in a healthy school-children population in Mallorca

Mª CONCEPCIóN SáEZ DE BARROSO[1], Mª DOLORES RODRIGO JIMéNEZ[2], FELIX GRASES[1], GUILLEM FRONTERA[3], CRISTINA GóMEZ[4], ANA MARIA GARCIA RAJA[1], JAVIER LUMBRERAS[2], Mª CONCEPCIóN MIR PERELLO[2]

[1]*LABORATORY OF RENAL LITHIASIS RESEARCH, UNIVERSITY OF BALEARS ISLANDS.*

[2]*PEDIATRIC NEPHROLOGY DEPARTMENT. SON ESPASES HOSPITAL.PALMA DE MALLORCA.*

[3]*RESEARCH INSTITUTE. SON ESPASES HOSPITAL. PALMA DE MALLORCA*

[4]*LABORATORY DEPARTMENT.SON ESPASES HOSPITAL. PALMA DE MALLORCA*

Introduction: Pediatric and adult lithiasic patients show similar underlying risk factors suggesting that predisposition to renal lithiasis may begin in childhood.The present study was conducted to evaluate the lithogenic risk in urine samples from a healthy school children population and determine which urine parameters were more associated with this risk.

Material and methods: Urine samples were obtained from 184 children (5–12 years): a spot sample collected in the afternoon, and a 12-h overnight sample. For each sample, stone risk biochemical parameters were measured as well as urine volume and pH values. Lithogenic urine was defined by the presence of some urine conditions that had previously demonstrated to be associated to stone formation.

Results: There was a high prevalence of lithogenic risk in the studied population. It was 15 % in the spot urine samples and 54 % in 12-h samples. Although metabolic abnormalities were more frequently detected in the group of children with lithogenic urines, the factor which was more strongly associated with a positive risk was a low urine volume. Children with a family history of lithiasis showed higher calcium excretion and calcium/citrate ratio.

Conclusions: This study reveals a high prevalence of lithogenic risk in urine among healthy children, especially in children with a family history of the disease. A low urine volume was the factor which was more strongly associated with the increased risk. Achieving an adequate fluid intake at early ages could be a simple and effective preventive measure to reduce the incidence of nephrolithiasis.

P56 - A RARE CAUSE OF URETERAL THICKENING: URETERAL LYMPHOMA

MERAL TORUN BAYRAM[1], SALIH KAVUKCU[1], MUSTAFA OLGUNER[2], ÖMER EGE[3], HANDAN CAKMAKCI[4], ALPER SOYLU[1], MEHMET ATILLA TURKMEN[1]

[1]*DOKUZ EYLUL UNIVERSITY MEDICAL FACULTY, DEPARTMENT OF PEDIATRICS, IZMIR, TURKEY*

[2]*DOKUZ EYLUL UNIVERSITY MEDICAL FACULTY, DEPARTMENT OF PEDIATRIC SURGERY, IZMIR, TURKEY*

[3]*KENT HOSPITAL, DEPARTMENT OF UROLOGY, IZMIR, TURKEY*

[4]*DOKUZ EYLUL UNIVERSITY MEDICAL FACULTY, DEPARTMENT OF RADIOLOGY, IZMIR, TURKEY*

Introduction: Ureteral thickening is a cause of urinary tract obstruction. Differential diagnosis includes infectious and inflammatory disorders, vasculitides and malignancies. Herein we present a case of hydronephrosis associated with ureteral wall thickening due to ureteral lymphoma.

Material and methods: 12-year-old male patient was referred for azotemia detected upon evaluation for anorexia, vomiting and weight loss fort he last 2 weeks. Physical examination was normal. Laboratory tests revelaed azotemia, anemia and elevated acute phase response; imaging studies showed bilateral hyroureteronephrosis.

Results: He was considered to have obstructive acute renal injury. Retrograde pyelography during cystoscopy revealed filling defects causing segmental narrowing in both ureters.

Ureteroscopy demonstrated a circular structure which is probably associated with muscular hypertrophy in the distal part of left ureter causing narrowing in that ureter segment. Right ureteral wall thickness was also found to be increased in MR urography. Renal functions improved upon insertion of ureteral catheters. Laboratory evaluation for the differential diagnosis of ureteral thickening including urine culture, PPD, chest x-ray, immunologic tests and mutational analysis of MEFV gene were normal. Pathoogic examination of the bladder and ureteral biopsy samples were consistent with lymphoma.

Conclusions: Primary malignant lymphoma of the ureter is rare and its diagnosis is difficult. However, it should be considered in the differential diagnosis of patients with ureteral wall thickening.

P57 - METABOLIC DISORDERS IN PEDIATRIC UROLITHIASIS

VALERIA ZANGARA, MARIA MICHELA D'ALESSANDRO, CIRO CORRADO, MARIA CHIARA SAPIA, SILVIO MARINGHINI

PEDIATRIC NEPHROLOGY. "G. DI CRISTINA" HOSPITAL. PALERMO

Introduction: The prevalence of urolithiasis (UR) in children has increased in the last years. Nowdays it is possible identify some predisposing risk factors for UR.

Material and methods: We enrolled 59 consecutive patients (37 M/ 22 F) with documented urinary calculi, by renal ultrasonography, median age 9 years (range 3–17 years), referred to our Department in the last 2 years. We measured, two months after hospitalization and without therapy, in 24-hour urine in toilet-trained patients and in a random urine sample in infants: Oxalate (Ox), Cytrate (Cit), Uric acid (Uric), Calcium (Ca) and Creatinine (Cr). In an urine sample taken two hours later, continuing fasting, we analyzed "fasting urine" levels of Ox, Cit and Ca. We used Ion-chromatographic (IC) techniques for determination of urinary Oxalate, enzymatic methods for determination of urinary Citrate. A group of 120 healthy children comparable for age and sex were used as control.

Results: We found a metabolic disorder (MD) in 57 patients (97 %). We documented Hypercalciuria (HyCa) in 16 patients (27,1 %), Hypocitraturia (HyCit) in 7 patients (11,9 %), Hyperoxaluria (HyOx) in 17 patients (28,8 %). Nobody had Hyperuricosuria. In 42 children we observed mixed MD: HyOx+HyCa, HyOx+HyCit, HyCa+HyCit, HyOx+HyCit+HyCa. Twenty three patients showed abnormalities only in fasting urine (UF): Hypercalciuria in 5 patients (8.5 %), Hypocitraturia in 10 patients (16,9 %), Hyperoxaluria in 8 patients (13.5 %). We didn't find any correlation of MD with age, sex and family history of UR.

Conclusions: In our study we found a high prevalence of MD in children affected by UR. The most common etiologic factors of calculus formation were Hypercalciuria and Hyperoxaluria in 24-hour urine or urine sample. We found elevated UF levels of Hyperoxaluria, Hypercalciuria and Hypocitraturia in a high percentage of our patients. We raccomend evaluation on UF in all children with urinary stones.

P58 - Microalbuminuria among children from families with Balkan Endemic Nephropathy

ANELIA BOUEVA, POLINA MITEVA, SVETLANA MARINOVA, DIMITER ROUSSINOV, MARIA GAYDAROVA, GALIA ZLATANOVA, STANISLAV STEFANOV, TONKA LISICHKOVA, SNEGANA GANEVA, TATIANA TSANOVA

MEDICAL UNIVERSITY, SOFIA, BULGARIA

Introduction: Objectives: Balkan Endemic Nephropathy (BEN) is a tubulointerstitial kidney disease. The final stage of BEN is characterized by renal failure. Cases of BEN were first described in Bulgaria in 1956. Its cause is still unknown. The exact number of patients has never been known. The mortality of endemic nephropathy in endemic villages is extremely high. The patients in the early and latent stages always remain undetected. Invariably these are children from families with BEN.

Material and methods: Methods: In a Bulgarian screening study performed between 2010 and 2012 almost 4000 children were included. 60 children were from families with a history of BEN. We investigated the prevalence of urine abnormalities- especially microalbuminuria, blood pressure, BMI, GFR by Schwarz formula and we also made a US of the kidney. Microalbuminuria was checked by dipstick measurement- Microalbu PHAN. Positive reaction was defined as albumin/creatinine ratio above 3.4 mg/mmol.

Results: Results: All of the children were positive for microalbuminuria.

Conclusions: Conclusion: The onset of BEN is in childhood.

P59 - Urinary stone disease in children- a single Croatian center experience

DANKO MILOSEVIC[1], DANICA BATINIC[1], MARIJA TOPALOVIC-GRKOVIC[2], LJILJANA NIZIC[1], KRISTINA VRLJICAK[1], ANJA TEA GOLUBIC[1], MIRJANA POROPAT[3], MAJA LEMAC[1], DANIEL TURUDIC[1]

[1]*UNIVERSITY HOSPITAL CENTER ZAGREB, DEPARTMENT OF PEDIATRIC NEPHROLOGY*

[2]*UNIVERSITY HOSPTAL CENTER ZAGREB, DEPARTMENT OF ANESTESIOLOGY AND INTESIVE CARE*

[3]*UNIVERSITY HOSPITAL CENTER ZAGREB, DEPARTMENT OF NUCLEAR MEDICINE*

Introduction: Urinary stone disease is not so rare in children. The aim of this study was to assess the demographic, clinical and biological characteristics, as well as outcome, of urinary stone disease among Croatian children.
Material and methods: We reviewed medical records of 76 children from various parts of Croatia who were diagnosed with urinary stone disease from 2002–2011.
Results: The average age (mean) were 9 yr 7 mo (toddlers 7.89 %) with approximately equal gender distribution (male 53.95 % vs female 46.05 %). Family affection was identified in 27 (35.53 %) children with the predominance of female transmission. The most stones were made of Ca oxalate dihydrate and monohydrate (75 %). Hypercalciuria were detected in 47.37 %, mild hyperoxaluria in (13.16 %), hypocitraturia in 1.31 % and 38.16 % remained of idiopathic origin. Urine saturation (EQUIL 2) were above the limits in 47 (61.84 %) children, urine volume less than average in 12 (15.79 %). For most of the children we recommended increased fluid intake and balanced food nutrition, citrate were administered in 20 (26.32 %), thiazides in 10 (13.15 %) and aldactone in 1 (1.31 %). Spontaneous evacuation were noticed in 51.32 %, surgical (operation and endoscopic removal) 11.84 %, ESWL in 11 .84 %, spontaneous resolution (ceftriaxone) in 1 (1.31 %) and in 13.16 % the stone was not removed from urinary tract.
Conclusions: The study gave insight in etiology of urinary stone disease in Croatian children. Main pathological factors were hypercalciuria, mild hyperoxaluria and increased urine saturation. Spontaneous evacuation of stones were notified for most of chldren.

P60 - Combined Calcium-sensing-receptor (CaSR) mutation and HNF1b deletion: additive effect on electrolyte abnormalities?

YVETTE KONIJNENBERG, LIANNE KRAB, JACQUES GILTAY, MARC LILIEN
UNIVERSITY MEDICAL CENTRE UTRECHT

Introduction: Benign familial hypocalciuric hypercalcaemia (FHH) is an established cause of hypercalcaemia. Patients generally exhibit mild to moderate asymptomatic hypercalcaemia with high-normal or slightly elevated magnesium and parathyroid hormone levels. Here we describe an aggravated phenotype in a child with both an inactivating CaSR mutation and a HNF1B deletion.
Material and methods: The child was diagnosed antenatal with a unilateral multicystic dysplastic kidney, which was removed at age 10 months. At follow-up the remaining kidney showed enlargement and multiple cysts which prompted us to test for abnormalities in the HNF1B gene. Routine laboratory check-ups revealed a severe hypercalcaemia (range 2.97–3.17 mmol/l) with hypocalciuria (calcium/creatinin ratio <0.17 mmol/mmol), mild hypophosphataemia (0.9-1.0 mmol/l) and low-normal magnesium (0.69–0.75 mmol/l). The child showed non-specific symptoms (mild constipation and fatigue) without polyuria or polydipsia. Her estimated GFR (Schwartz) was normal. Both the childs mother and maternal grandfather showed mild normocalciuric hypercalcaemia (calcium respectively 2.84 and 2.82 mmol/l). Mother had normal kidneys without cysts.
Results: The child, the mother and maternal grandfather were shown to harbour a heterozygous CaSR missense mutation (c.2383 C>T(p.Arg795Trp). Furthermore, arrayCGH showed a, de novo, 2.1 Mb deletion of 17q12, including the HNF1B-gene, in the child.
Conclusions: The severe hypercalcaemia in this child, opposed to the mild hypercalcaemia observed in her family members harbouring only the CaSR mutation, illustrates a more severe imbalance in electrolyte homeostasis. This might be due to the specific combination of aberrant CaSR and HNF1B signalling. The expected hypermagnesaemia in FHH is probably counteracted by the diminished HNF1B mediated FXYD2 transactivation in our patient. This case shows the in vivo interaction of two independent genetic defects on electrolyte patterns and serves to alert physicians to critically appraise unexpected electrolyte patterns even in the presence of a known mutation.

P61 - Long term prognosis of our cohort of patients with genetically confirmed Bartter syndrome (BS) type II & III

LEIRE MADARIAGA[1], ALEJANDRO GARCíA-CASTAñO[1], PéREZ DE NANCLARES GUSTAVO[1], INMA NADAL[2], MIREIA AGUIRRE[1], LUIS CASTAñO[1], GEMA ARICETA[1]
[1]*CRUCES HOSPITAL (BILBAO-SPAIN)*
[2]*VIRGEN DEL CAMINO HOSPITAL (PAMPLONA-SPAIN)*

Introduction: Few reports about long term prognosis of BS in adults are available. The aim of our study was to describe long-term clinical and renal outcome of 15 patients with BS II & III, genetically confirmed. Mean time of follow-up since diagnosis was 18±8.6 years (5 years minimum)
Material and methods: Two patients had mutations in ROMK (BS II) and 12 in CLCNKB (BS III) genes. We collected data of estimated GFR, height (SDS), serum potassium levels (K), proteinuria and nephrocalcinosis at diagnosis (i) and at the end of follow-up (f).
Results: Both BS II cases had prenatal onset and the diagnosis was made in the first month of life. Mean follow-up was 18.5 years. Collected data were: Ki 4.3 & 5.7 mEq/L, Kf 2.9 & 3.1 mEq/L; eGFRi 77 & 60 ml/min/1.73 m2, eGFRf 109 & 111 ml/min/1.73 m2; protenuria was absent at diagnosis and final visit. Severe nephrocalcinosis was present in both cases at diagnosis and persisted at long term.

Patients with BS III were diagnosed at a median age of 2.15 years (range: 0.6-16). Their median follow-up was 17 years (range 5.5-35). Mean eGFRi and eGFRf was 109.6 & 161.5 ml/min/1.73 m2, respectively. eGFRf was slightly below normal in 2 patients at final control (89 & 83 ml/min/1.73 m2). Mean and SD of Ki and Kf was 2.5 & 2.68 mEq/L, respectively. An improvement in growth from diagnosis was detected: mean SDSi −1.98 & SDSf −0.28. Nephrocalcinosis was present at diagnosis in 2 patients and persisted in one of them at the end of the follow-up. Proteinuria was only seen in one patient at diagnosis, and it became negative.

Conclusions: Unlike other reported series, long term renal prognosis in our BS patients was good, and persistant proteinuria was not detected in any case. However, hypokaliemia was constant throughout the follow-up despite treatment. Adequate clinical control could explain that evolution and the significant growth improvement. The persistence of nephrocalcinosis in both patients with BS II might compromise renal prognosis in adult life.

P62 - Determination in two moments of the day of two lithogenic risk factors in the urine of children with prelithiasis

MARIA ISABEL LUIS YANES[1], MARGARITA MONGE-ZAMORANO[1], MARIA JOSE HERNáNDEZ-GONZALEZ[1], FATIMA FRAGA- BILBAO[2], SILVIA GONZALEZ-CERRATO[1], VICTOR M GARCIA-NIETO[1]

[1]*PEDIATRIC NEPHROLOGY UNIT, HOSPITAL UNIVERSITARIO NUESTRA SEñORA DE CANDELARIA, SANTA CRUZ DE TENERIFE*

[2]*HOSPITAL UNIVERSITARIO DE CANARIAS.LA LAGUNA TENERIFE*

Introduction: Urolithiasis is a complex entity in which involved various genetic and environmental factors, especially the diet. Most children with kidney stones carry a metabolic abnormality among the hypercalciuria and hypocitraturia are the most prevalent. Citrate is a direct inhibitor of calcium phosphate precipitation and growth of crystals of calcium oxalate. Various procedures have been established to assess potentially crystallizing properties of urine.

Material and methods: We studied 48 children (18 V, 30 M) diagnosed prelithiasis in the metabolic study. None of them received drug treatment. The concentrations of calcium, citrate and creatinine in two urine samples collected one at bedtime and the other when the patient wake up. Calculations if they had scored in two successive scans and if there was a history of urolithiasis in relatives of 1 and / or 2 nd degree. To evaluate the results obtained using the criteria of Grases et al. establishing that urine is potentially a lithogenic if the calcium concentration is greater than 0.27 mg / dl. and / or the ratio of calcium / citrate is greater than 0.33

Results: At night, the calcium concentration ratio and the value of calcium / citrate were increased in 16.7 % (n=8) and in 33.3 % (n=16) of the samples, respectively . In the morning urine, the concentration of calcium and the value of the ratio calcium / citrate were elevated in 33.3 % (n=16) and 70.8 % (n=34), respectively. No differences in the parameters studied on the basis of the existence (n=21) or not (n=27) stones ultrasound. Relationship was observed between the ratio calcium / citrate morning high and a family history of urolithiasis (chi-square, p=0.02)

Conclusions: Like other body parameters, urinary calcium and citrate are changed throughout the day. The urine formed at night is more lithogenic, so you should take appropriate dietary measures and increased water intake at night to avoid, where possible, the possibility of crystallization of calcium salts.

P63 - MOLECULAR GENETIC DIAGNOSIS OF BARTTER SYNDROME (BS) TYPE III

ALEJANDRO GARCíA-CASTAñO[1], GUSTAVO PéREZ DE NANCLARES[1], ALVARO MADRID[2], INMA NADAL[3], ELENA LUCAS[6], LAURA ESPINOSA[4], JULIA FIJO[5], MAR ESPINO[7], LEIRE MADARIAGA[1], MIREIA AGUIRRE[1], LUIS CASTAñO[1], GEMA ARICETA[1]

[1]*CRUCES HOSPITAL (BILBAO-SPAIN)*

[2]*VALL D'HEBRON HOSPITAL (BARCELONA - SPAIN)*

[3]*VIRGEN DEL CAMINO HOSPITAL (PAMPLONA-SPAIN)*

[4]*LA PAZ HOSPITAL (MADRID-SPAIN)*

[5]*VIRGEN DEL ROCíO (SEVILLA - SPAIN)*

[6]*MANISES HOSPITAL (VALENCIA - SPAIN)*

[7]*FUNDACIóN ALCORCóN (MADRID-SPAIN)*

Introduction: The p.Ala204Thr mutation in the CLCNKB gene (exon 7) is a "founder" mutation responsible of most cases of Bartter syndrome (BS) type III in Spain. However, some patients have other different mutations. Aim: To perform the genetic diagnosis in our cohort of Spanish patients with BS type III

Material and methods: Population: 26 affected patients (18 women) belonging to 23 families with clinical diagnosis of BS type III. Methods: Diagnostic algorithm: first, detection of the founder mutation; second, MLPA and structural study of the whole CLCNKB gene.

Results: 15 patients from 15 families were homozygous for the p.Ala204Thr mutation (57.6 % of the overall patients). Further, 8 patients from 5 families were compound heterozygotes for the p.Ala204Thr mutation, and had associated other CLCNKB gene mutations: p.Met1_His654del in 3 cases (2 siblings); p.Val170Met in exon 6 in one case; and

p.Glu442Gly in exon 14 in 4 cases (3 siblings). The latter mutation has not been previously described. Another two patients had two not previously described mutations in compound heterozygosis: one presented the new mutation p.Ile398_Thr401del in exon 12, associated with the p.Met1_His654del mutation, and the other one carried the new c.1756+1 G>A splice-site mutation in exon 7, as well as the previously reported p.Ala210Val change. One case turned out to be negative in our genetic screening. Finally, 41 relatives with heterozygous mutations in CLCNKB were considered carriers.

Conclusions: BS type III is genetically heterogeneous in Spain. The high frequency of the founder mutation c.610 G>A; p.Ala204Thr justifies its initial detection, but the complete genetic study of the CLCNKB gene is required in many cases. We found three not previously described mutations in the CLCNKB gene: p.Glu442Gly (exon 14); c.1756+1 G>A (exon 7) and p.Ile398_Thr401del (exon 12).

P64 - A New Splicing Mutation of SCNN1A: Severe Neonatal Pseudohypoaldosteronism Type 1 with Normal Growth

ZELAL EKINCI[1], MEHMET BAHA AYTAC[1], HAE IL CHEONG[2]
[1]*KOCAELI UNIVERSITY SCHOOL OF MEDICINE*
[2]*SEOUL NATIONAL UNIVERSITY CHILDREN'S HOSPITAL*

Introduction: Pseudohypoaldosteronism Type 1 (PHA1) is characterised by mineralocorticoid hormon resistance and presents with hyponatremia, hyperkalemia, metabolic acidosis, high renin and aldosterone levels in the neonatal period. Excessive salt loss from the renal tubulus, colon, sweat and salivary glands is the hallmark of generalized form of the disease. Here we present a case of generalized pseudohypoaldosteronism type 1 whose genetical analysis revealed homozygous mutation in intron 4 of alpha ENaC gene (c.684+2 T>A).

Material and methods:

Results: Case report:A nine day-old girl from consanguinous parents, presented with dehydratation, failure to thrive, cyanosis, hypotermia and bradycardia. Hyponatremia (123 mEq/l), hyperkalemia (8.4 mEq/l), high renin (43 ng/ml/h), aldosterone levels (3500 pg/ml) and accompanying positive sweat testing (133 mmol/l) revealed the diagnosis of generalized pseudohypoaldosteronism type 1. Intravenous fluid therapy containing 60 mEq/kg/d of sodium, bicarbonate infusion for metabolic acidosis, polystren sulfonate and nebulised salbutamol against hyperkalemia were started. As dehydratation resolved, laboratory remission was maintained by oral sodium chloride (30 mEq/kg) and sodium bicarbonate (18 mEq/kg) administration. She was discharged on 35th day with 6x4 gr polystren sulfonate, hydrochlorothiazid (2 mg/kg) and indomethacin (1 mg/kg) therapy. The patient has been being followed up for 2 years without any deterioration on her clinical status and weight gain was appropriate even feeding with a nasogastric tube. Also, renin and aldosteron levels were relatively decreased. Analysis of SCNN1A (alpha ENaC) gene stated a homozygous mutation (c.684+2 T>A) in 4th intron, that was not reported previously for PHA1.

Conclusions: The mutation of the patient is located at the splicing site and is definitely a pathogenic one. This patient is a demonstrative example of distinct genotype-phenotype relationship in multisystemic PHA1 patients.

P65 - Native vitamin D supplementation in general populations : beware of genetic polymorphisms in the vitamin D-dependent genes

ODILE BASMAISON, JUSTINE BACCHETTA, AURELIA BERTHOLET-THOMAS, ANNE-LAURE LECLERC, DELPHINE DEMEDE, PIERRE COCHAT, BRUNO RANCHIN
CENTRE DE REFERENCE DES MALADIES RENALES RARES, HOPITAL FEMME MERE ENFANT, BRON, FRANCE

Introduction: Vitamin D supplementation is very effective in preventing rickets and, as suggested by recent studies, could have positive outcomes on general health, notably with beneficial effects on the immune and cardiovascular systems. These findings, along with the worldwide increase in vitamin D deficiency, should extend its use in the future. However, side effects can occur, when using high doses or in genetically predisposed patients.

Material and methods: We described 14 patients (9 families) suspected of vitamine D hypersensitivity.

Results: Children were aged from 2 days to 16 years at the time of diagnosis. Four had nephrolithiasis, 4 had nephrocalcinosis, 3 had both. Seven had experienced hypercalcemia, with severe episods (> 3 mmol/l) in 2 cases. Seven had hypercalciuria. Seven were asymptomatic (incidental discovery, or siblings of previously diagnosed patients). Eight had received Vitamin D prophylaxis. A familial history of nephrolithiasis was found in 6 families. 25OH vitamin D levels were normal or low in all cases, with PTH levels within or below the lower normal range. In contrast, 1,25 (OH)2 vitamin D levels were markedly increased in 6 cases, and were unexpectedly high for the low values of 25OH vitamin D in all patients. No symptoms of sarcoidosis was detected. These observations suggested that our patients have an abnormal metabolism of 1,25 (OH)2 vitamin D. The sequencing of CYP27B1 gene, encoding for 1α-hydroxylase, showed no mutation in the largest family (n=5 children). Analyses of CYP24A1 gene, encoding for 24-hydroxylase, are ongoing.

Conclusions: These data confirm the previous observations of genetic vitamin D hypersensitivity. Familial history of nephrolithiasis and/or hypercalcemia should therefore be ruled out in every child before beginning vitamin D supplementation ; in case of relevant familial history, the modalities of the supplementation should be discussed, so as to avoid potentially severe side effects.

P66 - Erythropoietin resistant anemia in an infant with end stage renal disease: Oxalosis.

CANER ALPARSLAN, ENGIN KOSE, SEDA SIRIN KOSE, ALKAN BAL, ONDER YAVASCAN, NEJAT AKSU

TEPECIK TRAINING AND RESEARCH HOSPITAL, PEDIATRIC NEPHROLOGY, IZMIR, TURKEY

Introduction: We report a 6-month old girl with erythropoietin (EPO) resistant anemia characterized by severe oxalate deposition in the bone marrow due to systemic oxalosis.

Material and methods: This girl was referred for evaluation of failure to thrive and episodes of cough and fast breathing for three days.

Results: Physical examination revealed a weight of 5700 gr (25–50 p), a height of 55 cm (3–10 p), a head circumference of 39 cm (3–10 p), a blood pressure of 80/50 mmHg (<90 p / <90 p), a pulse rate of 180 beats/min, a respiratory rate of 60/min, and a body temperature of 370 C. The patient was found to have skin pallor and altered sensorium. Chest examination showed wheeze and fine crackles. Her liver was palpable 2 cm below the right costal margin. Laboratory data were as follows; hemoglobin (Hb) 9.2 gr/dl, hematocrit (Htc) 28.5 %, white blood cells (WBC) 24.700/mm3, platelet count 499.000/mm3, erythrocyte sedimentation rate 58 mm/h, serum creatinine 4.4 mg/dl, urea 102 mg/dl, creatinin clearance 8 ml/min/1.73 m2, total protein 5.4 gr/dl, albumin 3.3 gr/dl, sodium (Na+) 141 mmol/l, potassium (K+) 3.5 mmol/l, calcium (Ca++) 9.6 mg/dl, phosphorus (P+) 9.8 mg/dl, pH 7.24, pCO2 28 mmHg, bicarbonate 11 mEq/l, base excess −14. Urinary sodium 54 mmol/l (N: 40–220 mmol/l) and chloride 126 mmol/l (N: 112–150 mmol/l) levels were normal. Plain abdominal radiography showed big and nearly bone density kidneys. Renal ultrasound scan and abdominal computed tomography demonstrated hyperechogenic kidneys with intensive medullary calcinosis and bilateral nephrocalsinosis, respectively. She experienced EPO resistant anemia.

Conclusions: Primary hyperoxaluria should be kept in mind that oxalate deposition in bone marrow should be considered in infants with end stage renal disease due to nephrocalcinosis, especially when they present with EPO resistant anemia.

P67 - A 7 month old girl with early diagnosed familial hypomagnesemia-hypercalciuria and prominent medullary nephrocalcinosis

HAVVA EVRENGÜL[1], ŞEBNEM ŞAHIN[2], ÖZLEM BUĞA[2], İPEK ÖZUNAN AKIL[3]

[1]*CELAL BAYAR UNIVERSITY, SCHOOL OF MEDICINE, DEPARTMENT OF PEDIATRIC NEPHROLOGY*

[2]*CELAL BAYAR UNIVERSITY, SCHOOL OF MEDICINE, DEPARTMENT OF PEDIATRICS*

[3]*PROF, CELAL BAYAR UNIVERSITY, SCHOOL OF MEDICINE, DEPARTMENT OF PEDIATRIC NEPHROLOGY*

Introduction: Familial hypomagnesemia with hypercalciuria and nephrocalcinosis is an autosomal recessive renal tubular disorder characterized by renal magnesium wasting, hypercalciuria, advanced nephrocalcinosis and progressive renal failure.

Material and methods: 4-month-old female infant was referred for investigation after a documented febrile urinary tract infection. Her growth and physical examination were normal. Her parents were 2nd degree relatives. Ultrasound examination of the kidneys demonstrated bilateral diffuse medullary nephrocalcinosis. Serum urea (26 mg/dl) and creatinine (0.3 mg/dl) were normal. Her serum and urine biochemistry revealed hypomagnesemia (1 mg/dl), and hypercalciuria (ca/cr 1.26 mg/mg) and hypermagnesuria (FeMg 6 %). Her parent's serum magnesium levels and urinary calcium excretion levels were normal. Arterial blood gas analysis was normal. Serum parathyroid hormone level was 63 ng/ml (normal: 15–65 ng/ml). Urinary excretions of oxalate and sistin were normal and urinary excretions citrate was decreased. The results of ophthalmologic examination and audiogram were normal. In our patient we thought that familial hypomagnesemic hypercalciuric medullary nephrocalcinosis with clinical findings of hypomagnesimia, hypermagnesiuria, hypercalsiuri and medullar nephrocalcinozis. We started oral magnesium citrate and hydrochlorothiazide treatment.

Results: Paracellin-1 gene mutation analyze was performed, but the result of the test has not yet completed.

Conclusions: Familial hypomagnesemia with hypercalciuria and nephrocalcinosis is a rare renal tubular disease. Clinical manifestations can vary from mild to severe symptoms. Thus a high index of clinical suspicion is needed, especially for the differential diagnosis of medullary nephrocalcinosis. Despite the absence of a specific treatment, early diagnosis, treatment and regular follow-up should be performed with the aim of reducing the complications of the disease. We want to present our case because of it was early diagnosed.

P68 - CLINICAL AND BIOCHEMICAL CHARACTERISTICS OF UROLITHIASIS IN CHILDREN BELOW 4 YEARS OF AGE.

BOCHNIEWSKA VIOLETTA[1], JUNG ANNA[1], KALICKI BOLESLAW[1], LITWIN MIECZYSLAW[1]
[1]*DEPARTMENT OF PEDIATRIC, NEPHROLOGY AND ALLERGOLOGY, MILITARY MEDICAL INSTITUTE, WARSAW, POLAND*
[2]*DEPARTMENT OF NEPHROLOGY &ARTERIAL HYPERTENSION, THE CHILDREN'S MEMORIAL HEALTH INSTITUTE, WARSAW, POLAND*

Introduction: The aim of the study was to analyze clinical and biochemical characteristics of urolithiasis in children below 4 years of age.
Material and methods: Patients and methods: retrospective analysis of cases of urolithiasis in 106 children (60 boys) in age from one month to 3 years.
Results: Results: 94 pts (88,68 %) had renal stones (in 19 bilateral), 9 (8,5 %) had ureteral stones, 2 had bladder stones and one in ureter. Urinary tract infection (UTI) was the first clinical presentation in 48/106 (45,28 %), abdominal pain in 11/106 (10,38 %), renal colic in 10/106 (9,43 %), hematuria in 8/106 (7,55 %), fever in 8/106 (7,55 %), poor weight gain in 8/106 (7,55 %) pts. 16 children were asymptomatic. Erythrocyturia was found in 36/106 (33,96 %), leucocyturia in 30/106 (28,30 %), and albuminuria in 21/106 (19,81 %) pts. Metabolic abnormalities were found in 87/106 pts (82,07 %): hypercalciuria 60/87 (68,97 %), hyperoxaluria 46/87 (52,87 %), hyperphosphaturia 41/87 (47,13 %), hyperuricosuria 32/87 (36,78 %), cystinuria 3/87 (3,45 %). Mixed disorders were present in 59/87 (67,82 %) pts: hypercalciuria and hyperoxaluria in 17/87pts (19,54 %), hypercalciuria, hyperoxaluria, hyperuricosuria and hyperphosphaturia in 12/87 pts (13,79 %), hypercalciuria and hyperphosphaturia in 7/87 pts (8,04 %), hypercalciuria, hyperoxaluria and hyperphosphaturia in 7/87 pts (8,04 %), hyperuricosuria and hyperphosphaturia in 4/87 pts (4,60 %), hypercalciuria, hyperoxaluria and hyperuricosuria in 3/87 pts (3,45 %), hyperoxaluria and hyperphosphaturia in 3/87 pts (3,45 %), hypercalciuria and hyperuricosuria in 3/87 pts (3,45 %), hypercalciuria, hyperuricosuria and hyperphosphaturia in 2/87 pts (2,30 %), hyperoxaluria and hyperuricosuria in 1/87 pts (1,15 %). 28/87 (32,18 %) pts presented isolated abnormalities: hypercalciuria in 9/87 (10,34 %), hyperoxaluria 3/87 (3,45 %), hyperphosphaturia in 6/87 (6,90 %), hyperuricosuria in 7/87 pts (8,05 %), and cystinuria in 3/87 (3,45 %) pts. Recurrent UTI was present in 47/106 (44,34 %), urinary tract abnormalities in 13/87 (12,26 %), and excessive vitamin D3 supply in 3/106 (2,83 %) pts.
Conclusions: Conclusion: hypercalciuria and recurrent UTI were the most frequent abnormalities. Complex metabolic disorders were two times more common than isolated abnormalities.

P69 - Osteopetrosis with renal tubular acidosis in a girl of Gypsy origin

VIKTOR JANKó[1], YAIR ANIKSTER[2], LáSZLó KOVáCS[1]
[1]*DEPARTMENT OF PEDIATRICS, COMENIUS UNIVERSITY MEDICAL SCHOOL, BRATISLAVA, SLOVAKIA*
[2]*SAFRA CHILDREN'S HOSPITAL, TEL-HASHOMER, ISRAEL*

Introduction: The rare bone thickening disease osteopetrosis occurs in various forms. One of them accompanied by renal tubular acidosis (RTA) is known as Guibaud-Vainsel syndrome. Clinical manifestations of this autosomal recessive syndrome comprise increased bone density, growth failure, intracerebral calcifications, facial dysmorphism, mental retardation, and hearing impairment. The majority of patients are of Arabic origin.
Material and methods: Case report. We present a girl of Gypsy origin with the syndrome. She was followed up from infancy for failure to thrive, psychomotor retardation, stunted growth and abnormal teeth. At age of 3, she was referred to our Department for evaluation. Laboratory tests revealed metabolic acidosis and mineral disbalance (pH- 7.27, plasma bicarbonate-16.1 mmol/l, anion gap-5.9, chloride-119 mmol/l), urine pH 7.0 and normal plasma creatinine (47 μmol/l). Failure to acidify her urine below pH 5.5 confirmed the diagnosis of distal type (type 2) RTA. Brain CT revealed osteopetrosis and calcifications in basal ganglions. Genetic analysis confirmed homozygous status of Gln92Pro mutation in CA2 gene, both her parents were heterozygotes for the mutation. Long term oral substitution of Shohl solution for metabolic acidosis stabilised her disease.
Results: This is the first case of Guibaud-Vainsel syndrome in Slovakia.
Conclusions: Several different loss of function mutations in in CA2 gene have been described. Usually, the RTA is of mixed proximal and distal type, but kindreds are reported in which either distal or proximal RTA predominate. Intracranial calcifications involving basal ganglions and cortex are developing in the age of 2–5. Around 50 % of patients have mental retardation. Treatment of osteopetrotic conditions is largely symptomatic with long term Shohl solution substitution, although haematopoietic stem cell transplantation is employed for the most severe forms with bone marrow failure.

P70 - Adipsic hypernatremia in a boy with agenesis of corpus callosum.

LASZLO KOVACS, VIKTOR JANKO
DEPARTMENT OF PEDIATRICS, COMENIUS UNIVERSITY MEDICAL SCHOOL

Introduction: Adipsic hypernatremia is characterized by chronic or recurrent episodes of severe hypernatremia with moderate volume depletion and lack of thirst. Hypodipsia or adipsia is the definitive abnormality, although in most cases, some defect in vasopressin (AVP) secretion without polyuria was also detected. This suggests that the syndrome is due to hypoplasia, destruction or impaired function of hypothalamic osmoreceptors that regulate thirst and AVP release.
Material and methods: 14-years old boy with absent corpus callosum, midline facial dysmorphism and moderate mental retardation was studied. He was recognized by the nursing home caregivers as a "weak-drinker".
Results: Patient complained of muscle weakness and became confused by the end of a whole-day summer-time excursion with limited water supply. Evaluation revealed severe hypernatremia (PNa 186 mmol/l, Posm 378 mOsm/kg), Uosm was 620 mOsm/kg. After i.v. fluid replacement, his general condition improved. He did not develop polyuria, however, due to lack of thirst sensation, hypernatremia could not be corrected and PNa remained above 155 to 160 mmol/l. Abnormally low vasopressin secretion was detected by means of plasma copeptin (C-terminal portion of vasopressin) levels to both osmotic (prolonged thirst) and nonosmotic (head-up tilt) stimuli. Our data indicate impaired osmoreceptor function with shifted osmotic threshold for AVP release to higher Posm values ("reset osmostat").
Conclusions: Chronic hypernatremia may be well tolerated. Many reported cases are asymptomatic, although neurologic and muscular problems may arise. Thirst deficiency is most dramatically apparent, when insensible fluid loss is increased (fever, increased ambient temperature). This abnormality can be diagnosed simply by observing that the subject does not drink spontaneously or even shows marked aversion to fluid intake at PNa>150 mmol/l. The therapy is alleviation of the degree of hypernatremia by increasing non-dipsogenic water intake. This is best accomplished by adopting water intake based on defined objective measure, e.g. body weight.

P71 - SIGNIFICANCE OF EXAMINATION OF CONCENTATION OF TNF-α IN 24 H URINE FOR EARLY DIAGNOSTIC OF RENAL SCARRING IN PATIENTS WITH VESICOURETERIC REFLUX

IGOR ZORIN[1], ALBINA VYALKOVA[1], ALEXANDER ZORIN[1], ALEXANDER KARPOV[2], LARISA GAJKOVA[2], OXANA USTINOVA[2]
[1]*ORENBURG MEDICAL ACADEMY*
[2]*PAEDIATRIC CLINIC N6*

Introduction: The aim of the study was to determine concentration of TNF-α in urine of patients with vesicoureteric reflux (VUR) and reflux nephropathy A (RN A) for early diagnostic of renal scarring.
Material and methods: We examined 60 children with RN A and VUR. All children were comparable on a gender and age. All patients underwent ultrasound, X-ray and DMSA scan. We examined concentration of TNF-α in 24 h urine of patients by ELISA. Children were divided into 2 groups: I – with unilateral RN A according to classification of Smellie J. et all, 1975 (n=30); II – with VUR without renal damage (n=30)
Results: We established that data of concentration of TNF-α in 24 h urine of patients with VUR without renal damage was 11,48±0,31 pg/ml. Concentration of TNF-α in 24 h urine of patients with unilateral RN A was 16,69±0,59 pg/ml. The ranges of concentration of TNF-α in 24 h urine of patients with VUR without renal damage were significant different with concentration of TNF-α in 24 h urine of patients with RN A ($p<0,05$).
Conclusions: So, we determined that concentration of TNF-α in 24 h urine increased in process of renal scarring. That's why data of concentration of TNF-α in 24 h urine can be used for early diagnostic of renal scarring in children with VUR.

P72 - Nephrocalcinosis and urolithiasis in children: an experience of a single center

RIMANTE CERKAUSKIENE[1], NERINGA UMBRASIENE[1], DOVILE JONAITYTE[1], DAURA RAUDONYTE[1], AGNE CERKAUSKAITE[1], AUGUSTINA JANKAUSKIENE[1], RIMANTE CERKAUSKIENE[2], AUGUSTINA JANKAUSKIENE[2]
[1]*1VILNIUS UNIVERSITY FACULTY OF MEDICINE*
[2]*2CHILDREN'S HOSPITAL, AFFILIATE OF VILNIUS UNIVERSITY HOSPITAL SANTARISKIU KLINIKOS, LITHUANIA*

Introduction: The prevalence of pediatric nephrocalcinosis (NC) and urolithiasis (UL) has increased in recent years worldwide. Aim of the study was to review the data of children with UL/NC and to analyse clinical symptoms leading to the diagnosis.
Material and methods: A retrospective study of 163 children (83 girls and 80 boys) with NC/UL who were referred Vilnius university Children's Hospital outpatient clinic between 2005–2011 was performed. The analysing criteria were (1) symptoms: hematuria, abdominal pain (colik like or non-specific); (2) urinary tract infection; (3) family history; (4) NC/UL associated diseases.
Results: The patients age varied from 0 to 18 years and they were divided in 3 age groups:<1 y(39); 1–7 y(72) and 8–18 y(52). The diagnosis of NC/UL from 8 in 2005 went up to 40 cases in 2011 (2 to11 infants respectively) per year. In 38.1 % of all cases NC/UL was detected incidentally, symptoms were in 25.7 %, urinary tract infection in 36.2 %. Family history was positive in 19.6 %. Hematuria as a presenting symptom was (8 %, 5.6 % and 7.8 %), abdominal

pain (5 %, 5.5 % and 48 %), urinary tract infections (28 %, 48.6 % and 25 %), and asymptomatic (59 %, 40.3 % and 19.2 %) for children in all age groups respectively. Nephrolithiasis associated diseases were found in 18 cases. The most frequent causes were hereditary disease and vitamin D intoxication.

Conclusions: Incidence rate of children, particularly of infants with NC/UL is growing. Early symptoms or conditions leading to NC/UL is helpful in the disease diagnostics. It seems necessary to do population based studies to find out the real prevalence of nephrolithiasis.

P73 - Mycophenolate Mofetil Therapy in Children with Idiopathic Membranous Nephropathy

RAJENDRA BHIMMA, ELAENE NAICKER, PRATISTADEVI RAMDIAL
UNIVERSITY OF KWAZULU-NATAL

Introduction: Idiopathic membranous nephropathy (IMN) is a rare form of childhood nephropathy. To date there are no standardised protocols of management for this condition in children. The aim of this study is to report on 4 children with IMN who were treated with mycophenolate mofetil (MMF).

Material and methods: MMF was given in combination with low dose steroids and angiotensin converting enzyme antagonists in a dose of 1200 mg/m2 body surface area in 2 divided doses for a minimum of 6 months.

Results: All children had histopathological findings in keeping with stage III membranous nephropathy. At the last hospital visit, 3 children had achieved a >50 % reduction of proteinuria with preservation of renal function. One patient who failed to respond progressed to stage III chronic kidney disease. None of the children who were treated with MMF experienced any major side effects of the drug.

Conclusions: MMF, administered over a limited period, provides safe and effective immune suppression in the treatment of this condition, in conjunction with low dose steroids and angiotensin converting enzyme inhibitors. Large multicentre randomised studies of children with IMN are necessary to assess the efficacy and long term safety of MMF.

P74 - Hemolytic uremic syndrome outbreak in Turkey in 2011

ZELAL EKINCI[1], CENGIZ CANDAN[3], HARIKA ALPAY[4], SARE GULFEM AKYUZ[5], ZUBEYDE GUNDUZ[6], İSMAIL DURSUN[6], SALIM CALISKAN[7], NUR CANPOLAT[7], KENAN BEK[1], HASAN DURSUN[8], EMEL ISIYEL[2], FARUK OKTEM[9], YILMAZ TABEL[10], IPEK AKIL[11], ALI DELIBAS[12], KAAN GULLEROGLU[13], NURVER AKINCI[14], NIDA DINCEL[15], OGUZ SOYLEMEZOGLU[2]

[1]*KOCAELI UNIVERSITY SCHOOL OF MEDICINE*
[2]*GAZI UNIVERSITY SCHOOL OF MEDICINE*
[3]*ISTANBUL MEDENIYET UNIVERSITY GOZTEPE TRAINING AND RESEARCH HOSPITAL*
[4]*MARMARA UNIVERSITY SCHOOL OF MEDICINE*
[5]*DR. SAMI ULUS TRAINING AND RESEARCH HOSPITAL*
[6]*ERCIYES UNIVERSITY SCHOOL OF MEDICINE*
[7]*ISTANBUL UNIVERSITY CERRAHPASA SCHOOL OF MEDICINE*
[8]*BAKIRKOY DR. SADI KONUK TRAINING AND RESEARCH HOSPITAL*
[9]*BEZMIALEM SCHOOL OF MEDICINE*
[10]*INONU UNIVERSITY TURGUT OZAL MEDICAL CENTER*
[11]*CELAL BAYAR UNIVERSITY SCHOOL OF MEDICINE*
[12]*MERSIN UNIVERSITY SCHOOL OF MEDICINE*
[13]*BASKENT UNIVERSITY SCHOOL OF MEDICINE*
[14]*SISLI ETFAL TRAINING AND RESEARCH HOSPITAL*
[15]*EGE UNIVERSITY SCHOOL OF MEDICINE*

Introduction: Hemolytic uremic syndrome (HUS) is a rare cause of acute renal injury in children in Turkey. However, in 2011 an unexpected number of D+HUS cases in the east Marmara region were observed. The aim of this retrospective multicenter study was to define the epidemiological, clinical features and prognostic factors of the HUS outbreak in Turkey in 2011.

Material and methods: All pediatric nephrology centers in Turkey were asked to send data of D+HUS patients diagnosed during 2011. A wide range of data was collected by a form via e-mail and results were analyzed using SPSS ver. 13.0.

Results: Fifteen centers and 70 D+HUS patients participated in this study. Mean age of the patients was 7.04± 4.60 (1–16.2) years. 34.3 % of the cases were ≥10 years. The seasonal peak was around the 7th, 8th and 9th months with 44 cases, centered in east Marmara region. Only 29 of the cases' stool specimen were sent for evaluation of shiga toxin-producing E.coli with a mean of 10.2±8 (1, 27) days after the onset of diarrhea. From these, two E.coli O104:H4 (from the epidemic region) one E.coli O145: H (−) and one E.coli ONT: H5 were identified. Rate of neurological complications was 21.4 %. Rate of mortality was 4.3 % and rate of chronic renal failure (CRF) was 5.7 %. Eculizumab was used in 4 cases, two of which had severe neurological complications despite plasma exchange. Outcome of these 4 patients were: CRF in two and hypertension in one. Elevated polymorphonuclear leucocyte count during hospital admission was the predictor of both severe disease (p=0,032) and poor outcome (0,016). Duration of prodrome was the predictor of poor outcome (p=0.023).

Conclusions: Although a dramatic increase occurred in D+ HUS cases in Turkey in 2011, any special cause could not be verified. Clinical features and outcome were similar to the previously reported D+HUS series.

P75 - Denosumab for Treatment of Refractory Hypercalcemia after Hematopoietic Stem Cell Transplantation for Osteopetrosis

MARTIN MRAZ[1], ORTRAUD BERINGER[2], KANCHANA RAO[3], ROBERT CHIESA[3], PAUL VEYS[3], LORENZ C. HOFBAUER[4], ANSGAR SCHULZ[2], RUKSHANA SHROFF[1]

[1]*RENAL UNIT, GREAT ORMOND STREET HOSPITAL FOR CHILDREN, LONDON, UNITED KINGDOM*

[2]*DEPARTMENT OF PEDIATRICS AND ADOLESCENT MEDICINE, UNIVERSITY MEDICAL CENTER ULM, ULM, GERMANY*

[3]*DEPARTMENT OF BLOOD AND MARROW TRANSPLANTATION, GREAT ORMOND STREET HOSPITAL FOR CHILDREN, LONDON, UNITED KINGDOM*

[4]*DIVISION OF ENDOCRINOLOGY, DIABETES, AND METABOLIC BONE DISEASES, DRESDEN TECHNICAL UNIVERSITY MEDICAL CENTRE, DRESDEN, GERMANY*

Introduction: In autosomal recessive osteopetrosis early hematopoietic stem cell transplantation (HSCT) is the only curative treatment. Recovery of osteoclast function post-HSCT leads to sclerotic bone resorption and hypercalcemia, particularly in patients with homozygous mutation in receptor activator of nuclear factor-κB (RANK). RANK together with its ligand, RANK ligand (RANKL), controls osteoclast differentiation and calcium (Ca) release from the bone. We present the first report of 2 cases of life-threatening hypercalcemia that were refractory to conventional treatment, but successfully treated with denosumab, a human monoclonal antibody against RANKL.

Material and methods: Two children aged 2.9 and 12.0 years, with homozygous mutation in RANK developed severe hypercalcemia (maximum serum Ca 4.1 and 5.0 mml/L, respectively) after successful HSCT. Conventional treatment (forced alkaline diuresis, calcitonin, bisphosphonates) and continuous dialysis only transiently reduced Ca levels. Hypercalciuria in patient 1 led to nephrocalcinosis and acute kidney injury. Patient 2 developed a rapid increase in Ca causing ventricular ectopic beats.

Results: Severe refractory hypercalcemia with renal and cardiac complications led us to use denosumab. Patient 1 received denosumab (10 mg; 0.27 mg/kg) subcutaneously on day 324 post HSCT, with rapid decrease in Ca and improvement in creatinine clearance. Denosumab (5 mg) was repeated every 4–7 weeks to maintain normocalcemia. Two years post-HSCT her GFR is 79 ml/min and urinary calcium/creatinine ratio is normal (nephrocalcinosis unchanged). In patient 2 denosumab (1 mg; 0.05 mg/kg) was given at 9 weeks post HSCT. Hypercalcemia corrected and continuous dialysis was discontinued after 24 hours. After 3 weeks, denosumab (0.5 mg) was repeated due to rebound hypercalcemia. The child developed severe pulmonary hypertension and died 6 weeks later.

Conclusions: Denosumab is an effective treatment for controlling severe hypercalcemia after HSCT in RANK homozygous osteopetrosis. Early use of denosumab to prevent hypercalcemia induced nephrocalcinosis or life-threatening events should be considered in these patients.

P76 - Eculizumab and successful living-donor liver transplantation in a patient with atypical hemolytic uremic syndrome (aHUS).

RAMON VILALTA, ENRIQUE LARA, ALVARO MADRID, SARA CHOCRON, MARINA MUñOZ, JOSE NIETO

HOSPITAL VALL D'HEBRON

Introduction: Background: Atypical hemolytic uremic syndrome (aHUS) is a rare, genetic disorder caused by chronic uncontrolled complement activation., characterized by systemic thrombotic microangiopathy (TMA) and multiple organ damage, which result in significant morbidity and mortality. Despite supportive management, including plasma exchange/infusion (PE/PI), 33-40 % of patients progress to end-stage renal disease (ESRD) or die at the first clinical manifestatations. Eculizumab is a humanized monoclonal antibody to terminal complement protein C5 that prevents activation of the terminal complement pathway, but lifelong maintenance of Eculizumab, treatment reintensification during triggering events (e.g. infective episodes) and possible emergence of anti-Eculizumab antibodies were considered. Because factor H is synthesized in the liver, living-donor liver transplantation (LDLT) seems to be a suitable procedure in a patient with CFH mutation and a severe aHUS phenotype, as previoulsly reported (1).

Material and methods: A 4 years-old girl with aHUS that had multiple severe clinical manifestations of thrombotic microangiopathy (TMA) including acute renal failure, dilated cardiomyopathy and cardiorespiratory arrest was managed with intensive plasma exchange and hemodialysis, which could not halt the progression of TMA. CFH heterozygous mutation (22 exon, mutation c.3355 G>A, 22) was identified. Sustained improvements of renal, hematological and cardiac values were achieved upon institution of chronic treatment with Eculizumab. During long-term treatment with eculizumab (>2,5 years), she has had no further clinical manifestations of TMA. Assumed that liver transplantation will restore and normalize plasma wild-type CFH blood

levels, and recurrences with subsequent renal loss prevented, the patient received a LDLT from her mother. C3 level was detected in the lower normality range after the surgery and one dose of Eculizumab was administered with no further doses required.
Results: An excellent immediate and sustained graft and renal function was observed with normal complement levels in a three months follow-up.
Conclusions: –LDLT should be considered as a treatment option for patients with a HUS and CFH mutations. –Eculizumab maintenance could be a step in the management of these patients. –Other approaches as infussion of H factor is being developed. (1) Successsful isolated liver transplantation in a child with atypical hemolytic uremic syndrome and a mutation in complement factorH. Haller, W et al. American Journal of Transplantation 2010; 10:2142–2147.

P77 - A severe case of diarrhea-associated hemolytic uremic syndrome: therapy with eculizumab
ZELAL EKINCI, MEHMET BAHA AYTAC
KOCAELI UNIVERSITY SCHOOL OF MEDICINE

Introduction: Eculizumab is proposed for diarrhea-associated hemolytic uremic syndrome (D+HUS) patients with accompanying evidence of complement activation. Afew cases have been reported to be resolved completely by this treatment. Here a case of D+HUS is presented to define favorable effect of eculizumab although no sign of complement activation was detected.
Material and methods: Results: Case report: A 9.5-year-old girl presented two days later from watery diarrhea, vomiting and abdominal pain. Anuria, somnolence and hallucinations rapidly developed. Low platelet count (82100/uL), presence of schystocyte on blood smear and high creatinine (5.82 mg/dl) revealed the diagnosis of D+HUS. On the day of hospitalization, plasma exchange (PE) protocol was performed together with the hemodialysis. Somnolence and hallucinations continued. During the 10th PE she developed a generalized tonic clonic convulsion and became unconscious. Although complement C3 level was normal, PE was terminated and eculizumab was started on the day of convulsion at a dose of 600 mg/week for three weeks. At that time her hemoglobin level was 9.13 g/dl, platelet count was 458x103 /uL, LDH level was 427 U/L and she was still anuric. Serum complement C3 and haptoglobin levels were normal. The next day she woke up with normal consciousness. The girl's neurological condition improved dramatically in 24 hours, however anuria resolved slowly. Nephrotic range proteinuria (63 mg/m2/h) and low GFR (44.9 ml/dk/1.73 m2) were persisting in her last control on the 6th month. Analysis of Factor I, H, and MCP did not identify any mutation.
Conclusions: In D+HUS patients, neurological findings that are resistant to PE could be treated successfully by eculizumab therapy even in the absence of any signs of complement activation. However the effect of eculizumab on renal involvement in D+HUS patients is under debate for now.

P78 - Heterozygous factor H mutation presented as diarrhea-associated hemolytic uremic syndrome
ZELAL EKINCI[1], MEHMET BAHA AYTAC[1], VEYSEL SABRI HANCER[2], REYHAN DIZ KÜÇÜKKAYA[2]
[1]*KOCAELI UNIVERSITY SCHOOL OF MEDICINE*
[2]*ISTANBUL BILIM UNIVERSITY SCHOOL OF MEDICINE*

Introduction: Clinically diagnosed diarrhea-associated hemolytic uremic syndrome (D+HUS) patients could have genetic abnormalities in complement regulators. Early identification of genetic complement regulator defects is usually not possible in the acute phase of D+HUS cases. Severe neurological signs are accepted as an indication for plasma exchange (PE) or eculizumab in D+HUS cases.
Material and methods:
Results: Case report:We report on a 17- year-old girl who presented with a history of bloody diarrhea, abdominal cramps and vomiting for three days. She was diagnosed as D+HUS with the presence of systocytes, high creatinine (5.82 mg/dL) and low platelets (82100/uL). Anuria rapidly developed and peritoneal dialysis (PD) was initiated. Serum complement C3 level was normal. Any other complication including neurological symptoms was not recorded. Multiple erythrocyte suspension infusions were required. After 45 days, she was still anuric, and PD was not enough to control her uremic symptoms and intermittent hemodialysis (HD) was performed concomitantly with PD. At this stage, for a chance for protection from chronic renal failure, eculizumab was started weekly at a dose of 900 mg for four weeks. Any favorable progression on her renal functions with eculizumab therapy was not recorded. PD catheter was removed and an HD program was arranged, and at the 75th day of her hospitalization she was discharged. On the 90th day's control she was still anuric and diagnosed as chronic renal failure. Analysis of the factor H gene revealed a heterozygous mutation on 20th exon (VIO89M).
Conclusions: Administration of plasma exchange (PE) and eculizumab were suggested only in severe cases with neurological signs in D+HUS. The experience in our case revealed that even in severe renal signs in D+HUS, a possibility of a defect in the complement system could be present and early effective therapy for complement regulation is mandatory.

P79 - Colchicine can Induce Remission in Atypical Hemolytic Uremic Syndrome

ZELAL EKINCI, MEHMET BAHA AYTAC
KOCAELI UNIVERSITY SCHOOL OF MEDICINE

Introduction: Management of atypical hemolytic uremic syndrome (aHUS) with plasma exchange (PE) protocols is technically difficult in small children. Now eculizumab is a very attractive therapeutic option, however it could be difficult to have access to the drug. As it is, colchicine could be an option. The idea from the hypothesis is that, colchicine could induce complement C5a inhibitor activity.

Material and methods:

Results: Case report: A 5.5 year-old previously healthy boy presented with bloody urine and low urine output. Coombs negative hemolytic anemia (Hb 5.5 g/dL), red blood cell fragmentation, trombocytopenia (74900/uL), high serum creatinine (4,15 mg/dL), heavy proteinuria (72 mg/m2/h), low haptoglobin (8 mg/dL) and decreased serum C3 level (61 mg/dL) without any history of preceeding infection, diarrhea or drug intake, revealed the diagnosis of aHUS. According to the guidelines by the Eurepean Pediatric Study Group (EPSG) for aHUS, PE was performed. At the end of one month he was discharged with normal physical and laboratory findings. Analysis of factor H, factor I and membrane cofactor protein genes did not identify any mutation. Despite continued prophylactic PEs once a week, he again presented with high creatinine (2,1 mg/dL), low hemoglobin (8,8 g/dL) and heavy proteinuria 265 mg/m2/h. PE protocol was restarted. After clinical and laboratory full remission was maintained, he was discharged with weekly prophylactic PE. 4,5 months later he presented again with low haptoglobin (8 mg/dL) and heavy proteinuria (71 mg/m2/h). During that time he took off his tunnelled hemodialysis catheter by himself. Colchicine was started as 2x0.5 mg depending on its inducable complement C5a inhibitor activity. Since then, although he had many infection attacks (upper respiratory tract infection, pulpitis) without any prophylactic PE, the child and all his laboratory parameters are fully normal including his haptoglobin level (124 mg/dL).

Conclusions: Colchicine could be an option with its effect on complement C5a inhibitor activity for prevention of aHUS attacks, but this hypothesis requires further investigations.

P80 - WHAT IS THE BENEFIT OF MEASURING ERYTHROCYTE THIOPURINE TRANSMETHYLTRANSFERASE ACTIVITY IN CHILDREN ?

ALISON LT MA[1], GREGORY BALE[2], HELEN AITKENHEAD[3], SUSAN PATEY[2], STEPHEN D MARKS[1]
[1]*DEPARTMENT OF PAEDIATRIC NEPHROLOGY, GREAT ORMOND STREET HOSPITAL FOR CHILDREN*
[2]*DEPARTMENT OF PHARMACY, GREAT ORMOND STREET HOSPITAL FOR CHILDREN*
[3]*DEPARTMENT OF CHEMICAL PATHOLOGY, GREAT ORMOND STREET HOSPITAL FOR CHILDREN*

Introduction: Azathioprine is an effective immunosuppressive agent for the management of a wide spectrum of diseases, including systemic lupus erythematosus, vasculitis and in renal transplantation. Myelosuppression is a known major side-effect so some authors advocate that erythrocyte thiopurine transmethyltransferase (TPMT) activity is required to identify those patients at increased risk. In such cases, the azathioprine dosage can be adjusted prior to prescribing. However, there is a lack of data to support routine TPMT monitoring in paediatric patients.

Material and methods: Retrospective study in a single paediatric centre of all patients who had TPMT enzyme assay measured over a three year period prior to the commencement of azathioprine therapy. Patients with TPMT enzyme activities of 26–50, 10–25 and <10pmol/h/mgHb were classified as normal, intermediate and deficient, respectively. Medical and electronic prescribing records were studied with record of patients' demographic data, diagnoses, dosages, and adverse drug reactions were monitored.

Results: 363 (51 % female) patients aged 1–19 (median 10.2) years were tested for TPMT activity of whom 228 patients were subsequently commenced on azathioprine. Erythrocyte TPMT activities were 14–76 (median 33.7) pmol/h/mgHb with 88 % and 12 % of patient having normal and intermediate activity respectively (none were deficient). The initial prescribed dosage of azathioprine was 0.7 - 3.5 (median 2.0) mg/kg/day. Only two patients required reduction of azathioprine dosage due to mild neutropenia in this cohort.

Conclusions: This is the first large paediatric cohort study which demonstrates that the majority of paediatric patients had normal TMPT activities and no patients developed severe neutropenia as a result of azathioprine treatment. We estimate the cost for testing this patient cohort was £16,000 without clinical benefit. We would recommend close monitoring of full blood counts after instituting azathioprine therapy but would question the value of pretreatment TPMT activity in paediatric practice.

P81 - Characteristics of cell-mediated immunity in children with glomerulonephritis, associated with herpesvirus infection (1, 2, 4, 5 types)

NATALIA NECHEPORENKO[1], NADEZDA SAVENKOVA[1], NATALIA KALININA[2]
[1]*SAINT-PETERSBURG STATE PEDIATRIC MEDICAL ACADEMY*
[2]*THE FEDERAL STATE INSTITUTE OF PUBLIC HEALTH " THE NIKIFOROV RUSSIAN CENTER OF EMERGENCY AND RADIATION MEDICINE"*

Introduction: Glomerulonephritis (GN), associated with herpesvirus infection (1, 2, 4, 5 types) is characterized by resistence to immunosupressive therapy, persistent course and serious prognosis.
Material and methods: 23 patients from 1 to 18 years old were examined: 17,4 % steroid-sensitive nephrotic syndrome (NS), 34,8 % NS with hematuria and hypertension, 47,8 % GN with hematuria and hypertension. 12 patients had increasing in blood specific and total IgE. 14 patients had morphological diagnosis: 50 % mesangioproliferative GN, 21,4 % membranoprolipherative GN, 28,6 % FSGS. 19 children were treated by prednisone. We used flow cytometry method, enzymelinked immunosorbent assay, immunohistochemical and immunocytochemical tests, polymerase chain reaction. Kidney biopsy, histological investigation of kidney tissue were performed in 14 patients.
Results: In kidney biopsy material herpes virus antigens were identified in 10 cases (71,4 %). Active herpesvirus infection (1,2,4,5 types) diagnosed in 18 patients: monoinfection in 12 (66,7 %), mixt infection in 6 (33,3 %). Dicreased quantity of cells with cytotoxic activity (cytotoxic-T-cells 20,6 %±0,74 %; NK-cells 4,4 %±0,42 %, activated NK-cells 0,76 %±0,17 %) was revealed in 16 cases (69,6 %). In 7 cases (30,4 %) Th 2-type of immunology answer was revealed. The investigation of lymphocytes subsets showed the presence of secondary cell-mediated immunodeficiency state in 9 patiens (39, 1 %). In 1 case (4,3 %) X-linked agammaglobulinemia was diagnosed. Increased amount of double negative T-lymphocytes was revealed in 80 %. In 19 (82,6 %) cases GN was resistent to immunosupressive therapy. The activation of cellular immune response and antivirus immunity were characterized for remission of GN and absence of active herpesvirus infection in 5 children.
Conclusions: Cell-mediated immunity in children with GN associated with herpesvirus infection (1, 2, 4, 5 types) is characterized by dicreased quantity of cells with cytotoxic activity. Increased amount of double negative T-lymphocytes may be sign of autoimmune component in pathogenesis of GN, associated with herpesvirus infection (1,2,4,5 types).

P82 - Eculizumab therapy for aHUS associated with heterozygous factor I mutation

ZELAL EKINCI[1], MEHMET BAHA AYTAC[1], VEYSEL SABRI HANCER[2], REYHAN DIZ KÜÇÜKKAYA[2]
[1]*KOCAELI UNIVERSITY SCHOOL OF MEDICINE*
[2]*ISTANBUL BILIM UNIVERSITY SCHOOL OF MEDICINE*

Introduction: Complement regulatory abnormalities should have to be suspected in atypical hemolytic uremic syndrome (aHUS) patients who were especially presented with low complement C3 levels. Eculizumab is preferred for infants as the first line management of aHUS, because plasma exchange protocols is difficult to perform. Here we present a case of aHUS in whom complement factor I mutation was detected to be the cause of the disease.
Material and methods:
Results: Case report: A 10 month-old girl was presented with paleness, weakness and vomiting for two days. High creatinine level (2.59 mg/dl), low platelet count (52.8x103/μl), hemolytic anemia (4.9 g/dl) with red cell fragmentation, increased LDH (4613 U/l) and low haptoglobin level (8 mg/dl) without any history of preceding infection, diarrhea or drug intake revealed the diagnosis of aHUS. Multiple erythrocyte suspensions were transfused to improve anemia. Low level of complement C3 (53 mg/dl), was thought to be an indicator of underlying genetic disturbance affecting the complement pathway. Although the patient was vaccinated against Neisseria meningitidis, Streptococcus pneumonia and Hemaphilus influenza, rifampicin prophylaxis was started as single dose of 20 mg/kg. Eculizumab therapy 300 mg per week for two weeks was performed initially. Serum creatinine decreased to 0.84 mg/dl and thrombocytopenia recovered dramatically only after one infusion. LDH level was 1632 U/l and haptoglobin level was still 8 mg/dl. It was planned to maintain eculizumab 300 mg every 3 weeks when the analysis of the Factor I gene revealed a heterozygous mutation on 11th exon (D401N).
Conclusions: The prognosis for patients with aHUS is poor. Although plasma exchange represents the first line therapy, it is difficult to perform in infants. As it is, eculizumab as a first line therapy was successful, easy and uncomplicated.

P83 - Effectiveness and safety of MMF in induction treatment for lupus nephritis in childhood: 28 cases

BENNOUR ANIA[1], PRUVOST ISABELLE[2]
[1]*1PEDIATRIC NEPHROLOGY DEPARTMENT, HôPITAL JEANNE DE FLANDRE, CHRU LILLE*
[2]*2PEDIATRIC DEPARTMENT OF INTERNAL MEDECINE AND INFECTIOUS DISEASE, HôPITAL JEANNE DE FLANDRE, CHRU LILLE*

Introduction: Lupus nephritis (LN) is a severe and rare disease in childhood. Mycophenolate Mofetil (MMF) is used in adult treatment, in the induction phase. Few paediatric data, even for the effectiveness, safety and terms of use of MMF, are available in the literature for induction treatment. This study was performed to determine the effectiveness and safety of MMF to induce remission, in LN.
Material and methods: Retrospective analysis of clinical and laboratory data was performed on 28 children with LN, in FSPN. At pre-induction, at 1 month, 3 months, 6 months and the end of follow-up, these parameters were recorded

and also relapses, adverse effects, terms of use, associated treatments and maintenance therapy.

Results: Twenty-eight patients, 12.8±5.3 years old, with a LN (63 % of classes (III-IV)), were included. MMF was effective: 57 % of complete remission and 22 % of partial remission at 6 months, with a significant decay of SLEDAI ($p<0,001$) and a significant improvement of activity biomarkers (albumin, proteinuria, haemoglobin, anti-DNA,VS) were noticed. There was a sparing of corticoids during induction ($p<0,001$). The adverse effects were rare, above all: hematologic and gastro-intestinal. No death or failure chronic renal evolution was observed. Four infectious events required hospitalisation. The terms of use were different between the units of nephrology, despite the initial dosage (1178±105 mg/m²/j). MMF was following for 89 % patients, who where in remission at the end of induction.

Conclusions: MMF is an effective induction treatment, well tolerated, and sparing corticotherapy, crucial for children. A harmonization of terms of use, mainly pharmacokinetics monitoring, is necessary.

P84 - Age-related differences in the clinical characteristics and outcome of Pediatric Lupus Nephritis: an Italian collaborative study

INES L'ERARIO[1], BARBARA RUGGIERO[3], MARINA VIVARELLI[3], ELISA BENETTI[4], LICIA PERUZZI[5], GIANCARLO BARBANO[6], FABRIZIA CORONA[7], GIOVANNA VENTURA[1], CARMINE PECORARO[8], LUISA MURER[4], GIAN MARCO GHIGGERI[6], MARCO PENNESI[2], ALBERTO EDELFONTI[7], ROSANNA COPPO[5], FRANCESCO EMMA[3], ALESSANDRA GIANVITI[3]

[1]INSTITUTE FOR MATERNAL AND CHILD HEALTH - IRCCS "BURLO GAROFOLO" – TRIESTE, UNIVERSITY OF TRIESTE, ITALY

[2]INSTITUTE FOR MATERNAL AND CHILD HEALTH - IRCCS "BURLO GAROFOLO" – TRIESTE, ITALY.

[3]BAMBINO GESù CHILDREN'S HOSPITAL AND RESEARCH INSTITUTE, DIVISION OF NEPHROLOGY AND DIALYSIS

[4]UNIVERSITY OF PADUA, DIVISION OF PEDIATRIC NEPHROLOGY,DIALYSIS AND TRANSPLANTATION, DEPARTMENT OF PEDIATRICS

[5]REGINA MARGHERITA CHILDREN'S HOSPITAL, DIVISION OF NEPHROLOGY

[6]GIANNINA GASLINI CHILDREN'S HOSPITAL, DIVISION OF NEPHROLOGY AND LABORATORY ON PATHOPHYSIOLOGY OF UREMIA

[7]FONDAZIONE IRCCS CA' GRANDA, MAGGIORE HOSPITAL POLICLINICO, PEDIATRIC NEPHROLOGY AND DIALYSIS UNI

[8]SANTOBONO HOSPITAL, DEPARTMENT OF NEPHROLOGY AND UROLOGY

Introduction: Lupus nephritis (LN) represents the most severe and frequent organ damage of children with systemic lupus erythematosus. To date, few studies have described the clinical characteristics, outcome and prognostic factors of pediatric LN, with particular reference to small children.

Material and methods:

The Italian retrospective collaborative study includes 161 pediatric patients with LN (1982 WHO classification) collected from 1987 to 2010, that were followed-up for a mean of 8.0 years (range 0.5-23.8). Patients were divided into 2 groups, depending on the age at diagnosis: group A (0–8 years) and group B (9–17 years). Survival curves were compared with the Log-Rank test. The impact of covariates (multivariate analysis) was analyzed by Cox proportional hazard regression.

Results:

No substantial difference was observed in the renal pathology among the two groups of patients. Despite similar induction and maintenance treatment regimens, small children were less likely to achieve partial (H.R. = 0.5 [0.3 - 0.9], $p<0.02$) and complete (H.R. = 0.5 [0.3 - 0.9, $p<0.02$) remission. This correlated with a worse outcome. By multivariate analysis, small children had a higher probability to develop stage III CKD (H.R.=4.4 [2.0 - 9.8], $p<0.001$) and ESRD (H.R. 5.6 [1.9 - 16.2, $p<0.02$).

Conclusions: This large retrospective study shows that very early onset of LN represents a negative prognostic factor and suggests that this sub-category of patients should receive targeted induction treatments.

P85 - THE CHALLENGE OF MANAGING HEMOPHILIA A AND STEC-INDUCED HEMOLYTIC UREMIC SYNDROME

DINEKE WESTRA[1], EISKE DORRESTEIJN[2], AUKE BEISHUIZEN[2], MARLIES CORNELISSEN[1], LAMBERT VAN DEN HEUVEL[1], PAUL BRONS[1], NICOLE VAN DE KAR[1]

[1]RADBOUD UNIVERSITY NIJMEGEN MEDICAL CENTRE, NIJMEGEN, THE NETHERLANDS

[2]ERASMUS MC–SOPHIA CHILDREN'S HOSPITAL, ROTTERDAM, THE NETHERLANDS

Introduction: The haemolytic uraemic syndrome (HUS) is a thrombotic microangiopathy leading to acute renal failure in children. In most cases it is triggered by a STEC infection (typical HUS). Endothelial damage plays a central role in the pathogenesis of disease. Haemophilia A is a genetic disorder, leading to Factor VIII (FVIII) deficiency, an important factor in the coagulation system. Here we describe a haemophilia A patient that developed typical HUS. Increased amounts of FVIII had to be administered during the acute phase of the disease.

Material and methods: At the age of two years, our patient developed abdominal pain, vomiting, and bloody diarrhoea. He was diagnosed with typical HUS (STEC O26). On the second evening he developed a tonic-clonic epileptic insult. Bilateral symmetric signal intensity changes in the basal ganglia were seen on MRI. Because of further deteriorating renal function continuous veno-venous haemofiltration was initiated as renal replacement therapy. Due to hemorrhagic colitis, severe neurological complications, hypertension, and bleeding at the exit site of the jugular catheter, all in combination with thrombocytopenia and persistently low FVIII levels in serum, FVIII treatment had to be increased enormously.
Results: It is known that shiga toxin induces the secretion of von Willebrand Factor (vWF) from microvascular endothelial cells, a protein important in adhesion of platelets at the site of injury and a carrier of FVIII in plasma. The adhesion of platelets by vWF will probably lead to increased thrombus formation in the microvasculature of the kidneys of HUS patients The supraphysiological dose of FVIII needed in this case may have contributed further to the thrombotic microangiopathy after shiga toxin-induced endothelial damage in the affected organs. Although his renal function recovered after 18 days of renal replacement therapy, surgical intervention was needed for resection of colorectal stenosis and invagination. For his severe neurological involvement, an intensive rehabilitation program was necessary in which clear neurological progress was made, but the boy is still not fully rehabilitated.
Conclusions: To our knowledge, this is the first report of a haemophilia patient that developed HUS after STEC infection. The treatment of haemophilia in the acute phase of the HUS could have contributed to the difficult management of the disease and to the development of severe gastrointestinal and neurological complications.

P86 - L-carnitine supplementation and plasma fatty acid status in patients with end-stage renal disease on regular hemodialysis

ENDRE SULYOK[1], BOTOND CSIKY[2], TAMáS MAROSVÖLGYI[3], TAMáS DECSI[3], JUDIT BENE[4], BéLA MELEGH[4]
[1]*INSTITUTE OF HEALTH SCIENCES,UNIVERSITY OF PéCS*
[2]*FMC DIALYSIS CENTER PéCS*
[3]*DEPARTMENT OF PEDIATRICS,UNIVERSITY OF PéCS*
[4]*DEPARTMENT OF MEDICAL GENETICS, UNIVERSITY OF PéCS*

Introduction: The response pattern of plasma fatty acids to l-carnitine supplementation was investigated in patients with end-stage renal disease (ESRD) on long-term hemodialysis (HD).
Material and methods: The study was performed at the FMC Dialysis Center Pécs. Ten non-diabetic adult patients with ESRD on HD for >7 months were selected for this longitudinal study. Patients underwent three HD sessions per week and received 1 g l-carnitine intravenously after each HD session for 12 weeks. Blood samples were taken for analyses before (week 0) and at the end of supplementation (week 12), as well as during the wash-out period (week 28). Fatty acids were determined in phospholipid (PL), triacylglycerol (TG) and sterol ester (STE) plasma lipid fractions by capillary gas chromatography. Changes in eicosapentaenoic (20:5n-3) and docosahexaenoic (22:6n-3) acid levels in plasma lipids were evaluated.
Results: In response to l-carnitine administration we found significant increases in values of eicosapentaenoic acid in TG and STE ($p<0.05$), docosahexaenoic acid in the TG ($p<0.05$) and the sum of n-3 polyunsaturated fatty acids (PUFA) in STE ($p<0.05$) lipid fractions. For months after the cessation of supplementation, both the sum of n-3 PUFA ($p<0.05$) and the ratio of n-3 to n-6 long-chain PUFA ($p<0.05$) were still significantly higher than the pretreatment values.
Conclusions: These data suggest that changes in plasma fatty acid composition may contribute to the beneficial effects of l-carnitine in patients with ESRD on regular HD.

P87 - "IDIOPATHIC" THROMBOCYTOPENIC PURPURA AS FIRST MANIFESTATION OF LUPUS NEPHRITIS

ANGELO MANNA[1], DANIELA MOLINO[1], FRANCESCA NUZZI[1], GABRIELE MALGIERI[1], MARIO BALLETTA[2], MARIA D'ARMIENTO[3], CARMINE PECORARO[1]
[1]*DEPARTMENT OF NEPHROLOGY AND UROLOGY, CHILDREN'S HOSPITAL SANTOBONO, NAPLES, ITALY*
[2]*DEPARTMENT OF NEPHROLOGY, UNIVERSITY FEDERICO II, NAPLES, ITALY*
[3]*DEPARTMENT OF PATHOLOGY, UNIVERSITY FEDERICO II, NAPLES, ITALY*

Introduction: Idiopathic thrombocytopenic purpura (ITP) is an autoimmune disorder characterized by a low circulating platelet count caused by destruction of antibody-sensitized platelets in the reticuloendothelial system. It's the most common form of thrombocytopenia in childhood. Systemic lupus erythematosus (SLE) is an autoimmune disorder which displays a broad spectrum of clinical and immunological manifestations, including thrombocytopenia. Mestanza-Peralta and colleagues have previously reported that thrombocytopenia is the initial manifestation of SLE in the 5 % of an adult population.
Material and methods: To evaluate the prevalence of ITP as isolated first manifestation in 50 children with Lupus

Nephritis (LN) and to characterize the nephropathy and the thrombocytopenia.

Results: Results are expressed as mean (range) values. Of the 50 patients with LN, 11 (10 F, 22 %) presented ITP as isolated initial manifestation of SLE. Age at presentation of ITP was 9.1 years (range, 6.3-12.7), while age at presentation of LN was 13.3 years (range, 9.7-15.5), with mean time interval of 4.2 years. The renal biopsy performed in the ITP-beginner population showed, according to the Weening Classification, LN class II, III, IV in 2 (18.2 %), 3 (27.3 %) and 6 (54.5 %) children, respectively. In all patients steroid and immunosuppressive treatment was started following SLE diagnosis: both thrombocytopenia and renal anomalies improved with stable remission.

Conclusions: In contrast to Mestanza–Peralta and colleagues, who reported that thrombocytopenia was the initial manifestation of SLE in the 5 % of an adult population, in our pediatric study ITP represents the isolated first manifestation of LN in a statistically larger population (22 %). This result leads to the hypothesis that in the pediatric population, ITP as isolated first manifestation of SLE may represent a predictive risk factor to the subsequent development of moderate-to-severe Lupus Nephritis. Risk factors in pediatric population with ITP are: chronic ITP, ANA positivity, female sex, and late presentation. These characteristics could determine a careful follow-up to promptly identify incipient signs of SLE.

P88 - Shigatoxin 2 induces apoptosis and a proinflammatory phenotype in human glomerular endothelial cells

CHRISTIAN BETZEN[1], THOMAS GIESE[4], KATHRIN PLOTNICKI[1], FARNOOSH FATHALIZADEH[1], SIMON SATCHELL[2], PETER MATHIESON[2], ANGELIKA BIERHAUS[3], BURKHARD TÖNSHOFF[1], NEYSAN RAFAT[1]

[1]*UNIVERSITY CLINIC OF HEIDELBERG, PAEDIATRIC DEPARTMENT*

[2]*ACADEMIC RENAL UNIT, SOUTHMEAD HOSPITAL, UNIVERSITY OF BRISTOL, UK*

[3]*UNIVERSITY CLINIC OF HEIDELBERG, MEDICAL CLINIC I AND CLINICAL CHEMISTRY*

[4]*UNIVERSITY CLINIC OF HEIDELBERG, IMMUNOLOGY DEPARTMENT*

Introduction: Hemolytic-uremic syndrome (HUS) presents as a clinical triad of hemolytic anemia, thrombocytopenia and acute renal failure. HUS is most commonly caused by infections with shigatoxin-producing strains of E. coli. So far, there is no specific treatment for this disease. Microvascular endothelial damage is a central hallmark of HUS pathology. Despite the pivotal role of glomerular endothelium in its pathogenesis, investigations into the interactions of shigatoxin with cell signaling pathways have largely been restricted to non-glomerular cell lines. Therefore, we studied the molecular mechanisms of Shigatoxin-induced endothelial dysfunction in a conditionally immortalized human glomerular endothelial cell line (ciGEnc).

Material and methods: Dose-dependent cytotoxicity of shigatoxin 2 (Stx2) on ciGEnc was determined at 24 h with a colorimetric assay (WST-1 assay). Using quantitative real time-PCR, we evaluated the influence of a cytotoxic dose of Stx2 on the gene expression of cellular adhesion molecules (ICAM, VCAM), mediators of apoptosis (CHOP, BCL-2) and transcriptional regulation (EGR1), proinflammatory cytokines (IL8, MCP-1, GRO1) and key enzymes of reactive oxygen species homeostasis (glutathione peroxidase, Cu,Zn-superoxidedismutase, catalase) after 3, 6 and 9 h of exposure to the toxin. In addition, we evaluated the effect of a pre-stimulation with TNF-alpha on Stx2-induced changes in gene expression.

Results: Stx2 had a dose-dependent cytotoxic effect on ciGenc with a CD50 of 7.5 μg/L. Incubation of glomerular endothelial cells with Stx2 markedly increased expression of transcripts for IL8, MCP-1 (both 44fold), GRO-1 (11fold), ICAM (12fold) and VCAM (2.6fold) as well as that of apoptosis regulator CHOP (21fold) and transcription factor EGR1 (158fold) at 6-9 h. No changes in expression were observed for Bcl-2 or enzymes of reactive oxygen species homeostasis. TNF-alpha pre-stimulation led to an additional increase in cytokine expression only.

Conclusions: Stx2 acts on glomerular endothelium to activate the cellular immune response by up-regulating adhesion molecules and chemotactic cytokines, together with a proapoptotic stress response involving CHOP.

P89 - ACTIVATION OF INNATE IMMUNITY IN CHILDREN WITH HENOCH –SHOENLEIN PURPURA: TOLL-LIKE RECEPTORS IN CIRCULATING MONONUCLEAR CELLS

ROBERTA CAMILLA[1], ELISA LOIACONO[1], MARIA ELENA DONADIO[1], MARGHERITA CONRIERI[2], MANUELA BIANCIOTTO[2], FRANCESCA MARIA BOSETTI[2], LICIA PERUZZI[1], GIOVANNI CONTI[3], ALESSANDRA BITTO[3], LUCA VERGANO[1], ALESSANDRO AMORE[1], ROSANNA COPPO[1]

[1]*NEPHROLOGY, DIALYSIS, TRANSPLANTATION, R. MARGHERITA HOSPITAL, TURIN, ITALY*

[2]*PEDIATRIC EMERGENCY, R.MARGHERITA HOSPITAL, TURIN, ITALY*

[3]*PEDIATRIC NEPHROLOGY, G. MARTINO HOSPITAL, MESSINA, ITALY*

Introduction: The course of Henoch-Schoenlein purpura (HSP) in children is often benign, but sometimes hematuria

and proteinuria develop. Only in a minority of children the renal involvement is long-lasting and severe. HSP is often triggered by a mucosal infection, but the pathogenesis is still unknown. Aim of this study was to investigate in children with HSP with and without renal involvement and in different phases of clinical activity the activation of innate immunity and the relationships with the regulatory T (Treg) cells and proinflammatory Th17 subset.

Material and methods: In 42 children with HPS (aged 3–14 years) and 35 healthy control subjects the innate immunity activation was investigated by detecting Toll-like receptor (TLR) expression in peripheral mononuclear cells (PBMC) with real time PRC (Taqman) to measure mRNA expression of TLR2, TLR3, TLR4, TLR9 and of regulation-associated genes of Treg including forkhead box P3 (Foxp3), Th17-related factors (IL-17), retinoid orphan nuclear receptor (RORc), and TFG-β1.

Results: PBMC of children with HSP had, in comparison to healthy controls (HC), significantly increased expression of mRNA encoding for TLR 2 (2.83±2.57 vs 1.42±0.77 in HC, P=0.042) and TLR4 (2.17±1.63 vs 1.37±0.73 in HC, P=0.011), while showed a significantly decreased expression of mRNA encoding for TGFβ1 (0.89±0.58 vs 1.44±0.5 in HC, <0.0001). A significant correlation was found between TLR4 and TGFβ1 mRNAs (p=0.033) and between TLR4 and foxp3 mRNAs (P<0.05). No differences were observed in cases with systemic purpura with or without renal involvement.

Conclusions: In children with HSP we observed a significant activation of innate immunity, with particular engagement of TLR4, which was correlated with down modulation of factors favouring the differentiation of Th17. This changes are coincident with the benign course of HSP in the children investigated.

P90 - MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS AND PRIMARY ANTIPHOSPHOLIPID SYNDROME

SYLVA SKALOVA[1], KATERINA LEJHANCOVA[1], LUDEK RYBA[2]

[1]*FACULTY HOSPITAL HRADEC KRALOVE AND FACULTY OF MEDICINE IN HRADEC KRALOVE, CHARLES UNIVERSITY PRAGUE*

[2]*HOSPITAL IN USTI N.ORLICI*

Introduction: Antiphospholipid syndrome (APS) is characterized by: a) venous and/or arterial thrombosis or tissue microthrombi, b) miscarriages, c) positivity of antiphospholipid antibodies. Primary APS not linked to autoimmune disease is very rare in children. Renal manifestations of APS include: renal artery stenosis or thrombosis, renal vein thrombosis, renal infarction, and thrombotic microangiopathy, representing the most frequently encountered APS nephropathy.

Material and methods: We present a case report of 14-year old boy with recent history of left vena poplitea thrombosis and confirmed primary APS who was admitted due to progressive proteinuria. On admision, his renal functions were normal, urine analysis revealed microscopic hematuria and non-selective proteinuria exceeding 3 g/24 hours. Serum levels of complement C3 and C4 were in normal range, cryoglobulin and tests for hepatitis B and C were negative. Imaging procedures ruled out renal vessel involvement. Histologic evaluation of kidney tissue sample obtained by renal biopsy did not show any signs of thrombotic microangiopathy or other vascular changes; the histological changes were consistent with membranoproliferative glomerulonephritis type III.

Results: After exclusion of secondary etiology, this type of glomerulonephritis is most probably associated with primary APS. Treatment with cyclosporin A was initiated and patient was maintained on long-term anticoagulation therapy.

Conclusions: Kidney involvement in APS patients may be heterogenous and according to recent reports it could include also some types of glomerular lesions. According to our knowledge this is a first report of pediatric primary APS associated with membranoproliferative glomerulonephritis.

P91 - PILOT TRIAL ON SYSTEMIC EVALUATION OF TREATMENT WITH PYRIDOXALPHOSPHATE IN PATIENTS WITH PRIMARY HYPEROXALURIA TYPE I (PH I)

HEIKE HOYER-KUHN[1], BARBARA HERO[1], SINA KOHBROK[1], BODO BECK[2], BERND HOPPE[1]

[1]*UNIVERSITY HOSPITAL COLOGNE, DEPARTMENT OF PEDIATRICS AND ADOLESCENTS MEDICINE, DIVISION OF PEDIATRIC NEPHROLOGY*

[2]*UNIVERSITY HOSPITAL COLOGNE, INSTITUTE OF HUMAN GENETICS*

Introduction: PH I is caused by an autosomal recessive inherited deficiency of liver specific peroxisomal enzyme alanine-glyoxylate:aminotransferase that requires pyridoxalphosphate (PLP) as a cofactor. The experience of treatment with PLP is limited to patient surveys, retrospective analyses and case reports. It should, however, be administered in all patients with PH I to evaluate its effect on the reduction of urinary oxalate (UOX) excretion. Primary objective of this pilot trial was to investigate the relative reduction of UOX excretion under increasing dosages of PLP at week 24 compared to baseline in a prospective setting.

Material and methods: We included 12 patients (7 males / 5 females; age 13.5 +/− 3.3 years; eGFR 139 +/− 37 ml/

1.73 m2/min) with confirmed PH I by mutation analyses: c.508 G>A homozygous (n=3), c.508 G>A heterozygous (n=6), c.508 G>A negative (n=3). In the 8/12 patients treated with PLP at study entry, medication was interrupted for 4 weeks or until serum levels were normal. PLP was started in a dosage of 5 mg/kg/day for 6 weeks and increased by 5 mg/kg steps to a final dosage of 20 mg/kg/day every six weeks until week 24. Two 24 h urines were collected at baseline and after each treatment episode.

Results: Preliminary data of an intention-to-treat analysis showed a mean relative reduction of UOX excretion of 25.0 %. UOX excretion declined from 2.14 +/− 0.54 mmol/1.73 m2/day at baseline to 1.57 +/− 0.58 mmol/1.73 m2/day ($p<0.02$) at week 24 and PLP levels increased from 24 +/− 10 ng/ml to 1228 +/− 813 ng/ml ($p<0.001$), respectively. Five patients showed a relative reduction of UOX≥30 %.

Conclusions: Preliminary results demonstrate that PLP treatment reduces UOX excretion, which is comparable to retrospective data. It underlines the need for further evaluation in a multicenter trial to analyze a genotype/phenotype related response to PLP treatment.

P92 - Successful treatment of membranoproliferative glomerulonephritis type I with monoclonal anti C5 antibody (eculizumab)

GARNIER ARNAUD[1], MODESTO ANNE[1], TELLIER STEPHANIE[1], BANDIN FLAVIO[1], FREMEAUX-BACCHI VERONIQUE[2], DECRAMER STEPHANE[1]
[1]*HôPITAL DES ENFANTS, CHU PURPAN*
[2]*HôPITAL EUROPéEN GEORGES POMPIDOU*

Introduction: Membranoproliferative glomerulonephritis (MPGN) is a rare and heterogeneous group of nephropathy, characterized by mesangial hypercellularity with increased matrix, splitting of the glomerular basement membrane and different pattern of deposit (type I, II and III). MPGN type I represent less than 5 % of primary glomerulonephritides and can be related to complement dysregulation.

Material and methods: We report the case of a 7 years old boy referred to our unit for nephritic syndrome. Renal biopsy displayed MPGN type I with subendothelial deposits of C3, C1q, IgG and IgM. Serum C3 level was low (0.11 g/L) and a C3 nephritic factor (C3NF) was present. No mutation was found in the complement alternative pathway factors H and I.

Results: A 6 months course of oral steroids together with angiotensin converting enzyme inhibitor (ACEi) and angiotensin II receptor blocker (ARB) did not improve proteinuria. After 3 years of sustained proteinuria, glomerular filtration rate (GFR) slowly decreased and a second renal biopsy was performed. Histological and immunological findings were similar to the first biopsy with global sclerosis concerning 20 % of the glomeruli. Low serum C3 level and C3NF were still present. A second course of steroids together with the maintenance of the ACEi and ARB did not succeed to reduce proteinuria. After tetravalent meningococcal vaccine and initiation of prophylactic penicillin V therapy, treatment with the anti C5 monoclonal antibody eculizumab was initiated as follows: 900 mg once a week for 4 weeks, then 1200 mg every 2 weeks. 10 months after the beginning of treatment, proteinuria is absent with normal albuminemia (35 g/L) and GFR.

Conclusions: This is the first report of successful treatment of MPGN type I with eculizumab, a monoclonal anti C5 antibody that blocks the terminal complement activation. In primary MGPN, dysregulation of complement activation is a frequent feature, and the treatment with eculizumab should be discussed in the most severe forms.

P93 - Increased serum IgA antiphospholipid antibody levels in childhood Henoch-Schönlein purpura

MAHMUT CIVILIBAL[1], OZGUN BASARAN KAYA[2], MURAT ELEVLI[2], NILGUN SELCUK DURU[2]
[1]*HASEKI EDUCATIONAL AND RESEARCH HOSPITAL, DEPARTMENT OF PEDIATRIC NEPHROLOGY, ISTANBUL, TURKEY*
[2]*HASEKI EDUCATIONAL AND RESEARCH HOSPITAL, DEPARTMENT OF PEDIATRICS, ISTANBUL, TURKEY*

Introduction: Henoch-Schönlein purpura (HSP) is a small-vessel vasculitis characterized by IgA-dominant immune complex deposition; and its pathogenesis is still controversial. Among IgA antibodies, serum IgA antiphospholipid antibodies (aPL) have been found in many diseases, including vasculitis. The aim of our study was to investigate a possible role of aPL antibodies in childhood HSP.

Material and methods: Thirty children with HSP and 30 healthy children were enrolled in this study. In addition to the levels of serum immunoglobulins, acute phase reactants, and other biochemical parameters; serum IgA class anticardiolipin antibodies (IgA aCL) and IgA class anti-β2-glycoprotein I antibodies (IgA aβ2-GPI) were measured. Blood samples from these patients were collected at both acute and convalescent stages. IgA aCL and IgA aβ2-GPI antibodies were measured by enzyme linked immunosorbent assay (ELISA).

Results: Serum IgA aCL and IgA aβ2-GPI levels were significantly higher in acute stage of children with HSP than controls (respectively, 2.12±0.56 U/ml vs. 1.57±0.31 U/ml, $p<0.001$ and 2.32±1.84 U/ml vs. 0.69±0.64 U/ml, $p<0.001$). The levels of these antibodies decreased significantly in remission stage of the disease. In regression analysis, serum IgA level was the only independent predictor of the

increased IgA aCL and IgA aβ2-GPI antibodies (β:0.549, p=0.002 and β:0.595, p=0.001, respectively).
Conclusions: The findings of the present study suggest that serum levels of IgA aCL and IgA aβ2-GPI antibodies are elevated in active stage of pediatric HSP, suggesting that anti-phospholipid antibodies may play role in the onset of disease. We believe that the levels of serum antiphospholipid antibodies might be an indicator of childhood HSP activity.

P94 - MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

ELIF COMAK[1], CAGLA SERPIL DOGAN[1], ARIFE USLU GOKCEOGLU[1], AKIF YESILIPEK[2], MUSTAFA KOYUN[1], SEMA AKMAN[1]
[1]*AKDENIZ UNIVERSITY MEDICAL FACULTY DEPARTMENTS OF PEDIATRIC NEPHROLOGY, ANTALYA, TURKEY*
[2]*AKDENIZ UNIVERSITY MEDICAL FACULTY DEPARTMENTS OF PEDIATRIC HEMATOLOGY AND ONCOLOGY, ANTALYA, TURKEY*

Introduction: Nephrotic syndrome developing after allogeneic hematopoietic cell transplantation (allo-HSCT) is rarely reported.
Material and methods: Case: A 4 year old boy presented with generalized edema and oliguria persisting for 3 days. His past medical history revealed that he underwent allo-HSCT from a HLA-one mismatched and unrelated donor 4 months ago because of a diagnosis of leukocyte adhesion defect since he was one year old and was on a treatment protocol of prednisolone, acyclovir and ciprofloxacin.
Results: On physical examination, he was afebrile, his blood pressure 100/50 mmHg, and there was marked pretibial and periorbital edema with ascites. Urinalysis revealed massive proteinuria (protein/creatinine ratio: 9.1 mg/mg) without hematuria. Serum albumin was 1.9 g/dL, total cholesterol level 327 mg/dL and serum creatinine level 0.29 mg/dL; serum complement C3 and C4 levels were 82.8 mg/dL and 10.1 mg/dL, respectively. Antibodies to hepatitis A, B, C and HIV viruses were studied and found negative. Other conditions associated with nephrotic syndrome such as allergy and vaccinations were not found. A renal biopsy was performed, showing mild mesangial expansion and diffuse thickening of the glomerular basement membrane with the appearance of double contours on light microscopy, and C3, IgG and IgM deposits on immunofluorescence examination, compatible with membranoproliferative glomerulonephritis (MPGN). After a therapy with 2 weeks of prednisolone 2 mg/kg/day, the need for albumin and furosemide infusions were still persisting and cyclosporin, 5 mg/kg/day, was started, after when remission was achieved.
Conclusions: Hematologists and nephrologists should be aware of this uncommon complication after allo-HSCT.

P95 - Monocyte Chemoattractant Protein 1 is expressed from kidney epithelial cells in Juvenile-onset Systemic Lupus Erythematosus (JSLE)

LOUISE WATSON[1], ANGELA MIDGLEY[1], LUCY BALLANTINE[1], CAROLINE JONES[2], RICHARD HOLT[2], STEPHEN MARKS[3], CLARISSA PILKINGTON[3], KJELL TULLUS[3], MICHAEL W BERESFORD[1]
[1]*UNIVERSITY OF LIVERPOOL, INSTITUTE OF TRANSLATIONAL MEDICINE*
[2]*ALDER HEY CHILDREN'S NHS FOUNDATION TRUST HOSPITAL, LIVERPOOL, UK*
[3]*GREAT ORMOND STREET NHS HOSPITAL FOR CHILDREN, LONDON UK*

Introduction: JSLE is a severe autoimmune condition. Upto 70 % develop renal involvement and some will progress to established renal failure (1). Diagnosing active lupus nephritis (LN) include the renal biopsy and urine protein quantification. We have previously identified increased urine monocyte chemo-attractant protein 1 (MCP1) in children with active LN compared to inactive LN or healthy controls (2), which may act as a novel biomarker. In addition, the glomerular presence of MCP1 is linked to a worse renal prognosis in LN (3). We aimed to determine whether podocyte cells can express the biomarker MCP1.
Material and methods: Using a human podocyte cell line (4), an in vitro model was developed in which podocytes were cultured in the presence of TNFα in different doses and over a time course. MCP1 protein/gene expression were quantified using ELISA/qPCR respectively. Results are expressed as mean+/−standard error. Probability (p) values <0.05 were significant.
Results: Podocyte MCP1 expression was up-regulated following increasing doses and time of TNFα exposure. MCP1 gene expression reached statistical significance at a concentration of 100 pg/ml (5.7x10-5+2.4x10-5, p<0.05), 1000 pg/ml (9.8x10-5+2.4x10-5, p<0.05) and 10 ng/ml (2.2x10-4+3.1x10-5, p<0.01) TNFα compared to control (1.9x10-5+5.1x10-6). MCP1 protein expression also increased and was significant at 1000 pg/ml (333.7+ 110.8 ng/ml, p<0.05). Podocyte MCP1 expression increased incrementally in response to the time exposure of TNFα compared to normal conditions (mRNA expression at 6 hours: 4.4x10-3+1.6x10-3,p<0.05; 8 hours: 1.2x10-3+ 8.2x10-5, p<0.01, 12 hours: 2.6x10-3+1.0x10-3, p<0.05; 24 hours: 2.3x10-3+9.4x10-4, p=0.05; 72 hours: 6.3x10-3 +1.8x10-3, p<0.05 compared to control: 1.9x10-5+5.1x10-

6; protein expression at 24 hours: 301.8+80.5 ng/ml, p< 0.05; 72 hours: 821.8+150.9 ng/ml, p<0.01; 96 hours: 1140.0+46.2 ng/ml, p<0.01 compared to control 38.6+ 3.2 ng/ml).

Conclusions: MCP1 in JSLE is associated with severe lupus nephritis (3) and may be a useful biomarker of disease activity. We have demonstrated that the podocyte cell is able to up regulate MCP1. Podocyte expressed MCP1 may contribute to the increased concentration of urinary MCP1 seen in patients with active lupus nephritis. Specific targeting of this pathway may be a novel therapeutic option. References 1. Baqi N, et al. J Am Soc Nephrol. 1996 Jun;7(6):924–9. 2. Watson L, et al. Lupus 2012; 21: 496–401 3. Marks SD, et al. Nephrol dial transpl. 2008 Nov;23(11):3521–6. 4. Saleem, M.A., et al., Journal of the American Society of Nephrology : JASN, 2002. 13(3): p. 630–8

P96 - CHRONIC URTICARIA CAN PRECEED SYSTEMIC LUPUS ERYTHEMATOSUS

SIBEL YEL[1], ZUBEYDE GUNDUZ[1], KENAN YILMAZ[1], ISMAIL DURSUN[1], RUHAN DUSUNSEL[1], HAKAN POYRAZOGLU[1], HULYA AKGUN[2], FULYA TAHAN[3]

[1]ERCIYES UNIVERSITY, MEDICAL FACULTY DEPARTMENT OF PEDIATRIC NEPHROLOGY

[2]ERCIYES UNIVERSITY, MEDICAL FACULTY DEPARTMENT OF PATHOLOGY

[3]ERCIYES UNIVERSITY, MEDICAL FACULTY DEPARTMENT OF PEDIATRIC ALLERGY

Introduction: Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by widespread inflammation that results in end-organ damage. Urticaria can be observed in lupus patients, at the beginning or during the course of the disease. Chronic autoimmune urticaria at the SLE onset is rare in even adults and so far this manifestation in a pediatric lupus population has been reported in only two patients.

Material and methods: We report here an unusual case presented as vasculitis with rash, and chronic urticaria and then diagnosed with 'full-house' nephropathy. A 12 year old girl presented with urticaria, purpuric rash and nephrotic range proteinuria suggesting systemic vasculitis. She had hypocomplementemia and positive antinuclear antibodies. Renal biopsy revealed full house nephropathy. The juvenile SLE diagnosis was established one year after onset of urticaria. Although fulfilling only three ARA criteria patient was accepted as lupus nephritis and treated with pulse methyl prednisolone and cyclophosphamide.

Results: A "full-house" immunofluorescence pattern on renal biopsy in a female patient is highly suggestive of a possible diagnosis of SLE. Chronic urticaria may preceed the classical manifestation of SLE.

Conclusions: The children with chronic urticaria should be followed carefully for other clinical and laboratory evidence of SLE to avoid any delay for diagnosis.

P97 - Clinicopathological characteristics and kidney outcome of childhood-onset lupus nephritis with acute kidney injury: from the multicenter study in Japan

SHINGO ISHIMORI[1], HIROSHI KAITO[1], HIROMI OTSUBO[1], FUSAKO HASHIMOTO[1], TAKESHI NINCHOJI[1], ICHIRO KAMIOKA[2], YUKO SHIMA[3], KIYOSHI HAMAHIRA[4], KOICHI NAKANISHI[3], RYOJIRO TANAKA[5], NORISHIGE YOSHIKAWA[3], KAZUMOTO IIJIMA[1]

[1]DEPARTMENT OF PEDIATRICS, KOBE UNIVERSITY GRADUATE SCHOOL OF MEDICINE

[2]DEPARTMENT OF PEDIATRICS, KAKOGAWA WEST CITY HOSPITAL

[3]DEPARTMENT OF PEDIATRICS, WAKAYAMA MEDICAL UNIVERSITY

[4]DEPARTMENT OF PEDIATRICS, HIMEJI RED CROSS HOSPITAL

[5]DEPARTMENT OF NEPHROLOGY, HYOGO PREFECTURAL KOBE CHILDREN'S HOSPITAL

Introduction: Lupus nephritis (LN) is the major important factor influencing the course of systemic lupus erythematosus (SLE). Some previous reports demonstrated that acute kidney injury (AKI) at the onset of SLE is a risk factor for end stage kidney disease (ESKD). However, there is scarce data of childhood-onset LN with AKI, especially after various sorts of new therapeutic approaches.

Material and methods: We retrospectively reviewed all the patient files of SLE below the age of 16 at the time of diagnosis from 1995 to 2010, and all the patients performed kidney biopsy promptly after diagnosis and their consent. AKI was defined with pediatric-modified RIFLE (p-RIFLE) classification. Estimated glomerular filtration rate (eGFR) was measured with Schwartz's formula below the age of 18 years and the modification of diet in renal disease study equation over 18 years.

Results: Thirty-six patients (10 males and 26 females) were enrolled. Mean age at diagnosis and mean observation period were 11.6±2.4 years old and 8.1±4.4 years, respectively. Seven (19 %) patients were identified as AKI at the onset of SLE. In comparison with the non-AKI group, patients with AKI had significantly higher proportions of nephrotic syndrome and proliferative LN, and significant lower C3. The systemic lupus erythematosus disease activity index (SLEDAI) scores at the onset of SLE were significantly higher in the AKI group. Regarding outcome, only 1 patient in AKI group had progressed to ESKD with no complete recovery of kidney function after AKI. There was statistically no

difference in eGFR at the last visit between two groups (106 ±29 ml/min/1.73 m2 in AKI group and 107±26 ml/min/1.73 m2 in non-AKI group; p=0.47).

Conclusions: Patients with AKI at the onset of SLE had more severe than non-AKI patients including extrarenal manifestation. Nevertheless, our study suggested a good kidney outcome of childhood-onset LN with AKI, at least in the near-to-mid term. It may be of great importance to induce a prompt and complete remission for preserving good kidney function.

P98 - Matrix metalloproteinase (MMP)-3, MMP-8 and interleukin-17 in children with systemic lupus erythematosus

SE JIN PARK[1], JAE IL SHIN[2], TAE-SUN HAA[3]
[1]*DEPARTMENT OF PEDIATRICS, AJOU UNIVERSITY SCHOOL OF MEDICINE, AJOU UNIVERSITY HOSPITAL, SUWON, KOREA*
[2]*DEPARTMENT OF PEDIATRICS, YONSEI UNIVERSITY COLLEGE OF MEDICINE, SEVERANCE CHILDREN'S HOSPITAL, SEOUL, KOREA*
[3]*DEPARTMENT OF PEDIATRICS, CHUNGBUK NATIONAL UNIVERSITY COLLEGE OF MEDICINE, CHEONGJU, KOREA*

Introduction: To determine whether matrix metalloproteinase (MMP)-3, 8 may have a role in the pathogenesis of childhood systemic lupus erythematosus (SLE).

Material and methods: In this study, we recruited 11 patients (8 female, 3 male) with SLE and 9 healthy controls (7 female, 2 male) who visited the Department of Pediatrics at Severance Children's hospital and Seoul National University Children's hospital from 2010 to 2011. Patients fulfilled the 1987 American Rheumatism Association revised criteria for SLE diagnosis.

Results: There were no differences in WBC, BUN, and serum cholesterol between the two groups. MMP-3 in SLE patients was significantly increased more than that in controls (195.3± 15.1 vs. 26.4±6.4 ng/mL, P<0.0001). However, the levels of MMP-8 and IL-17 did not significantly differ between the patients with SLE and healthy controls (38.6±13.7 vs. 16.8± 9.0 ng/mL, P<0.248; 62.8±52.2 vs. 91.0±44.5 pg/mL, P< 0.397, respectively). There were no differences in MMP-3, MMP-8, and IL-17 between SLE patients with or without nephritis. C3 and C4 levels were decreased in SLE children with positive anti-dsDNA antibody compared with SLE children without positive anti-dsDNA antibodies. (P<0.068; P< 0.028, respectively). There were no significant differences in MMP-3, MMP-8, and IL-17 between SLE children with and without positive anti-dsDNA antibodies. However, further studies are necessary to support these findings by a sufficient number of patients in the future.

Conclusions: The serum MMP-3 levels were significantly increased in children with SLE compared to normal controls and were positively correlated with serum total cholesterol and negatively correlated with serum albumin levels. However, serum MMP-3 levels did not correlate with disease activity of SLE or the presence of nephritis.

P99 - Lack of association between genetic polymorphisms of paraoxonase 1 192 and glutathione peroxidase 1 197 enzymes with Familial Mediterranean Fever

FARUK OKTEM[2], HÜLYA ANIL[1], RECEP SUTCU[3], AYÇA ESRA KUYBULU[1]
[1]*SÜLEYMAN DEMIREL UNIVERSITY FACULTY OF MEDICINE*
[2]*BEZMİ ALEM VAKIF UNİVERSİTY FACULTY OF MEDICINE*
[3]*KATIP CELEBI UNİVERSİTY FACULTY OF MEDICINE*

Introduction: The aim of this study was to investigate gene polymorphisms of important antioxidative enzymes, glutathione peroxidase (GPX) and paraoxonase (PON) frequencies in FMF patients, and their roles in the pathogenesis of FMF.

Material and methods: Sixty FMF patients on attack free period and 51 healthy children as control group were included in this study. PON1 Q/R192 and GPX1 Pro197Leu gene polymorphisms were studied. Blood urea nitrogen, creatinine and serum lipid profile of samples were measured.

Results: PON1 Q/R192 genotype distribution was 52 % QQ, 46 % QR and 2 % RR in the FMF group and 45 % QQ, 45 % QR and 10 % RR in the control group (P>0.05). GPX1 Pro197Leu genotype distribution was 28 % PP, 57 % PL, %15 LL in the FMF group and 18 % PP, 53 % PL, %29 LL in the control group (P>0.05). Blood urea nitrogen, serum creatinine, lipid levels, the distribution of PON1 Q/R192 and GPX1 Pro197Leu genotypes were similar in both groups.

Conclusions: PON1 Q/R192 and GPX1 Pro197Leu gene polymorphisms are not important risk factors in the development of FMF.

P100 - Evolution and concordance of FSGS histologic lesions in native kidney and renal allograft biopsies

ELISABETH A M CORNELISSEN[1], RUTGER MAAS[2], ERIC STEENBERGEN[3], BART SMEETS[3], JEROEN DEEGENS[2], JACQ WETZELS[2]
[1]*PED. NEPHROLOGY, RADBOUD UNIVERSITY NIJMEGEN MEDICAL CENTRE, NETHERLANDS*
[2]*NEPHROLOGY, RADBOUD UNIVERSITY NIJMEGEN MEDICAL CENTRE, NETHERLANDS*
[3]*PATHOLOGY, RADBOUD UNIVERSITY NIJMEGEN MEDICAL CENTRE, NETHERLANDS*

Introduction: The Columbia classification of FSGS defines five mutually exclusive histologic variants. It is unclear if these variants reflect pathogenetic differences. We questioned if the classification of FSGS remains unchanged in an individual patient. Therefore, we compared repeated biopsies, performed in the native kidney as well as in the allograft during recurrence after transplantation.
Material and methods: We identified 30 patients with a biopsy proven diagnosis of FSGS in the native kidney and FSGS recurrence in a renal graft. Twelve patients were excluded because slides from only one kidney biopsy were available. Biopsy specimens from native (n=22) and transplant kidneys (n=45) of 18 patients were reviewed according to the Columbia classification. Samples without FSGS lesions were classified as minimal lesions (ML).
Results: Median age at FSGS diagnosis of these patients was 15 (range 4–57) years. We evaluated 25 repeated biopsies (8 native kidney, 17 transplant kidney). A change in variant was observed in 16 (64 %). Fourteen patients with known native kidney histology developed a recurrent FSGS in 18 transplants. In the majority of patients the first allograft biopsy showed a ML pattern. We did not find any correlation between the variant in the native kidney and the first or second allograft.
Conclusions: In the majority of patients there was no concordance in FSGS variants between repeated biopsies or between native and transplant kidney biopsies. These data suggest that the morphological variants must reflect different stages in the evolution of lesions

P101 - TUBULAR-INTERSTITIAL NEPHRITIS CAUSED BY HANTAVIRUS INFECTION

ALEXANDER KOLSKY[1], SVETLA NAJMANOVA[2], ZDENKA VERNEROVA[3], HANA ZELENA[4], DUSAN KOTUS[1], ALZBETA BUHROVA[1], ZUZANA KOVAROVA[1], BARBORA KOCIANOVA[1], MONIKA KOLSKA[1], FELIX VOTAVA[1]
[1]*DEPT. OF PAEDIATRICS, 3RD MEDICAL FACULTY, CHARLES UNIVERSITY, FNKV, PRAGUE 10*
[2]*DEPT. OF PAEDIATRICS, DISTRICT HOSPITAL, KLADNO*
[3]*DEPT. OF PATHOLOGY, 3RD MEDICAL FACULTY, CHARLES UNIVERSITY, FNKV, PRAGUE 10*
[4]*INSTITUTE OF PUBLIC HEALTH, OSTRAVA*

Introduction: The authors report the case of a 15-year-old girl diagnosed to have glycosuria during a preventive check-up. At the same time, the girl had lost 5 kg of body weight over the last three months. The mother and girl are carriers of Leiden mutations. The girl´s history was otherwise unremarkable. In the past, her urinary sample findgings had always been negative.
Material and methods: On examination, her findings were physiological including blood pressure, height 172 cm, weight 45.7 kg, BMI 15.4 (below the 3rd percentile). The girl was feeling well and reported no complaints. Her body temperature was not elevated, nor had she been taking any drugs in recent months.
Results: Because of the glycosuria and weight loss, she was referred to her district department of pediatrics quickly ruling out the diagnosis of diabetes mellitus (glycemic profile, glycated HbA1C 4.2 %). However, the examination showed a reduced glomerular filtration rate (GFR) of 0.56 ml/s/1.73 m2 (=33.6 ml/min/m2) and s-Cys of 1.39 mg/l. C-reactive protein was 85 mg/l, with ESR being in the range of 60–85. Urinary findings were as follows: glykosuria (12.8 mmol/d), proteinuria (0.5 g/24 h), significant tubular proteinuria (ELFO); urinary sediment was negative, bacteriuria was repeatedly negative, N-acetyl-beta-D-glukoaminidase 59.03 nkat/l (norm 0–15.7), beta-2-microglobulin 16.68 mg/l (norm 0.3-0.36) and alpha-1-microglobulin 116.06 mg/l (norm 0–12). Hyperaminoaciduria was not present. Phosphorus and calcium excretion rates were within normal. Examination of the anterior eye segment was negative. Ultrasound revealed diffuse parenchymal lesions of both kidney, with normal kidney size. Static renal scintigraphy 99 m-Tc DMSA showed both kidneys with unequal lateral edges without obvious parenchymal defects. On day 9 post admission, renal biopsy was performed documenting acute tubulo-interstitial nephritis (TIN). Virological investigation revealed hantavirus positivity in blood. Subsequent immunoblotting identified a Puumala hantavirus strain. Given the renal biopsy finding and further progression of GFR to 0.41 ml/s/1.73 m2, corticosteroid therapy was initiated (six pulses of methylprednisolone with continued prednisone therapy). GFR values normalized during this therapy. As the girl´s clinical status was satisfactory, the dose of prednisone was gradually tapered to 20 mg every other day. While, at present, the girl has no complaints, her urinary findings do persist.
Conclusions: TIN of infectious origin is not common in childhood. Clinical manifestations of hantavirus TIN may include different forms of renal impairment that may eventually result in kidney failure.

P102 - Benefit of Eculizumab treatment in a child with severe D+HUS?

RIXT SCHRIEMER, JAAP GROOTHOFF, MICHIEL OOSTERVELD, JEAN-CLAUDE DAVIN, ANTONIA BOUTS
EMMA CHILDREN'S HOSPITAL, AMC, AMSTERDAM, THE NETHERLANDS

Introduction: To describe an atypical presentation of D+ HUS, with renal cortical necrosis on biopsy, treated with eculizumab.

Material and methods: An 8-month old girl presented with fever and prolonged convulsion. There was a two-day history of diarrhoea and vomiting. Blood pressure was normal and there were no signs of dehydration except for tachycardia and anuria since 24 hours. Antibiotics and anticonvulsive treatment was initiated.
Results: Blood results showed a serum creatinine of 366 umol/l, urea 23.6 mmol/l, LDH 2809 U/l, normal haptoglobin, Hb 5.5 mmol/l and no thrombocytopenia. An ultrasound showed normal sized kidneys without obstruction. A diagnosis of acute tubular necrosis secondary to gastroenteritis and dehydration was made. Renal replacement therapy was initiated. Two days after admission haptoglobin decreased and thrombocytopenia ensued. C3 and C4 were reduced. Blood, CSF and faeces cultures were still negative. Atypical HUS was considered and plasmapheresis started. Kidney biopsy showed massive renal cortical necrosis. MAG3-scan showed no renal uptake. On day 8 of admission stool cultures grew STEC, which led to the diagnosis of D+ HUS. Plasmapheresis was discontinued. Eculizumab was given on days 11, 18 and 25 of admission. C3 and C4 levels had returned to normal before the first dose of eculizumab. From day 18 diuresis resumed and dialysis was discontinued on day 27. However, renal function remains abnormal 2 months after presentation (serum creatinine 100 umol/L). Complement mutation analysis and CFH antibodies were negative.
Conclusions: In a child with D+HUS, massive renal cortical necrosis and anuria since 11 days, eculizumab treatment was followed by improvement -but not normalization- of renal function allowing dialysis discontinuation. The role of eculizumab in the favourable evolution of our patient remains questionable. Clear indications for the use of eculizumab and its timing to administration related to complement activation in D+HUS remain to be defined.

P103 - Long-Term Maintenance of Efficacy with Losartan in Children with Alport Syndrome: Results from a Subgroup Analysis of a Randomized Controlled Trial

NICHOLAS WEBB[1], SHAHNAZ SHAHINFAR[2], THOMAS WELLS[4], RACHID MASSAAD[3], GILBERT GLEIM[5], CHRISTINE MCCRARY SISK[5], CHUN LAM[5]
[1]*ROYAL MANCHESTER CHILDREN'S HOSPITAL*
[2]*CHILDREN'S HOSPITAL OF PHILADELPHIA*
[3]*ARKANSAS CHILDREN'S HOSPITAL*
[4]*MSD EUROPE*
[5]*MERCK SHARP AND DOHME*

Introduction: A 12-week, double-blind, multinational study showed that losartan significantly lowered proteinuria compared with placebo and amlodipine and was well tolerated in children aged 1–17 years with proteinuria secondary to Alport syndrome, with or without hypertension. The aim of the present open-label, extension phase of this study was to assess the long-term efficacy and tolerability of losartan versus enalapril after 3 years of treatment in this population. The aim of the present open-label, extension phase of this study was to assess the long-term efficacy and tolerability of losartan versus enalapril after 3 years of treatment in children with proteinuria secondary to Alport syndrome.
Material and methods: Patients with Alport syndrome who had completed the 12-week core study were re-randomized to remain on losartan or start enalapril, and followed for proteinuria and renal function. The extension study continued for up to 3 years.
Results: A total of 27 patients with Alport syndrome were randomized to losartan (0.44 to 2.23 mg/kg/d; N=15) or enalapril (0.07 to 0.72 mg/kg/d; N=12). The mean duration of follow-up was 997 days. The mean urinary protein/creatinine ratio (UPr/Cr) at the end of the 12 week core study was 1.9 (1.3) g/g for losartan and 1.6 (0.8) g/g for enalapril, and the mean estimated glomerular filtration rate (eGFR) was 145.8 for losartan and 149.0 for enalapril. The proteinuria reduction observed in losartan treated patients in the 12 week core study was sustained. After 3 years of treatment, the LS mean percent change from week 12 in UPr/Cr was an increase of 1.1 % in the losartan group vs. a further reduction of 13.9 % in the enalapril group [geometric mean ratio (95 % CI)=1.2 (0.7, 2.0)] and the LS mean change from week 12 eGFR was −6.4 ml/min/1.73 m2 in the losartan group vs. -9.1 ml/min/1.73 m2 in the enalapril group [treatment difference (95 % CI)=2.7 ml/min/1.73 m2 (−33.8, 39.2)]. The adverse event (AE) incidence was low and comparable in both treatment groups.
Conclusions: In children with proteinuria secondary to Alport syndrome, with or without hypertension, losartan maintained proteinuria reduction, and enalapril produced additional proteinuria reduction over the 3-year study period. Both agents were generally well tolerated.

P104 - RENAL INVOLVEMENT IN HIV INFECTED ROMANIAN CHILDREN

MIHAI GAFENCU[2], GABRIELA DOROS[2], RODICA COSTA[1], ADALBERT SCHILLER[2], NILIMA KUNDANI[1], IULIA ELENA JURCA- SIMINA[1]
[1]*"LOUIS TURCANU" CHILDREN EMERGENCY HOSPITAL, TIMISOARA, ROMANIA*
[2]*"VICTOR BABES" UNIVERSITY OF MEDICINE AND PHARMACY, TIMIŞOARA, ROMâNIA*

Introduction: Renal involvement in HIV infected children is various, appearing after many years of evolution, related to disease or to the nephrotoxic effect of HAART. The objective of this retrospective study is to establish the

existence of renal dysfunction after years of HIV infection in Romanian children.

Material and methods: We studied a group of 48 HIV infected patients from the western Romania, with ages between 16 and 20 years, admitted between 2010 and 2011. They were diagnosed at 10 to 20 years (10–15 years- 38 patients, 16–20 years- 10 patients) and half of them were non-Tenofovir HAART treated, the rest being on single or double antiretroviral drugs. 27.08 % were in stage B and 72.92 % in stage C of HIV. We detected the presence of hypertension, proteinuria, hematuria and other markers of renal dysfunction after years of HIV infection and response to treatment.

Results: Hypertension was present at 29.16 % patients (8.33 % in stage B and 20.83 % in stage C), proteinuria was documented in 6.25 % of cases and hematuria (Addis cell count) in 18.75 %, all in stage C of the disease. 33.33 % of patients presented metabolic acidosis and 8.33 % hyperkalemia in stage C. Low creatinine clearance (estimated with Schwartz/ Cockroft- Gault formula) was observed in 4.16 % of patients in stage C. Mild anemia was found at 8.33 %. 4.16 % had mild hydronephrosis but without significant ultrasound changes.

Conclusions: This study demonstrates that renal function was maintained in stage B patients compared with stage C patients. Renal dysfunction progresses in parallel with advancement of HIV infection under treatment but on a very slow rate. HAART proves to be beneficial not only in long term patient survival but also to delay renal complications.

P105 - RRENAL GROWTH AND FUNCTION OF THE RADIOLOGICALLY NORMAL SINGLE KIDNEY IN CHILDHOOD

EKATERINI SIOMOU[1], VASILEIOS GIAPROS[2], FREDERICA PAPADOPOULOU[3], MARIA PAVLOU[1], ANDREAS FOTOPOULOS[4], ANTIGONI SIAMOPOULOU[1]
[1]*DEPARTMENT OF PEDIATRICS, UNIVERSITY HOSPITAL OF IOANNINA, IOANNINA, GREECE*
[2]*NEONATAL INTENSIVE CARE UNIT, UNIVERSITY HOSPITAL OF IOANNINA, IOANNINA, GREECE*
[3]*DEPARTMENT OF RADIOLOGY, UNIVERSITY HOSPITAL OF IOANNINA, IOANNINA, GREECE*
[4]*DEPARTMENT OF NUCLEAR MEDICINE, UNIVERSITY HOSPITAL OF IOANNINA, IOANNINA, GREECE*

Introduction: The long-term outcome of patients with a single kidney (SK) remains a topic of concern, especially in children who may start their life with a SK.

Material and methods: In order to estimate growth/functional parameters of the radiologically normal SK, 38 children 8–16 years (9.2 ±4.9 years) were studied (23 with congenital SK, 9 with multicystic dysplastic kidney, and 6 with acquired SK from early infancy). The control group consisted of 40 healthy children age and sex matched to the patients (10.5 ±2.6 years).

Results: Kidney length, volume and the ratio of kidney length or volume to BSA were significantly higher in patients as a total, ≤10 or>10 years compared to controls ($p<0.0001$). No significant differences were found in resistive index (RI) of interlobar and arcuate arteries between patients and controls. Cre levels tended to be higher in patients as a total ($p=0.06$), and >10 years ($p<0.01$), while estimated GFR was significantly lower ($p<0.05$) in patients as a total and ≤10 years. There was no significant difference in Cre Clearance (CrCl), 24-hour protein and microalbumin urinary excretion in patients as a total, or ≤10 years, but a significant increase was noted in 24-hour protein excretion in patients >10 years. There was no significant correlation between years of SK and Z-score systolic/diastolic blood pressure, RI of interlobar/arcuate arteries, CrCl, DTPA-GFR, and 24-hour protein excretion. However, a significant independent positive correlation was found between years of SK and 24-hour microalbumin excretion ($p<0.05$).

Conclusions: The hyperfiltration of SK was not associated with findings of glomerulosclerosis, at least during the first 8–16 years of life. A follow-up is necessary to evaluate whether the higher 24-hour protein excretion in patients >10 years and the positive correlation of 24-hour microalbumin excretion with years of SK represents an early finding of future glomerulosclerosis.

P106 - Clinical and histopathological characteristics of renal diseases in children: our experience

SNEZANA ZULIC, NEDIMA ATIC
UNIVERSITY CLINICAL CENTER TUZLA

Introduction: The study was conducted in order to evaluate the clinical and histopathology findings in the diagnosis of renal diseases in children.

Material and methods: The study included 26 children of both sexes, aged up to 15 years, who were found to have a renal disease through percutaneous biopsy. Research was conducted at the Department of Paediatrics, University Clinical Center Tuzla in the period between 2000 to 2010. Age and sex of the child, clinical and laboratory features, indications for renal biopsy and histopathology findings were all analyzed.

Results: The most common indication for renal biopsy in our patients was nephrotic syndrome in 14(53,8 %), followed by asymptomatic hematuria and proteinuria in 11 (53,8 %) and chronic renal failure in 1(3,8 %) of patients. The most common were glomerular diseases in 21 (80,8 %), tubulointerstitial nephritis was found in 1(3,8 %) and systemic disease in 1(3,8 %) of our patients. The biopsy was

negative in 3(11,5 %) patients. Among patients with glomerulonephritis, in 19(73 %) it was primary, in 2(7,7 %) it was secondary and in 1(3,8 %) % it was congenital. The most frequent primary glomerulonephritis was focal segmental glomerulosclerosis (FSGS) in 7(26,9 %), mesangial proliferative glomerulonephritis (MEPGN) was found in 6 (23 %), membranoproliferative glomerulonephritis (MPGN) in 3(11.5 %), minimal change disease (MCD) in 2(7,7 %) and rapidly progressive glomerulonephritis (RPGN) in 1 (3,8 %) of patients. Among the secondary glomerulonephritis, 1(3,8 %) patient had biopsy- proven lupus nephritis (LN) and 1(3,8 %) had Henoch-Schönlein purpura nephritis (HSPN).

Conclusions: It is difficult to present a definitive epidemiological data on the incidence of renal diseases. Clinical and histopathology evaluation are important for clinical practice. Although the sample is not representative and the numbers do not correspond with those from other centres, this analysis provides insight into the the common occurence of renal diseases in our environment and points that there is a need to establish a registry of renal biopsies.

P107 - An uncommon presentation of hydatid cysts: Renal hydatid disease in two children

NESLIHAN CICEK DENIZ[1], IBRAHIM GOKCE[1], HALIL TUGTEPE[2], TUFAN TARCAN[3], HARIKA ALPAY[1]

[1]*MARMARA UNIVERSITY MEDICAL FACULTY, DEPARTMENT OF PEDIATRIC NEPHROLOGY*

[2]*MARMARA UNIVERSITY MEDICAL FACULTY, DEPARTMENT OF PEDIATRIC SURGERY*

[3]*MARMARA UNIVERSITY MEDICAL FACULTY, DEPARTMENT OF UROLOGY*

Introduction: Cyst hydatid is an important sestode infection caused by Echinococcus granulosus. It is prevelant worldwide, but especially in Mediterranean countries, Middle East and Australia. Hydatid cyst disease mostly involves the liver and the lung, while renal involvement is rare, comprising only 2 % of all cases. In this presentation we aimed to draw attention to cyst hydatid disease in differential diagnosis of renal cysts in children.

Material and methods: Two cases with renal hydatid disease are presented.

Results: CASES: First case was a six year old girl admitted with abdominal pain. A cystic lesion was visualized in the left kidney by ultrasonography. Indirect hemaglutination was positive (1/512). No cysts were vizualised in other organs by abdominal and cranial CT. After six months of mebendazol therapy, complete cyst resection was performed. She is currently followed as healthy. The second patient was a 17 year old boy admitted with respiratory distress and abdominal pain. Cystic lesion measured 82x65 mm was vizualised in the right hepatic lobe. One cystic lesion with 56x51 mm in size was detected in the right kidney and three cystic lesions measured 55x53 mm, 37x35 mm, 32x26 mm were detected in the left kidney. Indirect hemaglutination was found positive (1/320). PAIR (puncture, aspiration, injection, reaspiration) was performed for the cystic lesion in liver. He is on mebendazol therapy for 12 months, and is being followed for the reduction of cysts dimension.

Conclusions: Renal hydatid disease should be considered in children presenting with renal cyst, especially in areas where it is endemic. Prognosis is good with early diagnosis and appropriate treatment.

P108 - DENSE DEPOSITS DISEASE (DDD): FAVORABLE LONG-TERM OUTCOME ON ENALAPRIL DESPITE PERSISTENCE OF COMPLEMENT ACTIVATION

NIELS RUTJES[1], JAAP GROOTHOFF[1], ANTONIA BOUTS[1], NICOLE VAN DE KAR[2], JUDITH WILLEMSE[3], LISA STRAIN[4], TIM GOODSHIP[4], JEAN-CLAUDE DAVIN[1]

[1]*EMMA CHILDREN'S HOSPITAL / ACADEMIC MEDICAL CENTER (THE NETHERLANDS)*

[2]*RADBOUD UNIVERSITY NIJMEGEN MEDICAL CENTER (THE NETHERLANDS)*

[3]*ACADEMIC MEDICAL CENTER (THE NETHERLANDS)*

[4]*INSTITUTE OF GENETIC MEDICINE NEWCASTLE UNIVERSITY (UNITED KINGDOM)*

Introduction: Dense deposits disease (DDD) is a rare disease that carries a high risk for end-stage renal failure. It is thought to result from uncontrolled systemic activation of the alternative pathway of the complement cascade. This is most commonly caused by C3 nephritic factor (C3Neph) or less often by anti-Factor H antibodies (anti-FH Abs) or mutations of complement factor genes. We describe the favorable course of disease in a patient with DDD secondary to anti-FH Abs, treated with enalapril after unsuccessful plasma exchange (PE) therapy.

Material and methods: 16 year old girl with recurrent tonsillitis, fatigue and nephrotic proteinuria (>0.2 g/mmol creatinine) but normal renal function. Low C3 and AP50. High C3d. C3Nef was not present but anti-H Abs were detected. Pl, FH and FI concentrations were normal. No mutations of complement factor genes: CFH, C3, CFB, CFI and MCP. Renal biopsy showed typical features of DDD. Because the patient refused treatment with steroids, enalapril in standard dosages was initiated once PE therapy was completed (40 ml/kg fresh-frozen plasma, 3x/week, 8 weeks).

Results: Complement abnormalities did not change over time. Serum albumin levels normalized 5 months after discontinuation of PE therapy and proteinuria decreased to values<0.1 g/mmol creatinine after 8 months. After enalapril was stopped for 2.5 months, proteinuria increased (from 0.07 g/mmol creatinine to 0.16 g/mmol creatinine), but returned to 0.08 g/mmol creatinine after reintroduction. After 5 years on enalapril, plasma creatinine is 60 μmol/L and proteinuria 0.048 g/mmol creatinine.
Conclusions: 1. PE did not affect proteinuria. 2. No relationship was detected between proteinuria and complement activation, implicating other factors than complement activation in the pathogenesis of DDD. 3. A positive effect of enalapril on proteinuria is suggested by the recurrence of proteinuria after cessation of enalapril. 4. Spontaneous recovery of DDD can not be excluded.

P109 - TWO HISTOLOGICAL CLASSIFICATIONS IN THE EVALUATION OF HSP-GLOMERULONEPHRITIS

MIKAEL KOSKELA[1], HELENA AUTIO-HARMAINEN[2], OUTI JAUHOLA[1], JAANA RONKAINEN[3], MATTI NUUTINEN[1]
[1]*DEPT. OF PEDIATRICS, OULU UNIVERSITY HOSPITAL, OULU, FINLAND*
[2]*DEPT. OF PATHOLOGY, OULU UNIV. HOSPITAL, OULU, FINLAND*
[3]*OULU CITY HEALTH CARE CENTRE, OULU, FINLAND*

Introduction: Two kidney biopsy classifications were evaluated in nephrotic/nephritic Henoch-Schönlein purpura glomerulonephritis (HSP-GN).
Material and methods: Eleven HSP-GN patients (4 girls, 7 boys) with two kidney biopsies were included into analyses. Mean age (years) at the first and second biopsy and at the last control were 11.4 (range 5.1-16.8), 15.5 (7.1-25.6) and 23.1 (12.5-34.9), respectively. Mean follow-up time was 11.7 years (range 0.5-21.3). All biopsies were classified with ISKDC classification and a semiquantitative classification (1).
Results: In the last control 7/11 of the patients had no renal symptoms, one had proteinuria with normal kidney function, one proteinuria with reduced kidney function, one was in dialysis and one had died due to HSP-GN. At the time of the first biopsy and at the last control mean U-protein/creatinine ratio (g/mol crea) was 479.8 (range 47.7-1330) and 22.5 (4–113) and mean S-creatinine (μmol/l) 67.6 (range 33–153) and 80.7 (57–158), respectively. The time elapsed between the biopsies was by mean 4.1 years. The activity index according to the semiquantitative classification declined from the first biopsy to the second in 9/11 cases, stayed the same in one and increased in one. The chronicity index increased in ten patients, and declined in one. Overall score of the semiquantitative classification increased in 7/11 cases, declined in 2 and stayed the same in 2. In contrast, ISKDC classification increased in 3/11 cases from the first biopsy to the second, and declined in 8/11. Only in two cases the changes between the two classifications occurred to the same direction (the score increased).
Conclusions: The semiquantitative classification was more sensitive than ISKDC classification, which may be too rough to describe progression of HSP-GN. References: 1. Jaana Ronkainen et al. Long-term outcome 19 years after childhood IgA nephritis; a retrospective cohort study. Pediatr Nephrol 21: 1266–73, 2006.

P110 - An Unusual Case of Henoch Schonlein Purpura

MEHMET BAHA AYTAC[1], AYSEN AYDOGAN[2], KURSAT YILDIZ[1], ZELAL EKINCI[1]
[1]*KOCAELI UNIVERSITY SCHOOL OF MEDICINE*
[2]*DERINCE TRAINING AND RESEARCH HOSPITAL*

Introduction: Although Henoch Schonlein Purpura(HSP) has a benign character, life threatening presentations can be seen. Here we report a case of HSP in whom protein loosing enteropathy with severe life threatening gastrointestinal bleeding was found to be the leading cause of severe hypoalbuminemia.
Material and methods:
Results: Case report: A 14-year-old boy, who presented with purpuric rash, abdominal pain, swelling on ankle, revealed the diagnosis of HSP. Hypoalbuminemia(1.88 g/dl), hyponatremia(116 mEq/l) and normal serum creatinine level(0.51 mg/dl) were detected with normal urinalysis while he was on prednisolon therapy. He had bilateral pleural effusions. Pericardial effusion was determined on echocardiography. Increased excretion of fecal α1-antithyripsin and the absence of proteinuria revealed protein loosing enteropathy. As low levels of IgM(27 mg/dl), IgG(336 mg/dl) and serum complement C3(73 mg/dl) were attributed to the intestinal protein loss, IVIG was delivered. During that time nephrotic range proteinuria(124 mg/m2/h) was detected. Renal biopsy, indicating HSP nephritis, was performed. Endoscopic examination of the gastrointestinal tract demonstrated aphthous lesions on ileum, multiple mucosal ulcerations on colon and rectum, and necrotic ulcerations on antral mucosa. IgA deposits on biopsy revealed the gastrointestinal involvement. Pulse methylprednisolon therapy (30 mg/kg/d) was given for three days, then oral prednisolon (2 mg/kg) was initiated. Plasma exchange(PE) therapy was preferred because of coexisting pneumonia, when he had generalized convulsion. Cranial MRI showed posterior reversible encephalopathy indicating central nervous system involvement. When massive melena was noted, hemoglobin

decreased to 4.4 g/dl and 24 erithrocyte suspensions were required to recover anemia. After 6 PE therapies, he had still nephrotic proteinuria. Intravenous cyclophosphamid together with pulse methylprednisolon therapy improved gastrointestinal bleeding. Because of the persisting proteinuria and active cerebellar lesions on MRI despite of the long term use of corticosteroids, azathiopyrin was added for immunsupression. When he was discharged with prednisolon(2 mg/kg/d) and azathiopyrin(1.5 mg/kg/d), laboratory remission, including normal serum albumin(3.4 g/dl) and creatinine levels(0.68 mg/dl), was maintained except proteinuria.

Conclusions: Although HSP is a common disease, sometimes it presents with life threatening organ involvement. Severe gastrointestinal and central nervous system involvement in this patient could not be controlled even with methylprednisolon and PE. Early intravenous cyclophosphamid therapy is the most efficient way for suppressing severe diseases.

P111 - Childhood lupus nephritis: 10 years single center experience

INA KAZYRA[1], ALEXANDER SUKALO[1], TATJANA LETKOVSKAJA[1], NATALIA TUR[2], SVETLANA KROCHINA[2], JULIA SCHINKORENKO[2], ANZHELIKA BORYCHEVA[2]
[1]*BELARUS STATE MEDICAL UNIVERSITY*
[2]*2ND CHILDREN'S HOSPITAL*

Introduction: To analyze clinical, laboratory features and outcome of Belarusian children with lupus nephritis (LN) followed between 2002–2012 yrs.

Material and methods: 35 children (26 girls and 9 boys) with biopsy proven LN were observed at the Department of Pediatric Nephrology of the Republic Center.

Results: The disease was preceded by infections in 35 %, allergy (22,2 %), insolation (17 %), unknown (17 %), fatigue (11 %). The median age at the disease onset was 13, 5 yrs (9 – 17). The symptoms were present on average 3 months (0–96) before the diagnosis was made. The commonest presenting clinical features were: skin lesions in 22/35 (62 %), arthralgias (54 %), arthritis in 4/35, lymphadenopathy (34 %), cardiac (21 %), serositis in 21 %, neurological (17 %). Arterial hypertension was diagnosed in 27/35 (78 %). Renal disorders were marked in a debut of the disease in 12/35 -34 %, in most others developed during a year. Laboratory abnormalities included increased ESR (max 74 mm/h) – 94 %, cytopenia 73 %, low C3 (59 %) and C4 (38 %), positive anti dsDNA in 69 %, ANA (44 %), high IgG in 59 %, ACA in 34 % (66,7 % with active and in 41,6 % with class IV LN). AntiC1q antibodies (AB) were positive in 66,7 % (in 83,3 % with active LN). 50 % patients had low mannan-binding lectin (MBL) level (in 67 % with active and 42 % with class IV). Antiphospholipid syndrome was diagnosed in 8/35 patients. Renal biopsy revealed class II (n=7), III (n=3), IV (n=23), V (n=2) according to ISN/RPS criteria 2004. High levels of antiC1qAB, anti dsDNA, ANA with low C3 and MBL were associated with more active and severe morphological diseases and could be used as non-invasive markers in diagnostic of severe renal lesions. 9 patients were initially treated by oral corticosteroids (CS), 17 received puls-therapy (PS) CS and 10 PS cyclophosphamide (CYC) with plasmapheresis. Prednisolon (Pred)+azathioprin (AZA) received 17 patients (3 as induction therapy), switched on Pred+Cyclosporine A (CyA) – 11. Pred+CyA - 16 patents, switched on Pred+AZA – 8. Pred+Mycophenolate mofetil (after CYC PS as induction therapy) 1 girl. Leukeran+Pred −10 children. Intravenous immunoglobulin was prescribed in 13 children. 1 patient had experience with 2 infusions of Rituximab after CS PS, CYC PS and oral Pred. Outcome. 2 patients died (infection), acute renal failure developed in 4, chronic renal failure in 8 (end stage in 1), renal function impairment −5, remission during 5 yrs in 13.

Conclusions: Diagnostics, morphological interpretation and approaches to treatment of Belarus children with LN correspond to the international recommendations.

P112 - Pre-clinical diagnostics of Diabetic Nephropathy in children

INA KAZYRA[1], ANZHALIKA SOLNTSAVA[1], LUDMILA VIAZOVA[2]
[1]*BELARUS STATE MEDICAL UNIVERSITY*
[2]*2ND CHILDREN'S HOSPITAL*

Introduction: Diabetic nephropathy (DN) is the most severe complication and the leading cause of dialysis, renal transplantation and mortality in diabetes mellitus (DM 1) in adult patients. The aim of the study: to detect the correlation between serum cholesterol (C), triglycerides (TG), microalbuminuria levels, compensation degree and DM 1 duration as major risk factors for DN development in children.

Material and methods: 100 case histories of children with DM 1 (followed between 2007-2011y.y.) from the Republic Center of Pediatric Endocrinology 2nd Children's Hospital Minsk were retrospectively analyzed. Age, body mass index (BMI), diabetes duration, serum levels of C and TG, fructosamine (FA) (as a marker of DM 1 compensation) were analyzed. Statistical analyses were carried out using SPSS16 and MatLab, non parametric tests were applied.

Results: Depending on MA level patients were divided into 2 groups. Group 1 "without complications" included 86 children (median age 15,58 (8,3 - 17,97) yrs) with MA level 0–30 mg/day (7,4 (0–20,8)). Group 2–14 children (median age 15,8 (11,8 – 17, 44) yrs) with DN in a stage 3 of MA

(MA ≥30–300 mg/day): 62,5 (45–105). Diabetes duration was 5,6 (1,4 - 15,6) and 5,7 (2,31 – 12,6) yrs in groups 1 and 2, respectively (p>0,05). The pubertal status assessment has shown late Tanner stages (T4-5) in most children: early puberty (T2-3) in 16,7 %, late puberty (T4-5) 78 % in group 1, and 28,6 % and 71,4 % in group 2. There were no differences in BMI (19,9 (13,7 – 25,9) and 20,1 (13,8 – 24,6) kg/m2 in both groups, p>0,05), FA levels (395 (251,3 - 584,5) and 434 (266,0 - 637,0) mkmol/l, in group 1 and 2 respectively, p>0,05). There was a trend to increased C and TG level in group 2 compared to group 1 (5,17 and 4,77 mmol/l p=0,05, and 1,1 versus 0,69 (p=0,03), respectively. The comparison has low significance (p=0,05) due to small sample size and short follow-up period. Regression analysis of C, FA levels and DM 1 duration compared to MA value was performed. There was no statistically significant interrelation between MA concentration and observed values.

Conclusions: A complex of clinical, laboratory, instrumental data and genetic markers should be used for early diagnosis of DN in children with DM 1. Further research is required with enlarged sample size and prolonged follow-up period.

P113 - Polymeric IgA1 with galactose-deficient O-glycans binds to streptococcal IgA-binding M protein inducing IL-6 and C3 secretion by human mesangial cells: implications for the pathogenesis of IgA nephropathy

ROLAND SCHMITT[1], ANNE-LIE STåHL[1], ANDERS OLIN[2], RAMESH TATI[1], ANN-CHARLOTTE KRISTOFFERSSON[1], JOHAN REBETZ[1], JAN NOVAK[3], GUNNAR LINDAHL[4], DIANA KARPMAN[1]

[1]*DEPARTMENT OF PEDIATRICS, CLINICAL SCIENCES LUND, LUND´S UNIVERSITY, SWEDEN*

[2]*DEPARTMENT OF INFECTION MEDICINE, CLINICAL SCIENCES LUND, LUND UNIVERSITY, LUND SWEDEN*

[3]*DEPARTMENT OF MICROBIOLOGY, UNIVERSITY OF ALABAMA AT BIRMINGHAM, BIRMINGHAM, AL, USA*

[4]*DIVISION OF MEDICAL MICROBIOLOGY, DEPARTMENT OF LABORATORY MEDICINE, LUND UNIVERSITY, LUND, SWEDEN*

Introduction: IgA nephropathy, the most common form of primary glomerulonephritis, is characterized by mesangial cell proliferation and matrix expansion with mesangial immune deposits containing predominantly polymeric IgA1 with galactose-deficient O-glycans and complement C3 co-deposition. We have previously shown that IgA-binding regions of streptococcal M proteins co-localize with IgA in mesangial immune deposits in patients with IgA nephropathy.

Material and methods: See below.

Results: In the current study the IgA-binding M4 protein from group A streptococcus was found to bind to galactose-deficient polymeric IgA1 with higher affinity than to other forms of IgA1, as tested by surface plasmon resonance and a solid phase assay. Moreover, binding of M4 to mesangial cells was demonstrated by flow cytometry. When the mesangial cells were co-stimulated with M4 and galactose-deficient polymeric IgA1 a significant synergistic effect on IL-6 synthesis and secretion was demonstrated by real-time PCR and ELISA, respectively. In addition, galactose-deficient polymeric IgA1, but not M4, induced secretion of C3 from the cells.

Conclusions: These results indicate that IgA-binding M4 protein binds preferentially to galactose-deficient polymeric IgA1 and that these proteins induce excessive pro-inflammatory responses in human mesangial cells. Thus, tissue deposition of streptococcal IgA-binding M proteins may contribute to the pathogenesis of IgA nephropathy.

P114 - LOSARTAN INDUCED HEPATOTOXICITY IN CHILDREN

SING MING CHAO[1], WAI KANG LIEW[2], KONG BOO PHUA[3]

[1]*NEPHROLOGY SERVICE, KK WOMEN'S AND CHILDREN'S HOSPITAL*

[2]*RHEUMATOLOGY SERVICE, KK HOSPITAL*

[3]*HEPATOLOGY SERVICE, KK HOSPITAL*

Introduction: Losartan is widely used in treating hypertension and renal disease. It has an excellent safety profile but severe hepatotoxicity had been rarely reported in adults and none in children. We report 2 teenaged patients with lupus nephritis who developed Losartan-Induced hepatotoxicity.

Material and methods: First patient was a 14 year old Chinese girl diagnosed with Class III Lupus nephritis. She was treated successfully with Prednisolone and CyclosporinA but later developed persistent proteinuria. Losartan was added. After 3 weeks of Losartan, she developed a mild relapse of SLE but severe and progressive liver dysfunction which persisted even after clinical remission of SLE. Extensive investigations to exclude infective hepatitis, Wilson's disease, CTScan of hepatobiliary system and liver autoantibodies were all negative. Losartan was withdrawn and liver function improved remarkably over next few days and eventually normalized. Second patient was a 16 year old girl with Class IV Lupus Nephritis first diagnosed at 10 years old. She was successfully treated with IV cyclophosphamide pulses. After 2 years of remission, she had a flare and was treated with Mycophenolate mofitel with partial response. She continued to have significant proteinuria and was treated with Losartan. Liver dysfunction was noted 4 months later and investigations for acute liver injury were all

negative. Losartan was withdrawn and her Alanine Transaminase level peaked after a few days before improvement occurred.

Results: Drug induced Liver Injury (DILI) is a diagnosis by exclusion. An exhaustive search for other causes of acute hepatocellular disease were negative and Losartan was the only new medication introduced prior to liver injury in our patients. Marked improvement occurred upon its withdrawal. Losartan is thus the most likely culprit in accordance to the International Consensus Criteria for DILI

Conclusions: With increasing use of Losartan in children, clinicians should be aware of possible though rare DILI associated with Losartan which had been reported as potentially fatal in adults. Baseline and serial monitoring of liver function is mandatory especially in the early period of treatment.

P115 - COEXISTENCE OF ANTI-GBM ANTIBODIES (Abs) AND MYELOPEROXIDASE-ANCA IN A GIRL WITH PULMONARY RENAL SYNDROME (PRS)

RADOVAN BOGDANOVIć[1], PREDRAG MINIć[1], JASMINA MARKOVIć-LIPKOVSKI[1], NATAšA STAJIć[2], NATAšA SAVIć[2], MILAN RODIć[2]

[1]*FACULTY OF MEDICINE, UNIVERSITY OF BELGRADE, BELGRADE*

[2]*INSTITUTE OF MOTHER AND CHILD HEALTHCARE OF SERBIA „DR VUKAN ČUPIć“, BELGRADE, SERBIA*

Introduction: The term PRS denotes coexistence of diffuse pulmonary hemorrhage and glomerulonephritis, most commonly caused by ANCA-associated vasculitides, SLE, and anti-GBM disease. The concurrence of anti-GBM and ANCAs in children is extremely rare, with less than 10 cases reported to date.

Material and methods: Clinical-pathologic features, treatment and short term outcome in a girl with „double“ positive antibodies are presented.

Results: In a 10-year old girl experiencing malaise, pallor and blood-tinged sputum severe anemia (Hb=44 g/L) was found, together with patchy diffuse pulmonary infiltrates on chest X-ray and CT scan. FBS disclosed active pulmonary hemorrhage with hemosiderin-laden macrophages in BAL fluid, suggesting alveolar hemorrhage. Urinalysis: hematuria and proteinuria of 780 mg/24 hr; serum urea, creatinine, C3 and C4 were normal, ANA and anti-dsDNA Abs negative; pANCA titer was 1:80, anti-MPO Abs 52.7 U/mL (normal, < 5); anti-GBM (IgG) Abs 19.7 RU/mL (normal, < 20). Renal biopsy: diffuse mesangial cells proliferation with cellular crescents in 4/25 and fibrinoid necrosis in 1/25 glomeruli; IF: 3+ linear IgG staining of the GBM, consistent with anti-GBM disease. Treatment: 3 i.v. methylprednisolone (0.5 g) boluses continued with prednisone (2 mg/kg/day)+6 monthly i.v. cyclophosphamide (0.5 g/m2) boluses. Her condition rapidly improved, showing complete resolution of the pulmonary infiltrates as revealed by imaging. After 3 months of treatment her laboratory values were as follows: ESR 6 mm, Hb 120 g/L, serum urea 5,7 mmol/L, creatinine 47 μmol/L; pANCA titer 1:20, anti-MPO Abs 5.7 U/mL, anti-GBM Abs 0.02 RU/mL; urine microscopy showed numerous RBC and proteinuria was 940 mg/24 hr .

Conclusions: The exceptional coexistence of the ANCA and anti-GBM Abs in children with PRS should be bear in mind in order to obtain a rapid and acurate diagnosis. Contrary to other reported pediatric cases, renal disease was not the prominent part of clinical presentation in our patient. However, final renal prognosis is hard to predict owing to the posibility of relapses.

P116 - Hypertension and nephrotic syndrome as presentation of Takayasu arteritis in a 14-year-old girl

CLAIRE DOSSIER[1], MARYNE DEMOULIN[1], MIGUEL HIE[3], ALBERT FAYE[2], THERESA KWON[1], GEORGES DESCHENES[1]

[1]*DEPARTMENT OF PEDIATRIC NEPHROLOGY, ROBERT DEBRE HOSPITAL, PARIS FRANCE*

[2]*DEPARTMENT OF GENERAL PEDIATRICS, ROBERT DEBRE HOSPITAL, PARIS FRANCE*

[3]*DEPARTMENT OF INTERNAL MEDICINE, PITIé-SALPêTRIèRE HOSPITAL, PARIS FRANCE*

Introduction: Takayasu arteritis (TA) is a rare, chronic, large vessel vasculitis of unknown etiology, predominantly affecting the aorta and its major branches. In children, hypertension is the commonest finding at presentation (80-90 %), followed by systemic symptoms. Renal manifestations are uncommon.

Material and methods: Case report

Results: We report on a 14-year-old teenage girl, with no medical history, arriving from Congo. Severe hypertension (180/100 mmHg) was diagnosed on a systematic measure one month before. She had no general symptoms and physical examination was normal. Blood pressure and arterial pulses were symmetric on four limbs. Echocardiography and ocular fundus showed no organ damage. A nephrotic syndrome (proteinuria 7.7 g/24 h, hypoalbuminemia 27 g/l), with normal serum creatinine, and absence of hematuria was found, and inflammatory syndrome with elevated CRP, ESR and hypergammaglobulinemia. Renal ultrasound, and CT angiography showed a left renal artery occlusive stenosis with left kidney atrophy. It also showed artery inflammation with thickening of the wall of the whole abdominal aorta, the right renal artery and the superior mesenteric artery. Thoracic aorta, pulmonary arteries and cerebral vessels were normal, except thickening of the left extern carotid.

Takayasu arteritis was diagnosed based on the association of vascular imaging, hypertension and elevated acute phase reactants. A renal biopsy was performed on the right hypertrophic kidney, because of nephrotic range proteinuria, and showed minimal change disease and severe arteriolar hyalinosis. Immunofluorescence was negative. Oral prednisone, aspirin and statin were initiated, antibiotherapy for suspected tuberculosis was added. Severe hypertension persisted and required a tetra-antihypertensive therapy.

Conclusions: Renal manifestations are uncommon in Takayasu arteritis. Proteinuria has previously been reported secondary to glomerular disease such as mesengial proliferative GN, membranoproliferative GN, IgA nephropathy or amylosis, and may improve with immunosuppressive therapy. In our patient, nephrotic proteinuria was ascribed to hypertension and hyperfiltration and remained unchanged after two months glucocorticoïd.

P117 - SKIN INVOLVEMENT IN ATYPICAL HEMOLYTIC UREMIC SYNDROME

GIANLUIGI ARDISSINO, FRANCESCA TEL, SARA TESTA

CENTRO PER LA CURA E LO STUDIO DELLA SINDROME EMOLITICO-UREMICA, FONDAZIONE IRCCS CA' GRANDA OSPEDALE MAGGIORE POLICLINICO MILANO

Introduction: Skin involvement in atypical hemolytic uremic syndrome (aHUS) is very uncommon and, therefore, often unrecognized as a specific symptom aHUS. We describe here the case of a young adult patient on regular hemodialysis (HD) for aHUS who developed skin lesions that completely recovered when disease specific treatment with Eculizumab, was established.

Material and methods: In 2009, a 19 year old male, presented to an adult nephrology unit with severe hypertension and end-stage-renal failure. Renal biopsy was not diagnostic and HD was started. In 2010, he developed thrombotic mycroangiopathy (TMA) with refractory hypertension and he was referred to our Center for HUS Control. The diagnostic workout for aHUS was negative (CFH, CHI, CHB, MCP, THMD, C3, ADAMTS13, AbAntiFH) except for persistent low C3 level. The patient was addressed to high volume plasmaexchange (PEX) with FFP in combination with HD (Tandem PEX-HD) with remission of TMA. In 2012 the patient was again referred to our Center for persistent (as long as 10 months) skin lesions in the lower limbs characterized by numerous violaceous maculo-papules with a tendency to coalesce centripetally, several petechiae and slightly depressed necrotic eschars with well defined borders in the centre. Blood exams performed at our Center only showed thrombocytopenia and low C3 level (hemoglobin, haptoglobin, and LDH were normal). The patient underwent 1 Tandem session of high volume (150 %) PEX with FFP followed by Eculizumab 900 mg (3 doses) with the working hypotesis that the skin lesions were due to skin TMA.

Results: Thrombocytopenia recovered (from 105.000 to 252.000/mm3) and an impressive improvement was observed after Eculizumab was started.

Conclusions: This case suggests that, in patients with aHUS, when skin lesions of unknown origin are seen the possibility that they are specific of the TMA should always be taken into consideration.

P118 - Favorable outcome in a toddler with factor H mutation treated with plasmapheresis and eculizimab

MARTIN BALD[1], KIRSTEN TIMMERMANN[1], MARTIN HOLDER[1], BETTINA RUCKENBROD[1], CARSTEN BERGMANN[2], PETER F. ZIPFEL[3], HEINZ E. LEICHTER[1]

[1]*OLGAHOSPITAL, PEDIATRIC NEPHROLOGY, STUTTGART, GERMANY*

[2]*BIOSCIENTIA, INGELHEIM*

[3]*HANS-KNÖLL-INSTITUTE, JENA*

Introduction: A five month old boy with known dysplastic right kidney presented in our Nephrology Clinic with a 1 week history of diarrhea and vomiting. Lab tests revealed a hemoglobin of 5,7 g/dl, a blood smear showed schistocytes, white blood cell count and platelets were within normal limits. His creatinine was increased to 0.7 mg/dl and LDH was 1224 Ul/. Urinalaysis was positive for blood and protein.

Material and methods: Further investigations showed an activation of the complement-cascade, but excluded anti-factor H antibodies. Moleculargenetic analysis revealed a heterocygous mutation of the factor H gene (c.2596+1 G> A), which confirmed the diagnosis of atypic hemolytic syndrome.

Results: Kidney function deteriorated slowly in the following days, and hemodialysis was started on day 4 of admission; however, hemolysis persisted and creatinine rose to a peak of 2.0 mg/dl on day 9. Daily plasmapheresis was initiated after infection with EHEC could be excluded by serological tests. Renal function normalized within one week of treatment. The clinical course was complicated by hypertensive crisis, necessitating intensive care with three intravenous antihypertensive medications. With oral antihypertensive treatment and frequent plasmapheresis treatment (3 times /week) the boy could be discharged. Treatment with the monoclonal immunoglobulin G antibody eculizimab was started after meningococcal vaccination. Three months later, his kidney function remains stable and there are no

further signs of complement activation. The antihypertensive treatment could be discontinued.
Conclusions: This case shows that aggressive management with plasmapheresis can sustain renal function even in toddlers with factor H deficiency. Long term therapy with eculizimab might lead to a favorite outcome as the complement activation is completely blocked.

P119 - Eculizumab in post-bone marrow transplant hemolytic uremic syndrome

MARINA VIVARELLI[1], DARIA PAGLIARA[2], FRANCESCO EMMA[1], FRANCO LOCATELLI[2]
[1]*DIVISION OF NEPHROLOGY, IRCCS BAMBINO GESù PEDIATRIC HOSPITAL, ROME ITALY*
[2]*DIVISION OF ONCO-HEMATOLOGY, IRCCS BAMBINO GESù PEDIATRIC HOSPITAL, ROME ITALY*

Introduction: Post-bone marrow transplant hemolytic uremic syndrome (postBMT-HUS) is a rare complication of unclear etiology, arising most frequently in the first year following BMT and generally more insidious in its presentation compared to other forms of HUS.
Material and methods: We report the evolution of two patients with postBMT-HUS. Based on positive results obtained in other forms of HUS, they were treated with the anti-C5a antibody eculizumab (Alexion) following approval by the IRB. Patient 1 received an allogenic BMT for relapsing ALL at age 10, followed by engraftment and complete remission. After 5.5 months, she presented a decrease in hemoglobin and platelets, an increase in creatinine and LDH associated with severe hypertension. Aptoglobin was undetectable. Patient 2 received an autologous BMT for metastatic neuroblastoma at age 5, followed by complete remission. After 8 months, he presented a decrease in hemoglobin and platelets and an increase in creatinine and LDH. Despite treatment with steroids, i.v. high-dose immunoglobulins and plasmapheresis, both patients showed progressive renal failure requiring hemodialysis.
Results: In patient 1, Eculizumab treatment was started at 900 mg i.v. weekly for 4 weeks followed by 1200 mg weekly for 3 weeks. After 7 weeks treatment was discontinued. Platelet, hemoglobin and serum creatinine levels showed no significant improvement and hemodialysis was continued chronically. In patient 2, treatment was started at 600 mg i.v. weekly for 4 weeks followed by 900 mg weekly for 9 weeks and then 900 mg every 14 days for a total of 6 months. After 2 months platelet levels improved significantly, while aptoglobin levels normalized after 6 months. The patient remains dialysis-free with moderate chronic renal failure.
Conclusions: In contrast to other forms of HUS treated with Eculizumab, no rapid response was observed. Delayed remission in patient 2 requires further studies to establish the beneficial effects of Eculizumab.

P120 - Crescentic Glomerulonephritis and Dense Deposit Disease:A Case Report.

TINATIN DAVITAIA[1], GIULI MEGRELISHVILI[2]
[1]*M.IASHVILI CHILDREN CENTRAL HOSPITAL*
[2]*TBILISI STATE MEDICAL UNIVERSITY*

Introduction: Dense deposit disease (DDD) is a prototypical rare disease, which affects an estimated 2 to 3 people per million and accounts for 20 % of all cases of Membranoproliferative glomerulonephritis in children. The unifying feature of DDD is the presence of electron dense transformation of the glomerular basement membrane visualized by electron microscopy.
Material and methods: Herein, we report on a 15 years old patient clinically initially presented with nephrotic syndrome and based on pathological findings the diagnosis of crescentic glomerulonephritis and dense deposit disease was confirmed.
Results: A 15 years old boy was admitted to our hospital with nephrotic syndrome. He underwent a renal biopsy that revealed crescentic glomerulonephritis secondary to dense deposit disease. The C3 complement level was low and the patient for negative for C3-nephritic factor. Despite aggressive immunosuppressive treatment: high-dose corticosteroids and cyclophosphamide pulses patient developed End Stage Renal Disease (ERSD) within 3 month and was transferred to hemodialysis.
Conclusions: This is the only documented case of DDD in our unit. DDD causes significant morbidity, leading to ERSD in the majority of cases. Considering high rates of disease recurrence, renal transplantation cannot be considered as a reliable treatment option. Although recent advances has increased our understanding of the pathophysiology of DDD, the rarity of this disease still poses difficulties in establishing evidence based recommendations for its management.

P121 - Remission and recurrence free 2 year follow up in a patient with factor H antibody associated atypical HUS under induction therapy with Plasmapheresis and introduction of maintenance therapy with i.v.IgG and MMF

JOHANNES HOFER[1], THERESE JUMGRAITHMAYR[1], MAGDALENA RIEDL[1], ALEJANDRA ROSALES[1], THOMAS GINER[1], VERENA JELLER[1], BETTINA GADNER[2], REINHARD WÜRZNER[2], MICHAEL MORITZ[3]
[1]*CHILDRENS UNIVERSITY CLINIC INNSBRUCK, PEDIATRICS I*
[2]*MEDICAL UNIVERSITY INNSBEUCK, DEPARTMENT OF HYGIENE*
[3]*CHILDRENS MEDICAL UNIVERSITY PITTSBURGH*

Introduction: Factor H antibodies (FH Ab) develop in 6-10 % of aHUS patients. At present, evidence based therapy recommendations for this group of patients are missing. Many patients develop end stage renal disease (ESRD) and recurrence rates within the first year are up to 70 %.
Material and methods: A 10 year old boy was addmited to the hospital because of weakness, vommiting and decreasing amount of urine. 4 days ago he had gastroenteritis with vomiting and diarrhoea. On examination the patient showed peripheral oedema and arterial hypertension. Laboratory analysis showed anemia (Hemoglobin 68 g/l), thrombocytopenia (33x109/l), elevated serum creatinin (6,6 mg/dl), high LDH (2312 U/l), low haptoglobine (5.8 mg/dl) and low C3 (0,58 g/l). Hemodialysis (n=2) and plasmapheresis (n=7) were started. After 7 plasmapheresis sessions total remission (normalization of hematologic parameters and renal function) was achieved. 2 months later the patient presented a recurrent episode treated with FFP infusions. After remission the patient recieved weekly FFP infusions prophylactically. At that time FH Ab associated aHUS with homozygous deletion of the complement factor h related proteins 1 and 3 was diagnosed (FH Ab Titer 1500 AU/ml). After diagnosis of FH Ab and inclusion of the patient in the International HUS-Net registry Innsbruck (www.HUS-online.at) FFP was weened off, the patient recieved i.v. IgG 2 g/kg body weight and maintanance therapy with Mycophenolate mofetil was introduced. FH Ab titer and the terminal complement complex plasma concentration were monitored closely. The patient received additional i.v.IgG infusions when FH Ab Titers increased.
Results: 2 years after the first recurrence the patient is on total hematological and renal remission. The FH Ab titers are mainly in the low range (Titer cut off <100 AU/ml; low range <500 AU/ml). The measurement of C3 and the terminal complement complex in plasma reveal normal complement activation.
Conclusions: Early start and aggressive plasmapheresis, followed by maintance therapy with i.v.IgG and MMF in FH Ab associated aHUS is a reasonable alternative to an expensive therapy with regularly Eculizumab infusions or chronic Plasma prophylaxis.

P122 - Analysis of kidney stones by geoscience methods – helpful in diagnosis and in treatment strategies for primary hyperoxaluria?

MICHAELA GEßNER[1], DORRIT JACOB[4], BERND GROHE[2], BODO BECK[3], BERND HOPPE[1]
[1]*DEPARTMENT OF CHILD AND ADOLESCENT MEDICINE, UNIVERSITY OF COLOGNE*
[2]*SCHULICH SCHOOL OF MEDICINE & DENTISTRY, UNIVERSITY OF WERTERN ONTARIO, LONDON, CANADA*
[3]*INSTITUTE OF HUMAN GENETICS, UNIVERSITY HOSPITAL OF COLGNE*
[4]*EARTH SYSTEM SCIENCE RESEARCH CENTRE AND INSTITUTE FOR CERTAIN PROPERTIES, UNIVERSITY OF MAINZ*

Introduction: To date, three forms of primary hyperoxaluria (PHI-III) are distinguished. All are autosomal-recessive inherited disorders of the glyoxylate metabolism that manifest with varying degrees of nephrolithiasis and/or nephrocalcinosis and early progression to ESRD in PH I. The diagnosis, based on urine excretion parameters and mutation analysis, is frequently delayed and all too often only made in ESRD. Purpose of our study was to determine on whether more specific stone analysis using methods of geosciences allow a faster diagnosis and a deeper insight in stone pathology and growth, so that this data can later be used to develop new therapeutic approaches.
Material and methods: Kidney stones from five patients with idiopathic hyperoxaluria and urolithiasis were compared to stones from PH I (5) and PH III (2) patients. Fragments of stones were embedded in epoxy resin, polished with a diamond paste and analyzed by reflected light microscopy and additionally by Raman spectroscopy. Not embedded stone fragments were analyzed by scanning electron microscopy and X-ray microanalysis.
Results: Preliminary data show that PH I stones consists mainly of calcium-oxalate monohydrate (COM), while the white-yellowish porous PH III stones mainly consists of calcium-oxalate dihydrate (COD) and smaller COM inclusions. However, stones of patients with idiopathic hyperoxaluria, a clear dominance of COM and often an increased pigmentation was found. Also a well ordered crystal structure were found in the latter, in contrast to a looser and disordered crystal structure of PH-stones. Magnesium, phosphate, and sodium content of PH I stones are noticeably higher than found in PH III stones.
Conclusions: The more differentiated breakdown and understanding of the structure and composition of the stones can possibly help to foster early diagnosis of specific metabolic diseases, here PH. Differences in stones may also help to understand differences in clinical expression, finally leading to development of new treatment options.

P123 - MACROHEMATURIA-ASSOCIATED PROTEINURIA: HOW MUCH IS DUE TO BLOOD IN THE URINE OR TO REDUCED GLOMERULAR PERMSELECTIVITY?

GIANLUIGI ARDISSINO[1], FRANCESCA TEL[1], SARA TESTA[1], CRISTINA VERCELLATI[2], ANNA MARCELLO[1]
[1]*CENTRO PER LO STUDIO E LA CURA DELLA SINDROME EMOLITICO-UREMICA - FONDAZIONE IRCCS CA' GRANDA, OSPEDALE MAGGIORE POLICLINICO*

[2]UO EMATOLOGIA 2 - FONDAZIONE IRCCS CA' GRANDA, OSPEDALE MAGGIORE POLICLINICO

Introduction: Proteinuria is one of the most important biomarkers for severity and for evaluating treatment response in all kidney diseases particularly in acute glomerular ones. However, in patients with macrohematuria a certain degree of proteinuria is certainly due to the presence of blood in the urine. Although this concept is well-known and well-accepted, in individual cases, the exact extent of proteinuria to be referred to macrohematuria only as opposite to proteinuria due to a specific damage of glomerular permselectivity in all but clear. This limitation maybe particularly relevant in specific patients with glomerulonephritis and nephrotic range proteinuria.
Material and methods: To better understand the relationship between urinary protein and hematuria, when coexisting, urine from normal subjects was added with whole blood in increasing amounts from 0 to 20 %. Proteinuria (as urinary protein/creatinine ratio) and hemoglobinuria (describe method) were determined in each sample to identify the expected level of proteinuria for each level of hemoglobinuria.
Results: In the described experimental conditions, the relationship between proteinuria and hemoglobinuria is a linear one (y: 227,37x – r2: 0,9927). Whenever gross hematuria is present, the uPr/uCr ratio that can simply be ascribed to blood per se is as high as 6.
Conclusions: If hemoglobinuria is determined on the same urine sample where proteinuria has to be evaluated, the difference between the expected ratio of proteinuria for the amount of hemoglobinuria and the actual one can be ascribed to specific damages of glomerular permselectivity.

P124 - Fighting bloody diarrhea for HUS prevention and mitigation: Lombardy Regional HUS Network. An update.

GIANLUIGI ARDISSINO, FRANCESCA TEL, SARA TESTA, FABIO PAGLIALONGA, STEFANIA SALARDI, SILVANA TEDESCHI, NICOLò BORSA, ROSARIA COLOMBO, MANUELA COLOSIMO, ERMINIO TORRESANI
CENTRO PER LO STUDIO E LA CURA DELLA SINDROME EMOLITICO-UREMICA - FONDAZIONE IRCCS CA' GRANDA, OSPEDALE MAGGIORE POLICLINICO - MILANO, ITALY

Introduction: Typical hemolytic uremic syndrome (tHUS), although rare, still represents a major public health problem in industrialized countries caused by a Verotoxin-producing Escherichia coli (VTEC) intestinal infection often presenting with bloody diarrhea.
Material and methods: In order to identify patients at risk of tHUS early in the course of the disease, a network connecting pediatric hospitals in Lombardy Region (10 millions gp) was developed. Fifty-three units presently partecipate in the network and since May 28, 2010 (founding day) children with bloody diarrhea were centrally tested for Shigatoxin (Stx) 1 and 2 with a Reverse Dot Blot commercial kit (EHEC Arnika). The objectives of the project were: 1. to increase the ability of the surveillance system in identifying the sources of VTEC infection and its spreading; 2. to understand the mechanisms of Stx delivery to target organs endothelia; 3. to test the potential role of overhydration and/or leukoapheresis to prevent or mitigate renal and CNS involvement.
Results: So far 632 patients have been tested. Hereafter are the preliminary results concerning the 595 samples for which all the procedures were completed. Twenty-four out of 595 (4,1 %) were positive for VTEC. Among negative samples Salmonella (25,0 %), Campylobacter (14,6 %) and EPEC (8,4 %) were the most common identified bacteria. Among patients with negative colture (41,0 %) 2 patient had Henoch-Schonlein purpura, 2 Meckel diverticulum, 1 acute pancreatitis and 1 ulcerative colitis.
Conclusions: In conclusion, our findings point out an unexpected high frequency of VTEC among bloody diarrhea in children in our region and the action taken on Stx positive children seem promising in terms of prevention of HUS.
Acknowledgement: the project is feasible thanks to the collaboration of the members of the Regional HUS Network whose complete list is available at www.centroseu.org. The project has been supported by the " PROGETTO ALICE ONLUS – Associazione per la lotta alla SEU"

P125 - C3 DEPOSITION GLOMERULOPATHY (GNC3) ASSOCIATED WITH C3 NEPHRITIC FACTOR (C3NeF), HETEROZYGOUS MUTATION IN FACTOR I GENE (CFI) AND ANTI-FACTOR H AUTOANTIBODIES (antiCFH).

LAPEYRAQUE ANNE-LAURE[1], FREMEAUX-BACCHI VERONIQUE[2], LEDEIST FRANÇOISE[1], PATEY NATACHA[1]
[1]CHU SAINTE JUSTINE, UNIVERSITE DE MONTREAL
[2]HôPITAL EUROPEEN GEORGES POMPIDOU, PARIS

Introduction: Uncontrolled activation of the alternative complement pathway (AP) leads to development of membranoproliferative glomerulonephritis (MPGN). GNC3 was associated with AP dysregulation secondary to the presence of C3NeF and to heterozygous mutations in CFH and CFI.
Material and methods: We report a 6-year-old boy who developed GNC3 associated with C3NeF activity, heterozygous mutations in CFI and antiCFH.

Results: He presented with hematuria and mild proteinuria. Post streptococcal glomerulonephritis first suspected was confirmed by renal biopsy (RB) performed at 3 months because of persistent low C3 level. Optic microscopy revealed a segmental and focal mesangial cell proliferation with numerous polymorphonuclears in capillary with isolated mesangial and subepithelial C3 deposits and epimembranous humps. Complement analyses demonstrated undetectable C3 level associated with C3NeF activity, antiCFH and an heterozygous mutation (I398L) in CFI. RB after 10 months of follow up revealed GNC3 with MPGN (increased mesangial cell proliferation associated with focal reduplication of the glomerular capillary basement membrane and isolated mesangial and subendothelial C3 deposits). He was treated with the association anti-CD20 monoclonal antibodies-prednisone and mycophenolate mofetil (MMF) after CD20 cells recovery. Two years after the diagnosis, RB shows the same pattern of GNC3 with MPGN with more extensive reduplication of the glomerular capillary basement membrane. Eculizumab was initiated in association with MMF and prednisone (5 mg/48 h). One year after Eculizumab initiation, laboratory investigations show a significant decrease in proteinuria. C3 level is still low, C3NeF activity and antiCFH persists. RB results are pending.
Conclusions: To our knowledge, this is the first report of a GNC3 with MPGN associated with antiCFH autoantibodies, C3NeF and heterozygous mutation in CFI. The respective role of these 3 AP dysregulation factors in GNC3 pathogenesis needs to be elucidate in order to improve the therapeutic approach. The efficacy of Eculizumab needs to be confirmed.

P126 - Spectrum of biopsy-proven renal diseases in children from Norden Coastal Region of Croatia

GORDANA DJORDJEVIC[1], IVONA BUTORAC-AHEL[2], SANJA FLAJSMAN-RASPOR[1], MIRNA SUBAT-DEZULOVIC[1]
[1]*UNIVERSITY SCHOOL OF MEDICINE RIJEKA, DEPT.OF PATHOLOGY*
[2]*CLINICAL MEDICAL CENTRE RIJEKA*

Introduction: To evaluate the spectrum of renal diseases in the region of Norden Coastal part of Croatia we reviewed all kidney biopsies performed at our centre and compared with our national renal disease registry data started since 1999.
Material and methods: all native renal biopsies from January 1999 to December 2011 performed at a tertial pediatric centre (a region of 100.000 children <18 years) were retrospectively reviewed. Including only glomerular diseases, the diagnosis of each case was based on histological, immunofourescent, electronmycroscopy analyses and clinical features
Results: of a total 87 eligible patients (F40, M47), aged 1.5 to 17 years, who had kidney biopsy were analyzed. Indications for kidney biopsy were: hematuria in 32 %, non-nephrotic proteinuria in 14 %, nephrotic syndrome in 24 %, acute nephritic syndrome in 19 % and acute kidney injury 10 % of pts. Primary glomerular diseases were diagnosed in 63 % of all biopsies, secondary glomerular diseases in 18 % and hereditary glomerular diseases in 14 %. The most frequent primary glomerular diseases were focal and segmental glomerulosclerosis (FSGS) (31 %), mesangial proliferative glomerulonephritis (MEPGN) (22 %), IgA nephropathy (15 %) and minimal change disease (MCD) (11 %). Among primary glomerular diseases postinfectious glomerulonephritis (PIGN) accounted for 16 %. The most common secondary glomerular diseases were systemic lupus erythematosus (SLE) (38 %) and Henoch-Scholein purpura (HSP) (13 %). Alport syndrome corresponded to 8 % of the entire series. Of 9 pts with kidney biopsy findings indicative of PIGN, 2 pts presented with severe renal failure necessitating haemodialysis; others presented sub-clinically.
Conclusions: Comparing our results with Croatia registry of kidney biopsies data, the main difference included diagnosis of PIGN that still should be considered in any sub-clinical case or severe renal failure. Secondly, higher frequency of FSGS in comparison with our national registry and similar analyses from other countries deserves further evaluation.

P127 - 10-year follow up of pediatric Hennoch Schönlein purpura with renal involvement

ELENA TUDORACHE[1], CHRISTINE AZEMA[1], STéPHANE DECRAMER[2], GEORGES DESCHêNES[1], TIM ULINSKI[1]
[1]*UNIVERSITY PIERRE AND MARIE CURIE, PARIS 6*
[2]*PEDIATRIC NEPHROLOGY UNIT, CHU TOULOUSE*

Introduction: Henoch Schonlein purpura (HSP) is a common cause of renal disease in children, representing 10-15 % of glomerulonephritis. Only 1-3 % of affected children develop end-stage renal disease. The outcome seems less favourable for patients who require renal biopsy. In this specific population 7-50 % develop progressive renal disease. The treatment of HSP nephritis usually depends on the severity of histological lesions. The aim of this study was to determine the long-term clinical and biological outcome in children with HSP nephritis who underwent a renal biopsy and to identify possible correlation between disease development and treatment.
Material and methods: We included retrospectively all patients with renal biopsy proven IgA nephropathy related to HSP of three pediatric nephrology centers over a 10-year period. 142 children were included and fulfilled the criteria of HSP with renal involvement and mesangial IgA deposits on renal biopsy. Proteinuria and renal function were

monitored. Glomerular histopathologic changes were graded according to the ISKDC classification. Patient follow up period was 2 to 10.5 years.

Results: A total of 142 patients (68 males) with HSP nephritis underwent renal biopsy between 1999 and 2009. Mean (± SD) age at presentation was 7.6±2.8 years. Nephrotic range proteinuria was present in 28 % with grade II, 60 % with grade III and 90 % with grade IV lesions. Significant proteinuria >500 mg/L was found in 9/48 patients 3 years post renal biopsy, in 8/25 patients at 5 years and in 3/14 patients at 10 years. There was no correlation between risk for proteinuria at 3, 5, or 10 years with initial histological lesions or treatment modalities such as oral or pulse steroids.

Conclusions: Long term follow up is necessary even if renal involvement was rather mild or moderate. Prospective long term studies are required to determine if early aggressive treatment may reduce long term sequelae.

P128 - Adipocytokines and renal functions: Serum vaspin, apelin and urin NGAL levels in obese children

PINAR ERDOGAN[1], BILAL YILDIZ[1], NURAN CETIN[1], NURDAN KURAL[1], OMER COLAK[2]
[1]*ESKISEHIR OSMANGAZI UNIVERSITY, FACULTY OF MEDICINE,, DEPARTMENT OF PEDIATRIC NEPHROLOGY*
[2]*ESKISEHIR OSMANGAZI UNIVERSITY, FACULTY OF MEDICINE,, DEPARTMENT OF BIOCHISTRY*

Introduction: Obesity trends are causing serious public health concern. It is significantly increases the risk of morbidity and mortality. The aim of this study was to investigate serum levels of the newly discovered adipocytokines (vaspin, apelin) and their correlation of renal functions in obese children. We also investigated the relationship between renal functions and hypertension, insulin resistance (IR), dyslipidemia.

Material and methods: The 29 healthy and fifty-nine obese children were included according to the BMI (>25) in this study. The serum levels of vaspin, apelin, lipid profile and urine NGAL levels were studied. The creatinin (Ccr), β2MG and microalbumin excretion were examined in the 24-h-urine. We also calculated HOMA index as IR in all children. All subjects underwent 24-hour ambulatory blood-pressure monitoring.

Results: The levels of serum vaspin (13,2 ±1,16/7,7± 1 pg/ml; p=0,009), apelin (59,120±7590,9/36160,8± 5841 ng/ml; p=0,03), urine NGAL (6,63±1,08/4± 0,7 ng/ml; p=0.07) were significantly higher in patients than in the controls. Urine β2MG and microalbumin levels were similar in obese children than in those of the controls. Ccr were lower in obese children than in controls (119,3±4,9/166,8±6,9 ml/min/1,73 m²; p= 0,0001). There were positive correlations between the urine levels of NGAL with diastolic tension arterial levels (r=0.319, p=0.021). There were negative correlations between CCr and the tension arterial and vaspin levels and IR (P =0.01, r=− 0.370; p =0.025 r=−0.245; p=0.03 r=−0.232). Ccr levels were similar in child with and without dyslipidemia but urine NGAL levels were higher in patients with dyslipidemia than without dyslipidemia. Ccr were lower and serum vaspin levels were higher in patients with IR than in without IR (116±9,8/141,3±5 ml/min/ 1.73 m², p=0,03; 16,3±2,1/9,8±0,8 pg/ml, p=0,003).

Conclusions: Obesity is a potentially risk factor for the development of decreased Ccr. NGAL levels may be better indicator than Ccr for reduction in renal function in obese children with dyslipidemia.

P129 - TRPC6 mutation is a rare cause of steroid-resistant nephrotic syndrome in children

LION MATHILDE[1], BOYER OLIVIA[3], NIAUDET PATRICK[3], CHARBIT MARINA[1], ECKART PHILIPPE[5], NEVO FABIEN[4], KRUG PAULINE[3], GUBLER MARIE-CLAIRE[4], SALOMON REMI[3], ANTIGNAC CORINNE[2]
[1]*PARIS-DESCARTES UNIVERSITY, PARIS, FRANCE*
[2]*MEDICAL GENETICS, INSERM U983, IMAGINE, NECKER HOSPITAL, APHP, PARIS, FRANCE*
[3]*PEDIATRIC NEPHROLOGY, MARHEA, NECKER HOSPITAL, APHP, PARIS, FRANCE*
[4]*INSERM U983, IMAGINE, PARIS, FRANCE*
[5]*PEDIATRICS, CHU CAEN, FRANCE*

Introduction: Heterozygous mutations of the TRPC6 gene have been reported in ~5 % of autosomal-dominant podocytopathies with focal segmental glomerulosclerosis (FSGS). Most patients present with nephrotic range proteinuria in their thirties–fifties, and progress to end-stage renal failure within 10 years. Recently, TRPC6 mutations have been identified in 4 children; one of them had collapsing FSGS at 2 years of age with rapid progression to end-stage kidney disease.

Material and methods: A boy, born to non-consanguineous healthy parents presented at the age of 6 years with nephrotic syndrome (proteinuria 8 g/L, plasma albumin 19 g/L), chronic kidney disease (eGFR 19 ml/min/1.73 m²) and hypertension. The renal biopsy showed collapsing FSGS with 50 % of sclerotic glomeruli. The renal function rapidly worsened despite steroid therapy, and peritoneal dialysis was started within 2 months. He was transplanted one year later, with a deceased donor's kidney. Immunosuppressive regimen included anti-lymphocyte globulin, ciclosporin, azathioprine and steroids. There was no recurrence of the disease, but a delayed decrease of plasma creatinine resulting from urological complications.

The eGFR remained stable around 60 ml/min/1.73 m² until the last follow-up 20 years later.

Results: Genetic testing revealed a de novo heterozygous mutation c.2678 G>A (p.Ser893Asn) in the exon 13 of the TRPC6 gene. This missense mutation is predicted to be "probably damaging" by the Polyphen 2 software with a score of 1. The TRPC6 gene encodes a non-selective cation-permeable channel highly expressed in podocytes. It mediates intra-cellular calcium influx and plays a major role in signaling cascades of the slit diaphragm where TRPC6 interacts with nephrin and podocin. The mutation involves a highly-conserved residue located in the last cytoplasmic domain of the protein, that could participate in the assembly of subunits of TRPC6 and its interaction with membrane phospholipids.

Conclusions: TRPC6 mutations can be detected in early-onset and severe forms of familial and sporadic steroid-resistant nephrotic syndromes.

P130 - Alport Syndrome in a familial Corticoresistant nephrotic syndrome treated with Cyclosporine

CHEBL MOURANI, BERNARD GERBAKA
HOTEL DIEU DE FRANCE BEIRUT LEBANON

Introduction: We report a Lebanese family of three children born from consanguineous marriage with similar initial presentation : nephrotic-range proteinuria and microscopic proteinuria

Material and methods: The eldest child is a nine year old boy,he received four weeks of corticotherapy (2 mg/kg /day) with no response. A renal biopsy revealed marked irregularities in the glomerular basement membrane consistent with Alport syndrome. Despite angiotensin-converting enzyme inhibitor therapy, proteinuria remained in the nephrotic range associated with edema. Cyclosporine therapy was instituted, which resulted in partial response . Initially no deterioration of renal function was noted after 12 months of cyclosporine treatment than progressively renal function declined, cyclosporine was stopped but renal function continued to deteriorate. His first sister presenting similar clinical and histological findings suggesting Alport disease received corticotherapy for 4 weeks with no response followed by angiotensin-converting enzyme inhibitor and cyclosporine. Six months after the combined therapy renal function deteriorated despite the arrest of cyclosporine treatment. His second sister presented with also similar clinical symptoms. No electronic biopsy study was performed. She presented initially with moderate renal failure . She received corticotherapy and presented a progressive renal deterioration of the renal function after 13 months of follow –up . No cyclosporine was prescribed in this patient . All three children progressed to CKD and dialysis.One of the girls received a successful kidney transplant with no recurrence of the initial disease one year after the tranplantation procedure.

Results: Cyclosporine was reported as a treatment possibility in small pediatric series and on animal model with Alport syndrome presenting with nephrotic syndrome . The review of the literature showed beneficial effect on the resolution or reduction of proteinuria. No similar report in the literature about rapid progression to renal failure with or without cyclosporine in a same family. In the animal model the beneficial effect comes from a delayed deterioration of GBM structure which in turn may be related to glomerular hemodynamics altered by cyclosporine.

Conclusions: After seven year follow-up of this family with Alport disease and the unfavorable outcome with Cyclosporine treatment, we recommend that careful monitoring of renal function should be done in Alport patients receiving cyclosporine . Only a randomized prospective and well conducted study can answer the question on the beneficial effect of cyclosporine in this hereditary X linked nephritis

P131 - THE BENEFITS OF CYCLOSPORINE TREATMENT OF THE PATIENT WITH NPHS2 MUTATION

DUYGU OVUNC HACIHAMDIOGLU[1], FATIH OZALTIN[2], CENGIZ ZEYBEK[1], SULEYMAN KALMAN[1], ERKAN DEMIRKAYA[1], FAYSAL GOK[1]
[1]*GULHANE MILITARY MEDICAL ACADEMY MEDICINE SCHOOL DEPARTMENT OF PEDIATRIC, DIVISION OF PEDIATRIC NEPHROLOGY*
[2]*HACETTEPE UNIVERSITY MEDICINE SCHOOL DEPARTMENT OF PEDIATRIC, DIVISION OF PEDIATRIC NEPHROLOGY*

Introduction: The treatment response of nephrotic syndrome with mutation in podocin is expected to be resistant to corticosteroids and immunosuppressive agents. We present the benefits of cyclosporine treatment of the patient with nephrotic syndrome associated with NPHS2 mutation.

Material and methods: Twenty month-olds boy is second child of consanguineous parents. He had edema, proteinuria, hypoalbuminemia (0,9 g/dl), hypercholesterolemia, and serum creatinine level was 0,22 mg/dl. The results of molecular analysis of all NPHS2 exons was V165X (ins T 460→467) mutation in the exon 4. Since data on responses to cyclosporine or cyclophosphamide were available for patients with SRNS and homozygous or compound heterozygous mutations in NPHS2, the patient put on cyclosporine treatment.

Results: Partial remission was obtained and edema was disappeared in 2 months of cyclosporine treatment. Serum albumin level was rose and proteinuria decreased. After

sixth month of treatment, the laboratory finding were as fallows, Serum albumin 2,5 g/dl, urea 50,5 mg/dl, creatinine 0,32 mg/dl, and cholesterol 369,9 mg/dl.

Conclusions: It has been reported that the partial responses to cyclosporine achieved in some of nephrotic syndrome with podocin mutation, but none of them have complete remission. It was argued some opinions for the antiproteinuric effect of cyclosporine. Cyclosporine exerts an antiproteinuric effect by preventing the degradation of the actin organizing protein synaptopodin. However, cyclosporine's long-term effect and safety in children with hereditary forms of nephrotic syndrome have yet to be investigated.

P132 - OUTCOME OF STEROID SENSITIVE IDIOPATHIC NEPHROTIC SYNDROME (SSINS) PRESENTING AFTER THE AGE OF 12 YEARS

NIELS RUTJES[1], ADITI SINHA[2], ARVIND BAGGA[2], ELENA LEVTCHENKO[3], BENEDICTE ENEMAN[3], MARKUS KEMPER[4], ANNA ZAWISCHA[4], REZAN TOPALOGLU[5], JAAP GROOTHOFF[1], VALENTINA GRACCHI[6], MARTIN KÖMHOFF[6], JOANNA VAN WIJK[10], EISKE DORRESTEIJN[9], MARCIN TKACZYK[7], FRANCESCO EMMA[8], LAURA MASSELLA[8], JEAN-CLAUDE DAVIN[1]

[1]*EMMA CHILDREN'S HOSPITAL / ACADEMIC MEDICAL CENTER (THE NETHERLANDS)*

[2]*ALL INDIA INSTITUTE OF MEDICAL SCIENCES (INDIA)*

[3]*UZ LEUVEN GASTHUISBERG (BELGIUM)*

[4]*UNIVERSITY MEDICAL CENTER HAMBURG-EPPENDORF (GERMANY)*

[5]*HACETTEPE UNIVERSITY HOSPITAL (TURKEY)*

[6]*UNIVERSITY MEDICAL CENTER GRONINGEN (THE NETHERLANDS)*

[7]*POLISH MOTHER'S MEMORIAL HOSPITAL RES. INST. (POLAND)*

[8]*BAMBINO GESù CHILDREN'S HOSPITAL (ITALY)*

[9]*UNIVERSITY MEDICAL CENTER ERASMUS MC (THE NETHERLANDS)*

[10]*FREE UNIVERSITY MEDICAL CENTER (THE NETHERLANDS)*

Introduction: Clinical features and outcome in SSINS might be different according to age. Little is known about the course of SSINS with onset in late childhood, due to the low incidence of SSINS in this age group (1.6 % in the Amsterdam academic hospitals cohort of pediatric NS). Here we describe the clinical features and outcome of a multicenter cohort of patients with onset of SSINS between 12 and 18 years of age.

Material and methods: Data were retrieved from the Nephrotic Syndrome Registry (www.nsregistry.org) and from individual patient medical records. Inclusion criteria were as follows: 1) SSINS; 2) age at onset between 12 and 18 years; 3) ≥2 years of follow-up.

Results: The study included 21 patients. The mean follow-up was 5.2 years (2.0-13.9 years); the mean age at presentation was 13.5 years (12–17 years) and the M:F ratio was 1:3,2. Renal biopsy: 9 MCNS (43 %), 2 FSGS (9 %), 1 mesangial proliferation (5 %), 9 no biopsy (43 %). Clinical course: 8 infrequent relapses (38 %), 11 frequent relapses / steroid dependence (52 %), 2 secondary steroid resistance (10 %), one of the latter having reached end-stage renal failure. Treatment: 7 prednisone mono-therapy (33 %), 7 second line medications (levamisole, MMF or cyclophosphamide), 3 third line medications (calcineurin inhibitors) (14 %), 4 rituximab (19 %). At the last follow-up 14 patients were in complete remission (67 %) and 38 % were no longer receiving treatment. Except for one patient with secondary steroid resistant NS, renal function was normal in all tested patients.

Conclusions: A small percentage of children with SSINS have an onset of their disease between 12 and 18 yrs. Except for an inversion in the gender ratio, clinical characteristics and evolution in this population do not differ significantly from those reported in younger children. Confirmation of these findings in larger cohorts is necessary.

P133 - The bacterial microflora of gastrointestinal tract is imbalanced in children in nephrotic children treated with cyclosporine A

ROBERT SZLACHCIńSKI, MARCIN TKACZYK

NEPHROLOGY DIVISION, POLISH MOTHER'S MEMORIA HOSPITAL RESEARCH INSTITUTE

Introduction: Most of drugs applied in idiopathic nephrotic syndrome (INS) interfere with the natural immunity. Thus, the may induce changes in physiologic microflora of the intenstine. The aim of the study was to assess these changes in children with INS treated with different types of immunosuppression.

Material and methods: The study had a cross-sectional design. We analysed the commensal and indicative microflora of jejunum and colon. The total number of bacteria and number of pathogenic bacteria, Candida and other fungi species were measured. Additionally, physic-chemical stool analysis was performed. The data were gathered by Kyber-Myc and KyberStatus microbiology analysis sets. Basic clinical and lab data were gathered too. The study group comprised 15 INS children treated with cyclosporine A (CsA;Equoral) with or without steroids, 15 children treated with steroids. All the patients were in the remission induced by treatment. Children with antibiotics given 3 months prior to the study were excluded. 20 healthy age-matched children

served as controls. The statistical analysis was perfromed with descriptive and non-parametric analysis.
Results: Children treated with CsA had lower total number of microorganism, higher number of Clostridium sp and Candida sp when compared to the controls. Children treated with steroids only had increased number of Escherichia coli sp. and Bacteroides sp than healthy children. These pathological observations were accompanied by increased percentage of subjective complaints (constipation, flatulence, loose stools and abdominal pain in INS children despite the method of treatment.
Conclusions: Children with INS have their intestinal microflora changed when compared to health controls. The immunosupression (both steroids and CsA) plays a significant role in these disturbances. The administration of cyclosporine A induces deeper imbalance in the microflora reducing physiological number of bacteria and promoting colonization with pathologic species

P134 - Expression of nephrin and podocalyxin in kidney glomeruli in children with nephrotic syndrome and its association with development of proteinuria

IVAN SAKHARAU[1], NATALIA TUR[2], EVGENIY CHERSTVY[1], ALEKSANDR SUKALO[1], TATIANA LETKOVSKAYA[1], VIKTORIA SAVOSH[1]
[1]*BELARUSIAN STATE MEDICAL UNIVERSITY*
[2]*REPUBLIC CENTER FOR CHILDREN NEPHROLOGY AND RENAL REPLACEMENT THERAPY*

Introduction: Nephrin and podocalyxin are two podocyte proteins responsible for plasma proteins filtration. Their changes result in proteinuria. The aim of our study was to characterize the expression of nephrin and podocalyxin in patients aged up to 18 years and to reveal their role in pathogenesis of nephrotic syndrome.
Material and methods: Current and archive fine needle biopsy tissues were studied, clinical data were obtained. 47 children with nephrotic syndrome and isolated glomerular proteinuria were included in the first group. Some patients had no proteinuria at the moment of biopsy due to therapy. 17 children with isolated hematuria with no proteinuria were included in the second group. At histology minimal changes, mesangial proliferation and FSGS were diagnosed. Tissue samples were stained using anti human nephrin and podocalyxin antibodies. Digital images of five glomeruli of each sample were taken and analyzed using Aperio ImageScope software. The expression index (positivity) was calculated for each case.
Results: The staining levels were predominantly medium and low in the first group and high and medium in the second one. The positivity of nephrin and podocalyxin was significantly different in two groups. There was no difference in positivity between histological diagnoses. We found no difference in positivity between patients of the first group with and without proteinuria at the moment of biopsy. We found medium inverse correlation of nephrin expression and proteinuria level in the first group.
Conclusions: The revealed association of nephrin expression and proteinuria level shows the relation between podocyte slit diaphragm injury and clinical manifestations in nephrotic syndrome. Low podocalyxin expression indirectly indicates the reduction of glomerular filter negative charge in proteinuria.

P135 - WHETHER DIGENIC INHERITANCE OF TRPC6 AND NPHS1 VARIANTS ASSOCIATED WITH DEVELOPMENT OF FSGS IN CHILDREN WITH IDIOPATHIC STEROID-RESISTANT NEPHROTIC SYNDROME (SRNS)?

LARISA PRIKHODINA[1], OXANA RYZHKOVA[2], ALEXANDER POLYAKOV[2]
[1]*RESEARCH INSTITUTE OF PEDIATRICS & CHILDREN SURGERY, MOSCOW*
[2]*RESEARCH CENTER FOR MEDICAL GENETICS, MOSCOW; RUSSIA*

Introduction: To date, the clinical relevance of digenic inheritance of TRPC6 and NPHS1 variants in SRNS patients is unknown. The aim of the study was to investigate whether digenic inheritance of TRPC6 and NPHS1 variants contributes to development of FSGS among children with idiopathic SRNS.
Material and methods: Twenty-eight children (20 F/8 M) with primary non-familial SRNS were studied. Histological findings were FSGS in 17 (60.7 %), MPGN in 5 (17.9 %), mesangial proliferative glomerulonephritis in 3 (10.7 %), MN in 2 (7.1 %), MCD in 1 (3.6 %) patients. The median age at onset of SRNS was 9.0 (IQR: 4.3; 10.9) years. TRPC6, NPHS1 and NPHS2 mutation analysis was performed by PCR and direct sequencing of all 13, 29 and 8 exons, relatively.
Results: No mutations were found in TRPC6, NPHS1, NPHS2 genes in children with idiopathic SRNS. Digenic inheritance of TRPC6/NPHS1 variants was identified in 8/28 (28.6 %) patients, including three heterozygous TRPC6 variants (c.43 C>T, c.1211 C>T, c.1683 T>C) and two homo-/heterozygous NPHS1 variants (c.349 G>A, c.1223 G>A). There were no revealed NPHS2 variants among these patients. The frequency of FSGS was significantly higher in children with digenic inheritance of TRPC6/NPHS1 variants in comparison with only TRPC6 variants: 7/8 (87.5 %) vs. 4/11 (36.4 %) (p=0.037); OR= 12.3 (95%CI: 1.1 - 139.1). There were no differences in

frequency of FSGS between patients with digenic inheritance of TRPC6/NPHS1 variants and with only NPHS1 variants: 87.5 % vs. 50 % (p=0.18). Risk of FSGS developing in children with SRNS by testing of digenic inheritance of TRPC6/NPHS1 variants can be predicted with sensitivity=63.6 % (95%CI: 30.8 - 89.1 %), specificity= 87.5 % (95%CI: 47.4 - 99.7 %), likelihood ratio=5.1; AUC=0.76 (95%CI: 0.53 - 0.98).

Conclusions: We conclude that digenic inheritance of TRPC6 and NPHS1 variants can be associated with development of FSGS in children with idiopathic SRNS.

P136 - Unspecific increased levels of tumor markers in a girl with nephrotic syndrome after ovarian teratoma excision.

KATARZYNA KILIS-PSTRUSINSKA, URSZULA SZAJERKA, DANUTA ZWOLINSKA
DEPARTMENT OF PAEDIATRIC NEPHROLOGY, WROCLAW MEDICAL UNIVERSITY, POLAND

Introduction: Paraneoplastic nephrotic syndromes (NS) are rare in paediatric population. We present a case of a 16-year-old girl initially suspected with a paraneoplastic glomerulopathy. Eventually, co-occurrence of primary glomerulonephritis and mature ovarian teratoma were diagnosed.

Material and methods: A young female admitted due to proteinuria, oedema, hypoalbuminemia and hypercholersterolemia. Partial remission was promptly achieved with systemic corticosteroids. After two weeks the typical symptoms of NS aggravated. She developed significant oedema and ascites. Abdominal sonography revealed a thick-walled cystic structure in the right side of the minor pelvis, suggestive of an ovarian malignancy. The serum level of CA125 was 69 U/ml (normal range 0–35). An abdominal CT scan was performed. The patient was operated on and the right ovary with the tumor was completely removed (histopathologic evaluation: mature teratoma). A biopsy of the left ovary resulted normal.

Results: Following the operation no remission of NS was observed, and the serum levels of creatinine and urea, as well as of CA125 (173–200 U/mL) and CA19-9 continued to raise. An aggressive antioedematous therapy was required. Although in the second abdominal CT scan no tumor masses were observed, ascites and a thickened peritoneum suggested the presence of metastatic lesions; however, MRI showed no abdominal pathologies. The tumor markers demonstrated varying serum levels. Kidney biopsy was taken; the histopathological diagnosis: mesangial proliferative glomerulonephritis. Once the cyclosporine A was introduced the proteinuria receded, biochemical serum parameters typical of NS normalized and the serum levels of CA125 and CA19-9 decreased to the reference range.

Conclusions: Elevated levels of CA125 and CA19-9 in the serum of a patient with NS should be interpreted as increased glycoprotein secretion by the mesothelial cells stimulated by the peritoneal fluid. The NS in a patient suffering from neoplastic disease may occur over the course of a primary, non-paraneoplastic glomerulopathy.

P137 - Urinary alpha1-microglobulin in children with idiopathic nephrotic syndrome and progression of chronic kidney disease.

KATARZYNA KILIS-PSTRUSINSKA, ANNA MEDYNSKA, DANUTA ZWOLINSKA
DEPARTMENT OF PAEDIATRIC NEPHROLOGY, WROCLAW MEDICAL UNIVERSITY, POLAND

Introduction: In primary glomerulopathy not only glomeruli, but also renal tubules and interstitium are affected by pathological changes. They can lead to progression of chronic kidney disease (CKD). The aim of the study was to analyse the urinary alpha1-microglobulin (alfa1-M) in children with idiopathic nephrotic syndrome (INS) regarding the estimation of renal function based on serum cystatin C.

Material and methods: 80 children with INS, aged 2–18 as well as 20 healthy children were studied. In all INS patients 1 stage of CKD was diagnosed. Children with INS were followed up for 22 to 24 months and, on the basis of serum cystatin C, divided into two groups: group I (n=37) - children without glomerular filtration rate changes, group II (n= 43) - patients with impaired renal function. Urinary alpha1-M level was measured in the urine after a night by ELISA method and related to the creatinine concentration in urine. Measurements in children with INS were made in remission of the disease.

Results: Urinary alpha1-M levels were significantly higher in both groups of children with INS (gr. I: 0.014±0.005, gr. II: 0.016±0.008) compared to healthy controls (0.01±0.002; $p<0.05$). However, there were not significant differences in the mean levels of urinary alfa1-M between the two observed INS groups.

Conclusions: Increased urinary alpha1-M excretion in children with INS in remission indicates tubulointerstitial changes in the course of glomerulopathy. The urinary alpha1-M is not a sensitive marker of renal dysfunction in INS children.

P138 - A practical algorithm for molecular diagnosis of primary nephrotic/non nephrotic proteinuria

ELISA BENETTI[1], GIANLUCA CARIDI[2], MADDALENA GIGANTE[3], ELENA BRESIN[4], MARTA ALBERTI[4], MANUELA DELLA VELLA[5], LINA ARTIFONI[5], LUISA MURER[1]

[1]PEDIATRIC NEPHROLOGY, DIALYSIS AND TRANSPLANT UNIT, DEPARTMENT OF PEDIATRICS, A.O.U.OF PADUA, PADUA, ITALY
[2]LABORATORY OF PATHOPHYSIOLOGY OF UREMIA, ISTITUTO GIANNINA GASLINI, GENOA, ITALY
[3]DEPARTMENT OF BIOMEDICAL SCIENCES, FACULTY OF MEDICINE, UNIVERSITY OF FOGGIA, OSPEDALI RIUNITI DI FOGGIA, FOGGIA, ITALY
[4]MARIO NEGRI INSTITUTE FOR PHARMACOLOGICAL RESEARCH, CLINICAL RESEARCH CENTER FOR RARE DISEASES "ALDO E CELE DACCò", RANICA, ITALY
[5]LABORATORY OF KIDNEY IMMUNOPATHOLOGY AND MOLECULAR BIOLOGY, DEPARTMENT OF PEDIATRICS, A.O.U.OF PADUA, PADUA, ITALY

Introduction: Despite clinically similar, nephrotic/non nephrotic proteinuria-associated primary glomerulopathies are heterogeneous in terms of histological features, pathogenesis and prognosis. These forms may be immune-mediated or genetic. For genetic forms, molecular diagnostic pathways are mainly based on individual experience or knowledge in the fields of genetics. Our aim was to identify a clinical-molecular diagnostic pathway, starting from clinical features and the histological picture.
Material and methods: We retrospectively analysed clinical, molecular and histopathological features of 36 children with primary nephrotic/non-nephrotic proteinuria, who had undergone a genetic testing. Analysed genes included NPHS2, WT1, CoQ2, MTTL1, NPHS1, ACTN4, PLCE1, CFH, CFI, and MCP.
Results: Histological pictures were focal segmental glomerulosclerosis (FSGS) in 21/36 children (58 %), diffuse mesangial sclerosis (DMS) in 7/36 (19 %), membranoproliferative glomerulonephritis (MPGN) in 5/36 (14 %), Finnish congenital nephrotic syndrome (CNF) in 2/36 (5.5 %) and minimal change disease (MCD) in 1/36 (3 %). A genomic alteration was detected in 14/36 patients (39 %). NPHS2 was mutated in 3/21 (14 %) children with FSGS. WT1 was mutated in 5/7 children with DMS (72 %) and in one boy with FSGS. 3/21 children with FSGS (14 %) had a mitochondrial cytopathy (mutation in CoQ2 in 2 and in MTTL1 in 1). NPHS1 was mutated in 2/2 children with CNF (100 %). A girl with MPGN had a CFI novel mutation.
Conclusions: Based on clinical and genetic data of the patients, compared with the literature, a practical molecular-diagnostic algorithm for clinical assessment of children with nephrotic/non nephrotic proteinuria of suspected genetic origin is proposed. An appropriate diagnostic approach is essential to an accurate work up of the patient and may contribute to the optimization of health resources.

P139 - RANDOMIZED, DOUBLE BLIND, PLACEBO CONTROLLED TRIAL TO COMPARE THE EFFICACY OF 3-MONTHS VERSUS 6-MONTHS THERAPY WITH PREDNISOLONE FOR THE FIRST EPISODE OF IDIOPATHIC NEPHROTIC SYNDROME [CTRI/2010/091/001095]

ARVIND BAGGA[1], ADITI SINHA[1], ABHIJEET SAHA[2], MANISH KUMAR[3], KAMRAN AFZAL[4], AMARJEET MEHTA[5], PANKAJ HARI[1]
[1]ALL INDIA INSTITUTE OF MEDICAL SCIENCES, NEW DELHI
[2]RAM MANOHAR LOHIA HOSPITAL, NEW DELHI
[3]CHACHA NEHRU BAL CHIKITSALAYA, NEW DELHI
[4]JAWAHAR LAL NEHRU MEDICAL COLLEGE, ALIGARH
[5]SAWAI MAN SINGH MEDICAL COLLEGE, JAIPUR, INDIA

Introduction: Recommendations regarding prolongation of initial corticosteroid therapy for reducing the frequency of subsequent relapses are based on prospective studies, none of which were blinded. This double-blind placebo-controlled randomized trial intends to examine the efficacy and safety of 3-months (mo) versus 6-mo therapy with prednisolone in the first episode of idiopathic nephrotic syndrome (NS).
Material and methods: Following written consent, newly diagnosed patients with NS, 1–12 yr old, are enrolled. Patients that refused consent, presented with deranged renal function or gross hematuria, or received oral prednisolone for >10 days in past 4 weeks (wk) were excluded; reasons for late exclusion included initial steroid resistance, or relapse during initial 12-wks' therapy. Following standard therapy for 12-wk (prednisolone at 2 mg/kg/d x 6-wk, 1.5 mg/kg on alternate days x 6-wk) and re-consent, patients are randomized to receive prednisolone or placebo on alternate days in tapering doses (1 mg/kg x 4-wk, 0.75 mg/kg x 4-wk, 0.5 mg/kg x 4-wk). Primary outcome is the relapse rate during 1-yr following trial medication. Secondary outcomes include time to first relapse; cumulative prednisolone requirement (mg/kg/day), proportion with frequent relapses, requirement of alternative medications and corticosteroid side effects. Intention to treat analysis is planned for an estimated sample size of 180 patients.
Results: Of 199 patients enrolled since 2010, 170 (107 boys) have been randomized and 120 have completed 1-yr follow up. Fifteen patients were excluded later or were lost to follow up. At onset, mean±SD age was 52.8± 32.7 months. Blood level of creatinine was 0.56±0.29 mg/dl, albumin 1.9±0.7 g/dl and cholesterol 391.2±132.0 mg/dl. The urine protein to creatinine ratio was 4.7±1.2 mg/mg.
Conclusions: Randomization is continuing and assessment of outcomes shall happen at completion of follow up. Results of this study shall have substantial implications for guiding the duration of initial therapy for children with idiopathic NS.

P140 - Pancreas function evaluation with postprandial ultrasound in children with nephrotic syndrome

GULFIZAT BEKMURZAEVA[1], LUBOV POLESCHUK[2], ISMAIL OSMANOV[1]
[1]*RUSSIAN NATIONAL RESEARCH MEDICAL UNIVERSITY NAMED AFTER N.I. PIROGOV*
[2]*MOSCOW RESEARCH INSTITUTE OF PAEDIATRICS AND CHILDREN'S SURGERY*

Introduction: Nephrotic syndrome and its treatment can induce development of pancreas function alterations. Detection of these alterations by common ultrasound (US) can be quite difficult. Postprandial US allows to reveal pancreas pathology, such as chronic or reactive pancreatitis, with higher precision than common US investigation. The aim of the research was to investigate frequency and characteristics of pancreas lesion in children with nephrotic syndrome, using postprandial US.
Material and methods: We examined 50 children with nephrotic syndrome (35 boys, 15 girls), age 9±1,87 (range 3,0-18,0) years. Among them 24 (48 %) children had steroid dependent and 26 (52 %) - steroid resistant nephrotic syndrome. First, all children underwent fasting abdominal US and then repeated Doppler US, 120 min after usual breakfast. The postprandial index (PPI)>15 % evalued as normal pancreas function, PPI from 5 to 15 % - as inderect sign of reactive pancreatitis and PPI <5 % - as inderect sign of chronic pancreatitis.
Results: The analysis revealed that all children had pancreas alterations. All of them had echostructure abnormalities and increased pancreas, 74 % had hyperechogenicity. In the whole group 66 % of children had PPI <5 %, 63,6 % of them had steroid resistant nephrotic syndrome and 36,4 % - steroid dependent. 16 % of children had PPI 5-15 %, 25 % with steroid resistant nephrotic syndrome and 75 % with steroid dependent. Only 18 % of children had PPI >15 %.
Conclusions: We concluded that children with steroid resistant nephrotic syndrome show indirect signs of chronic pancreatitis 27 % more often than with steroid dependent variant. On the other hand, indirect signs of reactive pancreatitis were noticed in children with steroid dependent nephrotic syndrome 50 % more often than with steroid resistant. It can be connected with the fact that children with steroid resistant nephrotic syndrome use more immunosuppressive drugs.

P141 - Prevention of steroid induced bone disease in children with nephrotic syndrome: a systematic review

ANTONIA BOUTS[1], MARIKEN GRUPPEN[1], EISKE DORRESTEIJN[2], MICHIEL SCHREUDER[3], MARC LILIEN[4], MICHIEL OOSTERVELD[1], SHARON KRAMER[5], JEAN-CLAUDE DAVIN[1]
[1]*EMMA CHILDREN'S HOSPITAL, AMC, AMSTERDAM, THE NETHERLANDS*
[2]*ERASMUS MC SOPHIA, ROTTERDAM*
[3]*RADBOUD UNIVERSITY NIJMEGEN*
[4]*WILHELMINA CHILDREN'S HOSPITAL UTRECHT*
[5]*COCHRANE COLLABORATION CENTER, AMC, AMSTERDAM*

Introduction: Children with idiopathic nephrotic syndrome (NS) are at increased risk for developing osteoporosis mainly due to the use of glucocorticoids. The routine use of prophylactic therapy to prevent bone loss is uncommon. This review analyzed the effect of calcium and/or vitamin D, bisphosphonates (BF) in the prevention and treatment of bone loss in children with NS.
Material and methods: Search strategy: We searched Pubmed, MEDLINE, EMBASE and CENTRAL from 1961 up to 2010. Selection criteria: RCT's concerning children under the age of 18 years with NS requiring therapy with steroids. Due to the lack of published studies in this category we extended the search criteria to children<18 years with corticosteroid induced osteoporosis independently of the underlying disease. The primary outcome measure was a change of BMD. Secondary outcome measures concerned growth, fracture rate and side effects. Methodological qualities of the selected studies were evaluated by using the assessment form for randomized controlled trials from the Dutch Evidence Based Guideline Development Group (EBRO)
Results: The search strategy retrieved 1167 RCT's and systematic reviews. From these, 279 were selected on title and abstract (articles concerning steroid induced osteoporosis in humans, not in peri- or postmenopausal period only). Of these 279, 108 RCTs concerned patients with NS, transplantation, rheumatoid arthritis, inflammatory bowel disease or autoimmune disease. Extracting the studies concerning children yielded 6 RCTs. Two from these 6 studies were excluded because one was not qualified as RCT, the other because of trial completion failure. Four trials reporting 166 patients remained. All of them concluded to a significant improvement in bone mineral density in the treatment group compared to the control group.
Conclusions: Calcium and vitamin D supplements are recommended for children with NS treated with steroids to prevent osteoporosis. BF can be used in the treatment of severe osteoporosis.

P142 - Low Birth Weight as Risk Factor for Minimal Change Nephrotic Syndrome

INêS SIMãO, GUSTAVO QUEIRóS, MARGARIDA ABRANCHES
DONA ESTEFANIA HOSPITAL

Introduction: The reduced endowment of nephrons in low birth weight (LBW) is a risk factor for future chronic renal diseases. The influence of LBW in the course and outcome

of minimal change nephrotic syndrome (MCNS) may help clinicians during prognosis assessment.

Material and methods: A retrospective review of children with MCNS was analysed. MCNS was determined on clinical findings based on the response to corticosteroids or renal biopsy.

Results: The cohort consisted of 58 patients: eleven children had LBW with median weight of 2250 (850–2735) g; forty-seven children had normal birth weight (control group: median 3300 (2500–4420) g), all born at term. A similar age at the onset of MCNS was found in LBW and in control group, median 3.56 ±1.6 years and 4.65±2.2 years, respectively. On first episode, LBW children needed more days to achieve a remission (> 9 days), 72,8 % (8/11) versus 37 % (17/46) in control group (odds ratio (OR) 4,55 (95 % confidence interval (CI) (1,06-19,5), P 0,032). Occurrence of relapses was more frequent in LBW group (10/11, 90,9 %) than in control group (35/47, 74,5 %), (OR 3,82, P 0,195). No difference in corticosteroid-dependent patients could be determined on both groups: 4/11 (36,4 %) in LBW versus 14/47 (29,8 %) in control group (P 0,671). More LBW children had frequent relapsing episodes (27,2 % versus 6,4 %, P 0,041). One LBW child was corticosteroid-resistant and none on control group. More LBW children were treated with additional medication (cyclosporine, cyclophosphamide and levamisol) with no significant differences (72,7 % versus 46,8 %, OR 3,03, P 0,121).

Conclusions: More LBW children with MCNS were identified on this cohort compared to previous data. LBW children needed more days to remission, relapsed and were treated more frequently with cyclosporine or cytotoxic agents. Although absolute numbers were higher in LBW children, the small number of samples and its heterogeneity do not provide significant statistical differences.

P143 - The ARB role in the prevention of Idiopathic Nephrotic Syndrome relapse

TERESA PAPALIA, ROSITA GRECO, RENZO BONOFIGLIO

NEPHROLOGY DIALYSIS AND TRANSPLANTATION. ANNUNZIATA HOSPITAL. COSENZA

Introduction: Idiopathic Nephrotic Syndrome (ISN) is a therapeutic dilemma for Paediatric Nephrology. The long-term use of Cyclosporine (CyA) as treatment for nephrotic syndrome (SN) is controversial because of its potential nephrotoxicity and the disease relapse after its interruption. Our retrospective study examines the clinical outcome of children with NS treated with CyA.

Material and methods: A cohort of 45 children (30.5 %F, 69.5 %M) with ISN were examined between January 1998 and March 2008. The average age was 4.36 years. Medium follow-up was 7.2 years. All patients showed a normal renal function (according to Swhartz formula). Of the cohort, 12 were suffering from steroid resistant nephrotic syndrome (SRNS) and 18 from steroid dependent nephritic syndrome (SDNS). All patients had been treated with only CyA (3 mg/Kg/die) or combined therapy with CyA and small doses of Prednisone.

Results: Complete remission (proteinuria <4 mg/h/m2/body surface area) was observed in 23 children (28,5 %F, 71,5 % M) over a period of 2,4 months. The dosage of CyA C2 medium was 550 ng / ml. The average duration of the therapy was 3.5 years. During the period examined 3 children have suspended CyA because of EBV infection and chickenpox after an average of 16 months of treatment. In none of them was detected hypertension and/or deterioration of renal function (increase in Crs>30 %) and only 12 children presented evidence of gingival hyperplasia and hypertrichosis. Before the suspension of therapy with CyA, in all patients and despite the absence of proteinuria, a long-term therapy with ARB has been initiated. After 5 years from discontinuation of cyclosporine therapy, all patients are in complete remission.

Conclusions: This study further demonstrates the efficacy of CyA in inducing complete remission in NSRD and SDNS. We believe, however, that the initiation of ARB, at the end of the cycle employing CyA, is essential to prevent disease relapse after discontinuation of immunosuppressant.

P144 - Nephrotic syndrome of the Finnish type (CNF) displays changes in cell turnover and primary cilia associated with cysts formation

MIRNA SARAGA-BABIC[1], KATARINA VUKOJEVIC[1], MERICA GLAVINA DURDOV[2], MARIJAN SARAGA[3]

[1]*DEPARTMENT OF ANATOMY, HISTOLOGY AND EMBRYOLOGY, SCHOOL OF MEDICINE, UNIVERSITY OF SPLIT, SPLIT, CROATIA*

[2]*DEPARTMENT OF PATHOLOGY, UNIVERSITY HOSPITAL IN SPLIT, SPLIT, CROATIA*

[3]*DEPARTMENT OF PAEDIATRICS, UNIVERSITY HOSPITAL IN SPLIT, SPLIT, CROATIA*

Introduction: Nephrotic syndrome of the Finnish type (CNF) is a hereditary disease caused by mutation of gene for nephrin on the slit diaphragm. The renal histological picture varies greatly. Tubular atrophy and dilations are often found, while irregular microcystic dilations of proximal tubules are the most striking feature. By now, the process of dedifferentiation was suggested as possible pathogenetic mechanism of CNF.

Material and methods: Nephrotic kidneys in the second year of life and healthy kidneys of corresponding age were histologically analyzed using immunofluorescent method

for proliferation marker Ki-67, apoptotic caspase-3 marker and α-tubulin for detection of primary cilia. Increase in diameter of dilated proximal CNF tubules was measured and correlated with proliferation index in tubular epithelium. Data were analysed by the Kruskal–Wallis and Dunn's post hoc test. Probability values of $P<0.05$ were regarded as significant.

Results: In normal kidneys, distal tubules contained 2.65 % of proliferating cells, glomeruli contained 8.66 %, while proximal tubules showed no proliferation activity. CNF tubules with apparently normal diameter (12 μm), contained 81.54 % of Ki-67 positive cells, while in mildly dilated tubules (diameter 21 μm) their number increased to 89.47 %. In tubular cysts (diameter 54 μm), proliferation index decreased to 29.89 %, while in the largest cysts (diameter 73 μm) it dropped to only 11.54 %. Apoptotic cells were observed in the tubules and interstitium of CNF kidneys. Primary cilia were missing in the cysts, while in some tubules cilia were dimorphic and extremely long. The increase in tubular diameter was associated with changes in shape of tubular cells, from columnar to squamous.

Conclusions: The width (diameter) of proximal tubules is inversely proportional to proliferation index and shape of tubular cells. The increased proliferation in CNF tubules probably counteracts the initial cysts formation, while in large tubular cysts the exhausted cells lose their proliferation ability, shape and primary cilia function.

P145 - A new possibility for drug monitoring of prednisolone in saliva

NYNKE TEENINGA[1], ZHENG GUAN[2], JEROEN NAUTA[1], AN RUITER[1], MARIETTE ACKERMANS[3], JOANA E. KIST-VAN HOLTHE[4], TEUN VAN GELDER[5], JAN FREIJER[2]

[1]ERASMUS MC UNIVERSITY MEDICAL CENTER – SOPHIA CHILDREN'S HOSPITAL, ROTTERDAM, THE NETHERLANDS

[2]CENTRE FOR HUMAN DRUG RESEARCH, LEIDEN, THE NETHERLANDS

[3]DEPARTMENT OF CLINICAL CHEMISTRY, LABORATORY OF ENDOCRINOLOGY, ACADEMIC MEDICAL CENTER, AMSTERDAM, THE NETHERLANDS

[4]VU UNIVERSITY MEDICAL CENTER, AMSTERDAM

[5]ERASMUS MC UNIVERSITY MEDICAL CENTER, ROTTERDAM, THE NETHERLANDS

Introduction: It is well known that patients show variable responses to prednisolone in terms of therapeutic and side effects. Unfortunately, drug monitoring for prednisolone is hardly implemented in clinical practice. We aimed to develop a feasible method for drug monitoring of prednisolone by exploring the relationship between prednisolone levels in serum and saliva and to implement these results in a population pharmacokinetic (PPK) model.

Material and methods: We collected serum and saliva samples from 19 healthy volunteers before and 1–6 hours after oral ingestion of 80 mg prednisolone. We measured total and non-protein bound concentrations of prednisolone, prednisone and cortisol in serum, ultrafiltrate and saliva using liquid chromatography tandem mass spectrometry (LC-MS/MS). PK modeling was performed with NONMEM 7.2.

Results: The mean t1/2 of prednisolone was 3.4 hours, which is in agreement with previous reports. The unbound fraction of prednisolone gradually decreased from 40 % to 26 % within six hours. The ratio of prednisolone to prednisone, which was lowest in saliva, gradually decreased with time in all media. Salivary levels and free serum levels of prednisolone showed excellent correlation with total prednisolone levels in serum. This was best described in an exponential relationship. Age, serum albumin, and lean body mass significantly influenced this relationship and were kept in the final PPK model.

Conclusions: This study demonstrates that saliva can be used as a feasible and patient friendly method for drug monitoring of prednisolone.

P146 - Rituximab in steroid-dependent and resistant nephrotic syndrome patients

REZAN TOPALOGLU, BORA GÜLHAN, FATIH ÖZALTIN, ALI DÜZOVA, NESRIN BESBAS

HACETTEPE UNIVERSITY FACULTY OF MEDICINE DEPT OF PEDIATRIC NEPHROLOGY

Introduction: Idiopathic nephrotic syndrome is the most frequent glomerular disease in children Although most of the patients respond to steroids, development of steroid dependency/resistance causes important side effects. Rituximab (RTX) is a new therapeutic strategy for this group of patients.

Material and methods: We evaluated four steroid-dependent and one steroid resistant nephrotic syndrome patients who were on RTX treatment. At the time of first RTX treatment (375 mg/m2/dose), none of the patients had renal failure. Five patients (3 males and 2 females) were included to the study. The mean age of nephrotic syndrome diagnosis was 3.9±2.6 years (range 2–8.6). Initial renal biopsy revealed focal segmental glomerulosclerosis (FSGS) in three patients (1 female, 2 males) and minimal change disease (MCD) in two patients (1 female, 1 male). Before RTX, all patients were treated with prednisolone (3.7-11 years) and cyclosporine (0.8-7 years), Four patients had cyclophosphamide (1.5-3 months). One of the female patients with FSGS also used tacrolimus for 1 year and

mycophenolate mofetil (MMF) for 9 months as steroid sparing agents.
Results: The age of RTX treatment was ranged from 6 to 15.2 years (mean 11.2±3.6). Rituximab was given in relapse in all patients but one (male with MCD). In all of the patients, B cell depletion was observed after first dose of RTX infusion. One patient had four, three patients had three and one patient had two infusions. Median follow-up period was 3 months. Two patients were put on MMF therapy after RTX. All the steroid dependent patients who were in relapse got in the remission after the second dose of RTX. Although steroid resistant patient showed some improvement, he is still nephrotic after 3 doses of RTX.
Conclusions: Rituximab is an effective therapeutic option for steroid-dependent nephrotic syndrome patients without serious short-term side effects.

P147 - NEPHROTIC SYNDROME AND HYPERCOAGULABLE STATE. NEW DIAGNOSTIC TOOLS

DANIELA MOLINO[1], GABRIELE MALGIERI[1], MARIA ROSARIA LUPONE[2], CORRADO PERRICONE[2], FRANCESCA NUZZI[1], MARIA D'ARMIENTO[3], CARMINE PECORARO[1]
[1]DEPARTMENT OF NEPHROLOGY AND UROLOGY, CHILDREN'S HOSPITAL SANTOBONO, NAPLES, ITALY
[2]DEPARTMENT OF HEMATOLOGY, CHILDREN'S HOSPITAL PAUSILIPON, NAPLES, ITALY
[3]DEPARTMENT OF PATHOLOGY, UNIVERSITY FEDERICO II, NAPLES, ITALY

Introduction: Several studies showed that an imbalance of prothrombotic and antithrombotic factors and impaired thrombolytic activity contribute to the thrombophilia of the Nephrotic Syndrome (NS). However, it is not clear whether blood cell injury and/or activation is involved in hypercoagulability in NS patients.
Material and methods: To evaluate haemostasis and the main genetic mutations associated with thrombotic risk in children with Idiopathic Nephrotic Syndrome (INS), we have studied 20 children with INS aged 1 to 14 years, matched with 40 health-subjects. The following parameters were evaluated: PT, aPTT, platelet count, fibrinogen, antithrombin III, C- and S-proteins, plasminogen and homocysteine. Furthermore we have performed the molecular study for thrombotic risk (Factor V Leiden, MTHFR C677T, A1298C and Prothrombin G20210A) by the means of the analysis of subclasses of antiphospholipid antibodies (anticardiolipin, anti-Beta2GPI and anti Z-protein) and by the means of the thrombin generation test with thromboelastometer.
Results: In the studied population with NS PT, aPTT and homocysteine were into the normal range with no difference when compared with controls. On the contrary Fibrinogen and anticardiolipin, anti-Beta2GPI and anti Z-protein antibody serum levels and thrombin generation test values were significantly higher in NS children with respect to controls ($p<0.05$). Finally, there was not any significant difference in the incidence of genetic mutations related to the thrombotic risk between children with ISN and health-subjects group.
Conclusions: In INS children the coagulation cascade is greatly activated, as previously demonstrated by low levels of Antithrombin III and plasminogen and high levels of fibrinogen. This hypercoaogulable state is now confirmed by high values of thrombin generation test. More studies about haemostasis in NS are needed, to improve prognosis and therapeutic management of INS children.

P148 - Hyperkalemia in children with nephrotic syndrome: Two case reports

NURAN CETIN, BILAL YILDIZ, NURDAN KURAL
ESKISEHIR OSMANGAZI UNIVERSITY FACULTY OF MEDICINE DEPARTMENT OF PEDIATRIC NEPHROLOGY

Introduction: Nephrotic syndrome (NS) is the most common glomerulopathy in children. In contrast to hyponatremia, hyperkalemia is very rarely reported in GFR preserved nephrotic children.
Material and methods: Herein, we report 3 cases of severe edematous NS with hyperkalemia.
Results: Case-1: A 9-years-old male child with steroid-dependent NS was admitted due to severe edema. His follow up period was 2 years with non-specific renal biopsy findings and negative family history for NS or other renal diseases. On physical examination, he had generalized edema without respiratory distress and hypertension. Laboratory investigations showed serum creatinine:0.3 mg/dl, BUN:19.3 mg/dl, total protein:3.8 g/dl, albumin:1.2 g/dl, sodium:126 mEq/dl, potassium:6.5 mEq/dl and 4+ proteinuria in urine. Pulse-methyl-prednisolone (30 mg/kg/day) treatment was started. Nebulized salbutamol and albumin infusion with furosemide therapy was also started due to hyperkalemia. This treatment protocol induced prompt remission with resolution of clinical symptoms and normalization of laboratory findings. Case-2: A 3-years-old male child with relapse steroid-sensitive NS was hospitalized with severe generalized edema and decreased urine output. He has got severe peripheral edema with ascites, hypoalbuminemia (1.1 g/dl), hyperlipidemia and normal serum creatinine (0.05 mg/dl) and BUN (17.7 mg/dl) levels. He had hyponatremia (121 mEq/dl) and hyperkalemia (6.4 mEq/dl). This patient was treated with oral prednisolone (60 mg/m2/day), intravenous albumin infusions with furosemide and

nebulized salbutamol. His electrolytes levels were normalized on 4th days of hospitalization.
Conclusions: In conclusion, our patients showed hyperkalemia may be related to severe edema and/or proteinuria. Hyperkalemia seemed to be associated with the down-regulation of potassium channel due to abnormal protein occurrence in the tubular fluid or impaired potassium excretion due to the poor sodium delivery to the distal tubule. Our patients also showed that serum potassium levels and daily potassium intake should be controlled in patients with NS due to this potentially life-threatening complication.

P149 - Plasma and urine proteomic profiles in childhood idiopathic nephrotic syndrome

RENé ANDERSEN, BENTE JESPERSEN, SøREN RITTIG
AARHUS UNIVERSITY HOSPITAL, SKEJBY

Introduction: Idiopathic nephrotic syndrome (NS) is characterized by proteinuria, edema and hypoalbuminemia. The aim of the study was to identify differentially expressed proteins in urine and plasma during NS compared with remission.
Material and methods: Plasma and urine samples were collected during NS and at remission from four patients with the first episode of NS. Proteomic profiling was performed by iTRAQ labeling followed by nanoLC-MS/MS to yield data on relative protein amounts. Protein validation was performed by ELISA from 14 patients with NS.
Results: A total of 388 and 425 proteins were detected in plasma and urine, respectively. In total, 18 plasma and 38 urinary proteins were significantly altered ($p<0.05$). E-cadherin was one of the proteins with reduced urinary concentration during NS, a finding validated by ELISA. E-cadherin/total protein amount was 2.6 (CI95% 1.3 – 5.1) pg/mg at NS compared to 269.1 (157.6 – 459.1) pg/mg at remission, $p<0.001$. The slit diaphragm protein P-cadherin was identified by nanoLC-MS/MS and shown to be reduced in urine during NS by ELISA. The median P-cadherin/total protein amount was 6,000 (range 28 – 28,600) pg/mg at NS vs. a ratio of 209,000 (range 32,700 – 1,286,500) pg/mg at remission, $p<0.001$.
Conclusions: The present study identified more than 50 differentially altered proteins comparing NS with remission. Several proteins were found to be linked to the major clinical symptoms of NS, and further studies must elucidate if P-cadherin is involved in proteinuria during NS, and if low urinary E-cadherin level is linked to altered integrity of the epithelial cell to cell contacts in the distal part of the nephron.

P150 - The levamisole study in steroid sensitive idiopathic nephrotic syndrome (SSINS): Inclusion completed

MARIKEN GRUPPEN[1], ANTONIA BOUTS[1], PATRICK NIAUDET[2], THIERRY SCHURMANS[3], NOEL KNOPS[4], NADEJDA RANGUELOV[3], ELENA LEVTCHENKO[4], MARLIES CORNELISSEN[9], ANN RAES[5], JOHAN VANDE WALLE[5], MICHAL MATERNIK[6], ALEKSANDRA ZUROWSKA[6], FRANCESCO EMMA[7], LAURA MASSELLA[7], ARVIND BAGGA[8], ASHIMA GULATI[8], JEAN-CLAUDE DAVIN[1]
[1]*EMMA CHILDREN'S HOSPITAL/ACADEMIC MEDICAL CENTRE*
[2]*HôPITAL NECKER-ENFANTS MALADES, PARIS*
[3]*HUDERF, BRUSSELS*
[4]*GASTHUISBERG, LEUVEN*
[5]*UNIVERSITAIRE ZIEKENHUIS GENT*
[6]*MEDICAL UNIVERSITY GDANKS*
[7]*BAMBINO GESU OSPEDALE, ROMA*
[8]*ALL INDIA INSTITUTE, NEW DELHI*
[9]*UMC ST RADBOUD, NIJMEGEN*

Introduction: In order to interest pharmaceutical companies to bring back levamisole on the market, we have set up a multi-centre, double-blind, placebo-controlled, randomized clinical trial (RCT) followed by a cohort study, using the infrastructure of the RCT in order to study the efficacy of one year of alternate day levamisole 2.5 mg/kg in the prevention of relapses and in prolonging the time to relapse after cessation of corticosteroids treatment in children with SSINS.
Material and methods: Participating countries: Netherlands, Belgium (coordination T Schurman, HUDERF, Brussels), France (coordination P Niaudet, Hôpital Necker-Enfants Malades), Italy (Bambino Gesu Ospedale:L Massela, F Emma),India (All India Institute New Delhi : A Bagga, A Gulati),Poland: Medical University of Gdansk (A Zurowska, M Maternik). Financial support: ACE Pharmaceuticals (study medication manufacturing and distribution, pharmacokinetics), French Ministry of Health, Dutch Kidney Foundation, Emma Foundation, Dutch Orphan Disease Foundation, Dutch Agis Health Insurance. Authorizations: 2004: official ESPN study; 2005: Orphan Drug designation (EMEA), priority for ACE Pharmaceuticals to commercialize levamisol (EMEA),approval of study protocol (EMEA);2006: AMC and national Dutch Medical Ethical Commission;2007: Medical Ethical Commission Bambino Gesu Ospedale, Roma;2009: Belgian, French, Polish, Indian Medical Ethical Commissions.
Results: Inclusion: completed in March 2012 (100 patients) Interim analysis: performed on 65 patients: no efficacy or safety reason to stop prematurely or to extend to a higher number of patients than the originally calculated power.

Conclusions: Agenda: study completion in 2013. According to results of intermediate analysis, it might be expected that levamisole will be commercialized again for human use, registered for the indication of SSINS and available in tablets of different dosages adapted to age in a delay of 18 months

P151 - Congenital nephrotic syndrome of atypical development caused by a mutation in the gene NPHS1 splicing

MARIA ISABEL LUIS YANES[1], ELISABET ARS[2], SHEILA SANTíN[2], GEMMA BULICH[2], ROSER TORRA[2], VICTOR M GARCIA NIETO[1]
[1]*PEDIATRIC NEPHROLOGY UNIT, HOSPITAL UNIVERSITARIO NUESTRA SEñORA DE CANDELARIA, SANTA CRUZ DE TENERIFE*
[2]*LABORATORY OF MOLECULAR BIOLOGY **, PUIGVERT FOUNDATION, BARCELONA*

Introduction: The Finnish type congenital nephrotic syndrome, autosomal recessive,is caused by mutations in the NPHS1 gene encoding nephrin. Those affected are preterm infants with massive proteinuria starting in utero. This entity is resistant to any treatment and progresses rapidly to CKD.
Material and methods: Male patient, 19 years, four months, was valued by the incidental finding of proteinuria (1.9 g / l) and hypoalbuminemia in the absence of edema. Her birth weight was 2,700 g. Both parents come from the same geographic area. An ultrasound renal kidneys were symmetrical with marked renal pyramids. It was treated with steroids and, in the absence of response received cyclophosphamideand cyclosporine. We performed the first renal biopsy compatible with minimal change nephropathy. It was treated with ramipril, candesartan, indomethacin and fibrates. Proteinuria remained stable (1.9 to 3 g / l) without significant clinical manifestations. Recently, repeated renal biopsy without histological changes and were treated with mycophenolate without response .Throughout the monitoring period has maintained a normal renal glomerular function.
Results: The patient has homozygous sequence variant c.1930 +5 G>A (IVS14 +5 G>A) in intron 14 of the NPHS1 gene. This variant alters the pre-mRNAsplicing of NPHS1 causing the deletion of 31 nucleotides of exon 14 (r.1900_1930del31) as is expected to result in a nephrin protein truncated 645 amino acids instead of 1241 that has the normal protein . The parents and sister are heterozygous carriers of the same variant.
Conclusions: We establish the hypothesis that this mutation "mild" in homozygosityallows the coexistence of a certain proportion of wild-type NPHS1 mRNAs withmutated mRNA and thus with a certain level of functional nephrin. Most patients withNPHS1 mutations show very severe phenotype. In recent years patients have been reported with at least one mutation "mild" NPHS1 and a slower progression to CKD (Philippe et al., 2008, Santin et al. 2009).

P152 - The evaluation of treatment side effects in children with idiopathic nephrotic syndrome

HALUK ESMERAY, SEVINC EMRE, ALEV YILMAZ, ILMAY BILGE
ISTANBUL UNIVERSITY ISTANBUL MEDICAL FACULTY PEDAITRIC NEPHROLOGY DEPARTMENT

Introduction: Treatment of idiopathic nephrotic syndrome (INS) with immunosupressive agents and corticosteroids (CS) may cause several side effects leading to additional pathologic conditions requiring therapy and influence overall prognoses of the patients. The aim of this study was to assessed the frequency and prognosis of the side effects due to treatment of INS in children.
Material and methods: Two hundred and six patients (126 male, 80 female) were enrolled this retrospective study. Mean age was 3.8±2.8 years (1–13.8).
Results: All patients received oral CS, except one with spontaneous remission. Among these patients, intravenous pulse CS was administered in 47 patients, cyclophosphamide in 31, cyclosporine in 17 and chlorambucil in 4. One hundred and seventy one patients (83 %) had at least one side effect due to any of these agents. The most important advers effects of CS were growth retardation in 17 % of the patients, osteoporosis in 6.8 %, cataract in 6.8 % and hypertension in 23.4 %. Mean duration of CS treatment and mean total CS dose were significantly higher in the patients with growth retardation than in those without retardation (60.18±44.62 vs 29.56±37.83 months, and 25.4±26.8 vs 10.5±12.9 gram/m2; respectively)($p=0.0001$). Mean duration of CS therapy and mean total CS dose were also significantly higher in the patients with osteoporosis than in those without osteoporosis (69.82±50.27 vs 32.22±38.76 months, and 41.1±34.4 vs 11.0±12.9gram/m2; respectively)($p=0.0001$). Mean duration of CS therapy and mean total CS dose were found to be significantly higher in the patients with cataract than in those without cataract (68.31±49.21 vs 32.33±38.96 months, and 37.1 vs 11.3 gram/m2; respectively)($p=0.0001$). The most frequent side effects were neutropenia in the patients receiving cyclophosphamide and hypertension in those receiving cyclosporine.
Conclusions: Advers effects of therapy are an important determinant of the successful treatment in INS in children. Regular follow up the side effects are necessary in these patients in order to provide the optimal treatment.

P153 - Molecular characterization of Polish children with podocin-associated hereditary nephrotic syndrome: novel and recurrent NPHS2 mutations

BEATA S. LIPSKA[1], IRENA BAŁASZ-CHMIELEWSKA[2], LUCYNA MORZUCH[1], HALINA BORZęCKA[7], EWA GACKA[12], AGNIESZKA FIRSZT-ADAMCZYK[3], TOMASZ JARMOLIńSKI[4], JOANNA KSIążEK[5], ELŻBIETA KUŹMA-MROCZKOWSKA[6], ANNA MEDYŃSKA[8], IWONA OGAREK[9], MAGDALENA SILSKA[10], MARIA SZCZEPAńSKA[11], MARCIN TKACZYK[13], ANNA WASILEWSKA[14], JANUSZ LIMON[1], ALEKSANDRA ŻUROWSKA[2]

[1]*DEPARTMENT OF BIOLOGY AND GENETICS, MEDICAL UNIVERSITY OF GDANSK, POLAND*

[2]*DEPARTMENT OF PAEDIATRIC NEPHROLOGY AND HYPERTENSION, MEDICAL UNIVERSITY OF GDANSK*

[3]*DEPARTMENT OF PEDIATRICS AND NEPHROLOGY, TORUń*

[4]*DEPARTMENT OF PEDIATRICS, NEPHROLOGY AND TOXICOLOGY, DISTRICT CHILDREN'S HOSPITAL, SZCZECIN*

[5]*DEPARTMENT OF NEPHROLOGY AND HYPERTENSION, THE CHILDRENS' MEMORIAL HEALTH INSTITUTE, WARSAW*

[6]*DEPARTMENT OF PEDIATRICS AND NEPHROLOGY, MEDICAL UNIVERSITY OF WARSAW*

[7]*DEPARTMENT OF PEDIATRIC NEPHROLOGY, MEDICAL UNIVERSITY OF LUBLIN*

[8]*DEPARTMENT OF PEDIATRIC NEPHROLOGY, WROCLAW MEDICAL UNIVERSITY, WROCłAW*

[9]*PAEDIATRIC NEPHROLOGY AND DIALYSIS UNIT, JAGIELLONIAN UNIVERSITY MEDICAL COLLEGE, KRAKóW*

[10]*DEPARTMENT OF PEDIATRIC NEPHROLOGY, POZNAN UNIVERSITY OF MEDICAL SCIENCE, POZNAń*

[11]*DIALYSIS UNIT, SILESIAN MEDICAL UNIVERSITY, ZABRZE*

[12]*DEPARTMENT OF PEDIATRIC NEPHROLOGY, CHORZóW*

[13]*NEPHROLOGY DIVISION, POLISH MOTHER'S MEMORIAL HOSPITAL RESEARCH INSTITUTE, ŁODź*

[14]*DEPARTAMENT OF PAEDIATRICS AND NEPHROLOGY MEDICAL UNIVERSITY OF BIAłYSTOK, BIAłYSTOK*

Introduction: Hereditary nephrotic syndrome (HNS) is caused by mutations in a number of different genes, the most common being NPHS2 (podocin) gene mutations accounting for ca. 20 % of cases in childhood. The aim of the study was to identify the mutation spectrum of podocin-associated HNS in Poland.

Material and methods: Molecular analysis of NPHS2 was performed in a group of 113 NS patients, recruited from the 12 paediatric nephrology referral centres in Poland. All patients were clinically diagnosed with steroid-resistant NS according to the PodoNet consortium criteria. Mutational analysis included entire coding sequence and intron boundaries of the NPHS2 gene. RFLP and TaqMan genotyping assay were applied to detect selected NPHS2 sequence variants in a control group of 500 neonatal dried blood samples.

Results: 17 sequence variations were identified in 74 (65 %) NS patients. Of these, 1 novel and 8 previously reported pathogenic mutations were detected, the remaining 8 being single-nucleotide polymorphisms. 21 (19 %) patients carrying homozygous or compound heterozygous NPHS2 mutations fulfilled the criteria of podocin-associated HNS. The most frequent NPHS2 alteration was the non-neutral p.R229Q polymorphism detected in 24 (21 %) patients, including 2 homozygous and 13 compound heterozygous cases; followed by deletion c.1032delT found in 9 children (8 %), all compound heterozygous cases and p.R138Q point mutation in 5 patients (4 %), including 4 homozygous cases. A geographically skewed distribution of the c.1032delT allele was found with highest prevalence in North Pomeranian region suggestive of a founder effect origin.

Conclusions: 19 % detection rate of podocin-associated HNS is similar to observed in other populations. Non-neutral p.R229Q polymorphism and two point mutations (c.1032delT and p.R138Q) are the most frequent causes of podocin-associated HNS in Poland. However, the heterogeneity of NPHS2 mutations detected in the studied group confirms the requirement for complex molecular studies of Polish NS patients.

P154 - An abdominal presentation of disseminated varicella in children with chronic kidney disease: report of 3 cases

BOUCHIREB KARIM[1], LEROY VALERIE[3], OLIVIA BOYER[1], DAUGER STEPHANE[3], SALOMON REMI[1], DESCHENES GEORGES[3], DE PONTUAL LOIC[2]

[1]*NECKER HOSPITAL*

[2]*JEAN VERDIER HOSPITAL*

[3]*ROBERT DEBRE*

Introduction: Varicella in immunocompromised children is a rare but often fatal event. Except for skin rash, other clinical signs of disseminated varicella infection are not well known by pediatricians. Currently, there is no clear consensus about immunization and treatment of varicella in immunocompromised children.

Material and methods: We report 3 cases of disseminated varicella in immunocompromised children with chronic kidney disease, hospitalized in a pediatric nephrology department in Paris, between 2006 and 2009. Clinical

presentation, biological and radiological findings, management and outcomes were all reviewed.
Results: Varicella occurred at 6, 14 and 16 years of age after a duration of immunosuppression of 1, 160 and 96 months respectively. Abdominal and/or back pain was the first symptom in all cases, preceding from 48 to 72 h the characteristic skin rash. All children received intravenous acyclovir between 2 to 3 days after first symptoms, whereas only one received varicella zona immune globulin. Two out of the 3 patients died. The last one recovered completely.
Conclusions: Varicella should be considered in the differential diagnosis of abdominal pain in immunocompromised patients. Blood PCR VZV can help to make early diagnosis in the absence of typical skin rash. Intravenous acyclovir should be started as soon as the other differential diagnosis is excluded and varicella is considered. Prompt initiation of therapy with acyclovir can be life saving.

P155 - Posterior reversible encephalopathy syndrome and elevated intraocular pressure: a case report
HELENA PINTO, ANA TEIXEIRA, CALDAS AFONSO
PEDIATRIC NEPHROLOGY UNIT, PEDIATRIC DEPARTMENT, S. JOãO HOSPITAL, OPORTO, PORTUGAL

Introduction: Childhood posterior reversible encephalopathy syndrome (PRES) has been increasingly recognised, despite its rarity and poorly defined pathophysiology. It has been described in association with acute hypertension and renal disease including nephrotic state, but its correlation with elevated intraocular pressure is not established.
Material and methods: We describe a 6-year-old girl previous asymptomatic who was admitted due to inaugural nephrotic syndrome.
Results: At first she was treated with intravenous methylprednisolone because of vomiting. At day 6 she was transferred to our Pediatric Nephrology Unit due to sudden onset of headache, vomiting, lethargy and blurred vision. Blood pressure was 177/99 mmHg. Cerebral MRI revealed moderate right fronto-temporal cortical thickening compatible with vasogenic oedema. Ophthalmologic observation demonstrated open angle glaucoma with significant elevation of intraocular pressure in both eyes, without papilloedema, which was treated with timolol, iatanoprost and bromonidine ophthalmic solutions. Arterial hypertension was controlled with captopril. At day 10 of disease she showed significant improvement of symptoms, intraocular pressure control and response to oral prednisolone. During follow-up consultation she stopped captopril, maintaining normal blood pressure. A slow tapering of steroids coincident with tapering of ophthalmic medication was performed during a six-month period without any complication. Two months after the acute episode cerebral MRI didn't evidenced any lesion. At present, one year later, she is asymptomatic without medication.
Conclusions: With this case report the authors aim to highlight one of the possible side effects of steroids, namely open angle glaucoma, which requires early diagnosis and treatment to prevent irreversible damage of optic nerve. In addition, clinical and radiological features of PRES coupled with elevated intraocular pressure, raise the question of a coincident development of both entities or less probably a causal relation. It is suggested that patients being treated with prolonged high dose of systemic steroids and patients with PRES should have an adequate ophthalmological examination.

P156 - Are polymorphisms of multidrug resistance gene 1 responsible for interindividual differences in therapeutic outcome to glucocorticoids in paediatric patients with idiopathic nephrotic syndrome?
MARTINA CIZMARIKOVA[1], LUDMILA PODRACKA[2], LUCIA KLIMCAKOVA[3], JAN MOJZIS[1], LADISLAV MIROSSAY[1]
[1]*DEPARTMENT OF PHARMACOLOGY, FACULTY OF MEDICINE, UNIVERSITY OF PAVOL JOZEF SAFARIK, KOSICE, SLOVAKIA*
[2]*DEPARTMENT OF PAEDIATRICS, FACULTY OF MEDICINE, UNIVERSITY OF PAVOL JOZEF SAFARIK, KOSICE, SLOVAKIA*
[3]*DEPARTMENT OF MEDICAL BIOLOGY, FACULTY OF MEDICINE, UNIVERSITY OF PAVOL JOZEF SAFARIK, KOSICE, SLOVAKIA*

Introduction: Multidrug resistance gene 1 (MDR1) is the most notable gene encoding the efflux pump P-glycoprotein (P-gp), which is involved in the transport of a wide range of substrates including glucocorticoids (GC). Recent studies have demonstrated that single nucleotide polymorphisms (SNP) of MDR1 gene can contribute to interindividual differences in P-gp levels and/or P-gp function. The main aim of the study was to determine the role of MDR1 polymorphisms: C3435T, G2677T, and C1236T in relation to therapeutic response (TR) to GC in paediatric patients with idiopathic nephrotic syndrome (INS).
Material and methods: Forty three patients with INS (13 girls, 30 boys, mean age at disease onset 6.04 years) were enrolled into the study. Minimal change nephropathy was found in 32 children, and focal segmental glomerulosclerosis in 11 remaining patients. The polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) method was used for genotyping. Patients were labelled according to their initial TR as "responders" (RE: 3 steroid-sensitive and 28 steroid-dependent individuals) and "nonresponders" (NR: 12 steroid-resistant individuals).

Results: The therapeutic outcome to GC was not influenced by any of the allele variations of the C3435T, G2677T, and C1236T polymorphisms (P=0.467, OR=1.54 (95 % CI= 0.58-4.14); P=0.477, OR=1.47 (95 % CI=0.56-3.85); and P=0.342, OR=1.67 (95 % CI=0.64-4.38), respectively, Fisher´s exact test). Moreover, no significant difference between genotype frequencies of all three tested SNP and TR was found.

Conclusions: According to our preliminary results, particular MDR1 polymorphisms (C3435T, G2677T and C1236T) are not main factors responsible for therapeutic failure of initial GC therapy in children with INS. Further data are needed to confirm our findings. Supported by Norway grant through the EEA and the Norwegian Financial Mechanisms, VEGA project No. 1/0715/11 and by VVGS UPJS grant No. 5/2011.

P157 - A girl with isolated diffuse mesangial sclerosis and WT1 mutation

KRISTINA VRLJIČAK[1], DANICA BATINIć[1], DANKO MILOšEVIć[1], MARIJANA ĆORIć[1], LJILJANA NIžIć STANčIN[1], HRVOJE KNIEWALD[1], JASNA SLAVIčEK[1], MAJA LEMAC[1], SONJA HODžIć[1], FRIEDHELM HILDEBRANDT[2]

[1]*UNIVERSITY HOSPITAL CENTRE ZAGREB*

[2]*UNIVERSITY OF MICHIGAN, DEPARTMENT OF PEDIATRICS*

Introduction: Isolated diffuse mesangial sclerosis (IDMS) is a histologically distinct variant of nephrotic syndrome with early onset and progression to end-stage kidney disease. Mutations in PLCE1, WT1 and LAMB2 genes may cause IDMS. Carriers of a WT1 mutation are at risk for the development of Wilm's tumor and gonadoblastoma.

Material and methods: Our patient is a female, born from a normal pregnancy, healthy; BW 3900 g. Family history is unremarkable. At the age of 4 months proteinuria was detected during a febrile respiratory infection. Methods: laboratory analysis, renal biopsy, ultrasound, abdominal MRI, genetic analysis.

Results: When she was 8 months old, she was admitted to our Department and we found proteinuria (1.4 g/dU), hypogammaglobulinemia (IgG 0.83 g/l) and a patent foramen ovale. Ultrasound showed hyperechoic kidneys of normal size Renal biopsy revealed diffuse mesangial sclerosis and multifocal nephroblastic proliferative lesions. Her karyotype is 46,XX,1qh+(population variant). She has a WT1 mutation (Ex9: c.1165 C>T), heterozygous. In the follow up period she received intravenous immunoglobulin and underwent ultrasound screening for tumors monthly. At the age of 3 years and 3 months she is a well developed girl, with normal blood pressure and without edema. Laboratory findings show non-selective glomerular proteinuria (2.47 g/dU), hypoproteinemia (49 g/l), hypogammaglobulinemia (1.72 g/l) and hypercholesterolemia (9.1 mmol/l). Other findings are within reference ranges. There are no detectable expansive lesions at abdominal MRI and ultrasound examination.

Conclusions: Our patient has a favorable course of the disease so far. She has a persistent hypogammaglobulinemia in spite of substitution. Patients with IDMS do not respond to corticosteroid and immunosuppressive therapy. It was reported that one child with PLCE1 mutation responded to cyclosporine therapy. So, patients with IDMS should be tested for mutations to find those who might benefit from the therapy. Those with WT1 mutation should be carefully observed because of the risk of tumor development.

P158 - EFFECT OF SIMVASTATIN AND CYCLOSPORIN A ON GLOMERULUSCLEROSIS IN ADRIAMYCIN INDUCED NEPHROPATHY

YONCA ACIKGOZ[1], KENAN BEK[2], OZAN OZKAYA[1], BILGE CAN[3], BIRSEN BILGICI[4], ABDULLAH ACIKGOZ[5], MURAT HOKELEK[6], SUKRU ARSLAN[1]

[1]*ONDOKUZ MAYIS UNIVERSITY FACULTY OF MEDICINE, DEPARTMENT OF PEDIATRIC NEPHROLOGY*

[2]*KOCAELI UNIVERSITY FACULTY OF MEDICINE, DEPARTMENT OF PEDIATRIC NEPHROLOGY*

[3]*ONDOKUZ MAYIS UNIVERSITY FACULTY OF MEDICINE, DEPARTMENT OF PATHOLOGY*

[4]*ONDOKUZ MAYIS UNIVERSITY FACULTY OF MEDICINE, DEPARTMENT OF BIOCHEMISTRY*

[5]*GAZI STATE HOPSPITAL, DEPARTMENT OF UROLOGY*

[6]*ONDOKUZ MAYIS UNIVERSITY FACULTY OF MEDICINE, DEPARTMENT OF MICROBIOLOGY*

Introduction: Focal segmental glomerulosclerosis (FSGS) is a specific pattern of chronic renal injury characterized by the progressive depletion of podocytes. Adriamycin (ADR) induced nephropathy is the experimental model for FSGS. The aim of this study is to investigate the individual and additive effects of Simvastatin (simv) and cyclosporin A (CyA) on glomerulosclerosis and inflammation in ADR-induced-nephropathy.

Material and methods: In our study 42 Sprague Dawley rats, weighing 300–350 gr on average, were used. Rats were randomly divided into 3 groups and their controls as Simv-treated ADR nephrosis, CyA-treated ADR nephrosis and CyA and Simv-treated ADR nephrosis. Adriamycin nephropathy was induced by single-tail intravenous injection of ADR (6,5 mg/kg). Anti-inflammatory effects of Simv, CyA and Sim+CyA were evaluated by the expression of transforming growth factor-β (TGF-β) and glomerulosclerosis index (GSI) at 8 weeks after ADR injection. At the 0,

2, 4, 6 and 8 weeks, renal functions, serum lipid and albumin levels were measured and compared between the controls and treatment groups.

Results: Simvastatin decreased neither TGF-β expression nor GSI. CyA, on the other hand decreased GSI but did no effect on TGF-β expression. However, Simv+CyA combination decreased TGF-β expression and GSI at 8 weeks after ADR injection. Additionally this combination ensured better albumin and cholesterol levels than Simv or CyA individually at the 4, 6 and 8 weeks.

Conclusions: These results suggest that CyA and Simv together seem more effective than CyA or Simv on decreasing GSI and inflammation in ADR-induced-nephropathy. Moreover, combined administration of CyA and Simv obtained better albumin and cholesterol levels than their single use. Therefore Simv might be added to therapy in patients where CyA is indicated. Obviously this recommendation needs further clinical evidence.

P159 - Nephrotic syndrome: Next Generation Sequencing (NGS) as a new diagnostic tool

JULIA HOEFELE[1], ANJA BÜSCHER[2], CHRISTIAN HEBERLE[1], MARTIN KONRAD[3], HANNS-GEORG KLEIN[1], STEFANIE WEBER[2]

[1]*CENTER FOR HUMAN GENETICS AND LABORATORY MEDICINE DR. KLEIN & DR. ROST, MARTINSRIED, GERMANY*

[2]*UNIVERSITY CHILDREN'S HOSPITAL, DEPARTMENT OF PEDIATRIC NEPHROLOGY, ESSEN, GERMANY*

[3]*UNIVERSITY CHILDREN'S HOSPITAL, DEPARTMENT OF PEDIATRIC NEPHROLOGY, MÜNSTER, GERMANY*

Introduction: 10-20 % of children with idiopathic nephrotic syndrome (NS) are steroid-resistant (SRNS) and develop end-stage renal disease. Mutations in a number of genes highly expressed in podocytes have been identified causing SRNS.

Material and methods: We established NGS for genetic testing of SRNS patients. NGS was performed on DNA samples of 31 patients, who already underwent DNA analysis by the Sanger sequencing method following the mutational algorithm of the Podonet network (www.podonet.org). These patients were reexamined by NGS in all hitherto known SRNS relevant genes (ACTN4, CD2AP, COQ6, INF2, LAMB2, NPHS1, NPHS2, PLCE1, TRPC6, WT1) using the Roche 454 technology. In 18/31 patients pathogenic mutations had been already detected by Sanger sequencing. 13/31 patients did not show mutations in the examined genes (Sanger detection rate 58 %).

Results: With NGS, we could confirm the mutations in 16/18 genetically characterized patients. However, two mutations that localize to homopolymer regions were missed by NGS. In 4/13 (31 %) so far negative patients new mutations in one of the following genes were now identified by NGS: CD2AP (1 patient), INF2 (1 patient), and NPHS1 (2 patients). These genes had not been analyzed by Sanger sequencing because they were not included in the mutation algorithm of the original approach. Interestingly, the INF2 mutation localizes to exon 6 within the DID domain of the INF2 protein. Altogether, causative mutations were identified in 20/31 patients by NGS (detection rate 65 %).

Conclusions: We conclude that NGS is a useful tool for rapid and reliable genetic testing of SRNS patients. However, mutations within homopolymer regions can be missed by the Roche 454 technology. Therefore, these critical regions should be reanalyzed by Sanger sequencing. Overall, the mutation detection rate in SRNS patients is high amounting to 65 % in the present pilot study.

P160 - Mn-SOD Ala–9Val gene polymorphisms in childhood nephrotic syndrome

OZLEM OZSOY[1], FARUK OKTEM[2], AYÇA ESRA KUYBULU[1], RAMAZAN YILMAZ[1], HARUN PERU[1]

[1]*SÜLEYMAN DEMIREL UNIVERSITY FACULTY OF MEDICINE*

[2]*BEZMİ ALEM VAKIF UNIVERSITY FACULTY OF MEDICINE*

Introduction: The aim of this study is to evaluate the association between the clinical characteristics and Mn-SOD- Ala-9 Val genotypes of Turkish children with idiopathic nephrotic syndrome (INS).

Material and methods: The study is consisted of three groups: steroid resistant nephrotic syndrome group (SRNS) (n=12), steroid sensitive nephrotic syndrome group (SSNS) (n=51), and healhy voluntary controls (n=72). Patients with SRNS and SSNS further classified into two groups: patients with well prognosis and bad prognosis; patients with less frequent relapses and more frequent relapses, respectively. Mn-SOD Ala-9 V gene polymorphisms of patients and controls were evaluated.

Results: Most frequent genotype was Mn-SOD VV homozygotes in INS and it was comparable with controls (44 % vs 31 %, OR: 1.7, $p>0.05$). Frequency of VV genotype was similar between males and females also (52.5 % vs 30.4 %, OR: 3.9, $p>0.05$). However frequency of V allels was more common in male patients than female patients (70 % vs 52 %, $p<0.05$). Frequency of VV genotypes of male INS cases were higher than male controls (52 % vs 27 %, $p<0.05$). There was no difference in the frequency of VV genotype between children with SRNS and controls (OR: 2,9, $p>0,05$). The difference between SRNS patients with bad prognosis and control group in view of frequency of VV genotype is nearly significant (32 % vs 80 %, OR: 8.52, p>

0.05). The distribution of genotype and allelle frequency of Mn-SOD genotype between SSNS and controls are not different. The frequency of VV genotype is similar between less and more frequent relapsers.
Conclusions: In conclusion Mn-SOD Ala-9 V gene polymorphisms have not any direct correlation with INS. However, VV genotype may be a risk factor for males with the disease and the development of progressive renal impairment in children with INS; however, further studies are needed to confirm this result.

P161 - HYDATID CYST DISEASE PRESENTING WITH NEPHROTIC SYNDROME IN A CHILD

HULYA NALCACIOGLU[1], DEMET TEKCAN[1], ATAKAN COMBA[2], GURKAN GENC[1], GONUL CALTEPE[2], OZAN OZKAYA[1], AYHAN GAZI KALAYCI[2]
[1]*ONDOKUZ MAYIS UNIVERSITY FACULTY OF MEDICINE, DEPARTMENT OF PEDIATRIC NEPHROLOGY*
[2]*ONDOKUZ MAYIS UNIVERSITY FACULTY OF MEDICINE, DEPARTMENT OF PEDIATRIC GASTROENTEROLOGY, HEPATOLOGY AND NUTRITION*

Introduction: Hydatid disease is a parasitic infection caused by a parasite, echinococcus granulosus, characterized by cystic lesion in the liver, lungs and rarely in other parts of the body. Secondary renal involvement such as minimal change lesion, Ig A and mesangiocapillary glomerulonephritis as a response to hepatic hydatidosis was rarely reported.
Material and methods: We report a case who presented with nephrotic syndrome with a hepatic hydatid cyst that eventually responded to albendazol treatment.
Results: A 14-year-old boy was admitted to the hospital with the complaint of edema for 7 days. His physical examination was normal except periorbital edema. Proteinuria, Hypoalbuminemia, hypertriglyceridemia, hypercholesterolemia was found in laboratory examination. He was excreting 183 mg/m²/h of urinary protein in 24 hours. Nephrotic syndrome was diagnosed and during the work-up for the biopsy of the nephrotic syndrome a cystic mass in the right upper abdomen was found by ultrasonography, consistent with echinococcal disease was discovered. The serum ELISA for Echinococcus was positive. Renal biopsy revealed diffuse proliferative glomerulonephritis. Treatment was started with antiechinococcal drug albendazole. One mouth after the albendazol treatment, laboratory findings returned to normal and excessive proteinuria disappeared.
Conclusions: The hydatid cyst should be considered in the etiology of nephrotic syndrome especially in the endemic areas. Treatment with albendazole induced complete remission of the nephrotic syndrome, suggesting an etiopathogenic role for a hydatid antigen in the development of an immune-mediated glomerulonephritis.

P162 - Effect of Levamisole in Children with Steroid-Dependent Nephrotic Syndrome (SDNS)

ELZBIETA KUZMA-MROCZKOWSKA, MALGORZATA PANCZYK-TOMASZEWSKA, PIOTR SKRZYPCZYK, MARIA ROSZKOWSKA-BLAIM
DEPARTMENT OF PEDIATRICS AND NEPHROLOGY, MEDICAL UNIVERSITY OF WARSAW

Introduction: Levamisole is a therapeutic option in SDNS in children but results of therapy are inconsistent.
Material and methods: The aim of the study was to assess the results of levamisole treatment in children with SDNS. The study group included 72 children with NS (31 girls, 41 boys) aged from 2 to 15.6 mean 6.4±3.0 years. Age of NS onset - form 0.9 to 10.7 mean 3.2±2.0 years, duration of disease from 0.5 to 11 mean 3.2±2.8 years, number of relapses from 2 to 17. Renal biopsy showed minimal change disease - 16, diffuse mesangial proliferation - 28 patients; in 28 patients renal biopsy was not performed. Patients were divided into 2 groups according to prednisone tapering during levamisole therapy: group I: 27 children with slow tapering of prednisone (0.1-0.2 mg/kg/month); group II: 45 children with fast tapering of prednisone (0.1-0.2 mg/kg/10 days). Levamisole was administered orally 2.5 mg/kg/48 h during first month, then two times a week the same dose from 0.5 to 31 mean 12.0±8.1 months. The clinical outcome analysis included absence of proteinuria and adverse events of the treatment.
Results: Time without proteinuria was significantly lower in group I compared to group II (group I: from 0.5 to 10, median 2.5 months, group II: from 1 to 27, median 7 months, $p<0.01$) and number of relapses during levamisole therapy was significantly higher in group I compared to group II (group I: from 0 to 9, median 2; group II: from 0 to 4, median 1, $p<0.0005$). Adverse events were found in 16 (22.2 %) patients: allergic rash in 6, joint pains in 2, abdominal pains in 3, hypertransaminasemia in 3, leukopenia in 1, thrombocytopenia in 1 patient.
Conclusions: 1. Levamisole seems to be effective in prolonging maintenance of remission in children with SDNS. 2. Better results are observed in patients with fast prednisone tapering.

P163 - Regressive nephrotic syndrome (NS) in 3 children with nephrin mutation

JULIEN HOGAN[1], RAPHAELLE CAMPAIT[2], FRANCISCA YANG[3], JEAN-PIERRE BENAMENYO[4], JEROME PASCHE[3], DALIA REKLAITYTE[1], CORINNE ANTIGNAC[5], VERONIQUE BAUDOUIN[1]
[1]*PEDIATRIC NEPHROLOGY, HOPITAL ROBERT DEBRé, APHP, PARIS, FRANCE*
[2]*DEPARTMENT OF GENETICS, NECKER HOSPITAL, APHP, PARIS, FRANCE*

[3]PEDIATRIC DEPARTMENT, CENTRE HOSPITALIER TERRITORIAL, PAPEETE, FRENCH POLYNESIA
[4]PEDIATRIC UNIT, HOPITAL D'ENFANTS, MARGENCY, FRANCE
[5]INSERM U574, UNIVERSITé PARIS DESCARTES, PARIS, FRANCE

Introduction: Congenital NS secondary to nephrin mutation is usually a severe and life threatening condition which motivates a bilateral nephrectomy then transplantation when children reach a sufficient size.
Material and methods: We report 3 children from French Polynesia with the same NPHS1 mutation and a favorable outcome.
Results: For these children, the diagnosis was made at 3 weeks, 1 and 5 months respectively. Renal biopsy was performed in only one patient diagnosed at 5 months. They all presented severe NS. Two children received the standard conservative treatment with high dose albumine infusions (4 g/kg/d) and a combination of angiotensin converting enzyme (ACE) inhibitors and indomethacin, whereas the third one, diagnosed later received only ACE inhibitors. Two of them presented several episodes of bacterial and viral infections during the first 6 months. However, in these 3 patients, after a few months, we observed a decreased proteinuria and an increase of serum albumin, which allowed us to stop albumin infusion at age of 5 and 8 months respectively. At last follow-up, patients are 16 months, 3 and 7 years old, with normal growth status and the actual treatment is ACE inhibitor. They all have a normal creatininemia and an albuminemia above 25 g/L while proteinuria/creatiniuria ratio is 0.1, 0.22 and 0.04 g/mmol respectively. In these patients, genetic analysis found a missense mutation in the homozygous state in exon 6 of NPHS1 (c.2131 C>A) resulting in a serine for arginine substitution in the extracellular domain of nephrin (p.Arg711Ser). The identification of the same mutation in the 3 children originating all from French Polynesia suggests a founder effect.
Conclusions: This report shows that a conservative treatment procedure must be considered in patients with NS secondary to non Finish NPHS1 mutations, as milder clinical forms with spontaneous favorable outcome could occur.

P164 - Are serum vitamin D levels related to vaccine response in idiopathic nephrotic syndrome patients?

MARIE-EMILIE DOURTHE, JULIEN HOGAN, BILAL AOUN, TIM ULINSKI
PEDIATRIC NEPHROLOGY UNIT, TROUSSEAU HOSPITAL, APHP, PARIS

Introduction: Vitamin D serum levels have been shown to impact immune reaction by multiple pathophysiological mechanisms. We have previously reported that pediatric idiopathic nephrotic syndrome patients have a normal serological response after one 23-valent pneumococcal vaccine injection at disease onset despite steroid therapy and nephrotic proteinuria. However, there was a huge variability ranging from 2.5 – 100-fold increase of pneumococcal antibody levels 1 month post vaccine. We tested the hypothesis that vitamin D serum levels are related to vaccine response.
Material and methods: We measured 25OHD and 1,25 (OH)2D serum levels in 25 serum samples from patients one month post vaccine. All patients had negative proteinuria and normal serum albumin levels at the time of sampling.
Results: Patients' age was 7.3±3.2 yrs at the time of 23-valent pneumococcal vaccine. 25OHD levels were decreased 7 (3–35) ng/ml (normal 30–74) and 1,25 (OH)2D levels were 41 (13–175) pg/ml (normal 25–76). There was a strong correlation between 25OHD and 1,25OH2D levels ($p<0.0001$), but we did not find any correlation between antipneumococcal antibody levels at one, three and six months post vaccine with 25OHD and 1,25OH2D serum levels.
Conclusions: This pilot study did not show any relation between serological vaccine response and 25OHD and 1,25OH2D serum levels in children with idiopathic nephrotic syndrome.

P165 - Long term outcome in children with idiopathic focal segmental glomerulosclerosis

ADITI SINHA, SIDDHARTH JAIN, SONIA SHARMA, AMIT DINDA, PANKAJ HARI, ARVIND BAGGA
ALL INDIA INSTITUTE OF MEDICAL SCIENCES, NEW DELHI, INDIA

Introduction: Information on long-term management and outcome of focal segmental glomerulosclerosis (FSGS) in children is limited. We report disease course & therapies in children with FSGS evaluated at a single center over 1998–2010.
Material and methods: Clinic records were reviewed to include patients 1-18-yr-old, with steroid resistant or steroid dependent nephrotic syndrome (NS), idiopathic FSGS and followed for ≥2-yr. Therapies included oral or IV corticosteroids or cyclophosphamide (CP), calcineurin inhibitors (CNI), and ACE inhibitors; response was categorized as complete or partial remission or non response. Hazard ratios with 95 % confidence interval (95%CI) following Cox regression assessed the impact of baseline variables and therapies on adverse outcome, defined as chronic kidney disease (CKD) stage 4–5 (estimated GFR <30 mL/min/1.73 sq.m).
Results: Mean age at onset of NS for 140 patients (42 girls) was 60.9±42.5 months. 57 (40.7 %) and 65 (46.4 %)

patients showed initial or late steroid resistance, respectively; 15 and 3 underwent biopsy for steroid dependence or renal dysfunction. Biopsy, performed 22±29.5 months from onset, was classified as FSGS not otherwise specified (55.6 %), hilar (34.4 %), collapsing (7.5 %), and cellular & tip variant in 1.3 % each. Therapy was associated with complete/partial remission in 69.9 % after CNIs (n=73) and 48.4 % after IVCP (n=42). At 88.6±59.7 mo, outcomes included sustained remission (28.7 %), steroid sensitive relapses (21.3 %), non-nephrotic proteinuria (15.6 %), non response (17.2 %), and CKD 4–5 (17.3 %). Survival without adverse outcome with late resistance was 100 % at 1- and 5-yr, 87.7 % at 8-yr & 80.9 % at 10-yr; corresponding rates for initial resistance were 93.4 %, 72.0 %, 64 % & 64 % respectively. Predictors of adverse outcome included initial resistance [HR 3.23; 95%CI 1.18-8.87; P=0.022] and non-response to CNI [12.1; 3.19-45.96; P<0.001] or IVCP [P<0.001].

Conclusions: Children with FSGS have satisfactory responses to immunsuppression, and the majority do not progress over 10-yr. The presence of initial steroid resistance and non-response to therapy predict adverse outcomes.

P166 - DISCREPANCY BETWEEN GFR ESTIMATED BY CREATININE CLEARANCE AND CYSTATIN C IN CHILDREN WITH NEPHROTIC SYNDROME

GIANLUIGI ARDISSINO[1], FRANCESCA TEL[1], SARA TESTA[1], ALBERTINO TARTARA[2], TIZIANA CHIONNE[2]

[1]*CENTRO PER LO STUDIO E LA CURA DELLA SINDROME EMOLITICO-UREMICA - FONDAZIONE IRCCS CA' GRANDA, OSPEDALE MAGGIORE POLICLINICO*

[2]*M.A.D. ANALISI MEDICHE S.R.L. - VOGHERA (PV)*

Introduction: It has been reported that serum creatinine overestimates renal function in children with nephrotic syndrome but the extent of this overestimation and its impact on the clinical management is poorly documented particularly when renal insufficiency coexists. The present study is aimed at analyzing the difference between GFR estimated by serum creatinine and by Cystatin C in children with nephrotic syndrome including patients with impaired renal function.

Material and methods: Eight patients (6 males - mean age of 9.7 years) with nephrotic syndrome (congenital minimal change, FSGS and chronic glomerulonephritis), with different level of renal function (4 patients with CKD II-V), of proteinuria (median uPr/uCr ratio of 8.7; range 0.6-38) and of plasma albumin level (median 1.85; range 0.6-2.7), were tested for serum creatinine and Cystatin C and their GFR estimated.

Results: The mean discrepancy between creatinine clearance and GFR as calculated with Cystatine C was +63 %. This discrepancy has an higher Person's correlation coefficient with proteinuria (r: 0.7) than with albumin plasma level (r: 0.4).

Conclusions: In patients with nephrotic syndrome, creatinine clearance heavily overestimates GFR. Such important overestimation if not taken into serious consideration may have dangerous consequences when nephrotoxic drugs are prescribed or when indications to renal replacement therapy are considered

P167 - Sequencing analysis of genes SOCS3 and SOCS5 in steroid-resistant nephrotic syndrome children

DANUTA OSTALSKA-NOWICKA

POZNAN UNIVERSITY OF MEDICAL SCIENCE

Introduction: Structural and functional abnormalities in the glomerular filtration barrier result in proteinuria and are responsible for idiopathic nephrotic syndrome (INS). There is strong evidence in the role of the immune system in pathophysiology of INS. Recently, also the role of genetic factor have been considered. Glucocorticoids (GCs) are effective drugs in most cases of INS and steroid responsiveness is the major determinant of prognosis. Approximately 10-15 % patients have partial or no response to GC therapy. SSNS (steroid sensitive nephrotic syndrome) patients are usually of favorable prognosis, whereas 50 % of children with SRNS (steroid resistant nephrotic syndrome) progress to end-stage renal failure. There is evidence that in SSNS/SRNS group of patients several elements of the Jak/Stat signaling pathway are being excited. After 6-week glucocorticoid treatment expression of all analyzed elements in the SSNS group is back to the level compared to the control group, whereas in the SRNS group there are still high levels of only two elements – SOCS3 and SOCS5 transcripts, coding for suppressor proteins of the Jak/Stat pathway. Increased transcription of these genes correlated with proteinuria.

Material and methods: Sequencing analysis of coding regions of genes SOCS3 and SOCS5 was conducted in study group 1 counting 40 SRNS patients, study group 2 counting 30 SSNS patients and control group of 30 healthy individuals. All results were establish in terms of Hardy-Weinberg Equilibrium. Odds ratio value (OR) was based on frequencies of alleles and genotypes and SNP (single nucleotide polymorphism) analysis was provided with gene structure based on Haploview software.

Results: The results showed no significant differences in OR value among the three groups.

Conclusions: The aim of the study was to analyze genetic basis of steroid resistance in idiopathic nephrotic syndrome in children. SOCS5 gene structure showed weaker linkage

between heterozygous SNPs in SRNS group than in SSNS and control group.

P168 - Cyclosporine dependence in nephrotic syndrome.

ELENBERG EWA
BAYLOR COLLEGE OF MEDICINE

Introduction: Cyclosporin A (CyA) is used in the treatment of patients (pts) with frequently relapsing or steroid-dependent nephrotic syndrome (NS). In pts who are responsive to CyA therapy, there is high relapse rate following CyA withdrawal. Therefore, prolonged treatment with CyA is needed, which increases the risk of nephrotoxicity. Commonly CyA therapy is continued for several years (y) and then slowly weaned. There are some patients though, who become CyA dependent and relapse with attempts to wean.
Material and methods: This is a case report of 3 NS pts who have been treated with CyA for 15–16 y, with minimal side effects
Results: Three pts developed new onset of NS at young age, all developed steroid resistance and were started on CyA at age 2 - 4y. All had multiple relapses with weaning attempts, never off CyA. All maintain stable renal function and respond to steroid therapy with relapses. All pts had FSGS on initial biopsy (Bx), on f/up Bx no CyA toxicity and no FSGS in 2 pts and mild FSGS in1pt. Pt #1, 16y old male, on CyA since 1997. Initial Bx in 1997 revealed FSGS, f/up Bx in 2008 with global sclerosis (3/11) and mild interstitial fibrosis. Currently in remission on Sandimmune 3 mg/kg/day, serum creatinine (scr) 0.6 mg/dl. Pt #2, 19y old female, on CyA since 1996, multiple relapse with wean attempts, 2 relapses with AKI (scr 1.7 mg/dl). Initial Bx 1994 mild FSGS, f/up Bx in 2004 FSGS (2/12), global sclerosis (4/12), focal tubular atrophy and interstitial fibrosis. Currently on Sandimmune 2.5 mg/kg/day, scr 0.9 mg/dl. Pt #3, 17y male, on CyA since 1996. Initial Bx in 1998 revealed FSGS, f/up Bx in 2009: 40 % global sclerosis (11/25), focal tubular atrophy and mild interstitial fibrosis, no FSGS. Currently on Neoral 3 mg/kg/day, scr 0.8 mg/dl.
Conclusions: All pts were initially dgn with FSGS and steroid resistance. CyA therapy lead to resolution of FSGS in 2 pts and presence of minimal FSGS in 1 pt, with no CyA toxicity in any. CyA dependence can be seen in pts who start CyA therapy at early age. CyA dose wean should be done very slowly and pts monitored closely. Relapses respond to therapy with prednisone and increased CyA dose. Maintaining pts on small CyA dose for years is safe, allows pts to maintain renal function within normal and no CyA toxicity on Bx.

P169 - Ouantitative mRNA Expression of Podoctye Proteins in Children With Steroid Resistant Nephrotic Syndrome

NİDA DİNÇEL[2], AFİG BERDELİ[1], SEVGİ MİR[2]
[1]*EGE UNIVERSITY MOLECULAR GENETIC*
[2]*EGE UNIVERSITY PEDIATRIC NEPHROLOGY*

Introduction: The recent description of gene defects of the podocyte resulting in hereditary nephrotic syndrome has provided a completely new understanding of the glomerular filter and unrevealed important aspects of the pathogenesis of proteinuric kidney diseases.The aim of this study is to evaluate mRNA expressions of genes encoding proteins that are located in the glomerular filtration barrier(GFB) and to search the relation of these between glomerulosclerosis.
Material and methods: Renal biopsy specimens of 15 steroid resistant nephrotic syndrome patients, were included into the study. mRNA expressions of genes encoding podoplanin(PDPN), dystroglycan(DAG), actinin-4(ACTN-4) and podosin(NPHS2) proteins were evaluated. After isolation of mRNA, expression studies were done by quantitative real time PCR techniques.Levels of mRNA expression were determined according to the internal control:GAPDH.
Results: Renal biopsy findings of 12 patients were FSGS, other 3 were MCNS. We used to MCSN patients as control group,all 3 was without NPHS2 mutation. Only, three patients in FSGS group had mutation.NPHS2 mRNA expression level of FSGS patients was 3 times lower than MCNS patients.Similarly, PDNP mRNA levels was 1 times, ACTN-4, DAG mRNA levels were below 1 times, lower in FSGS patients. The lowest mRNA level was found in patients with NPHS2 mutation(n=3).The highest mRNA level was in MCNS group.Also, among the FSGS group, ACTN-4,DAG and PDNP mRNA expression levels were higher than NPHS2 mRNA levels.
Conclusions: We emphasized that, besides the functional and structural changes, quantitative changes of proteins both lead a localised effect, and affect almost all 3 regions (basal, apical, apicolateral) of podocyte causes proteinuria via dysfunctioning of GFB especially in FSGS.

P170 - The analysis of selected gene LRP5 single nucleotide polymorphisms as the osteoporosis risk factors in children with idiopathic nephrotic syndrome treated with glucocorticoids.

MAGDALENA SILSKA, DANUTA OSTALSKA-NOWICKA, JACEK ZACHWIEJA
DEPARTMENT OF PEDIATRIC NEPHROLOGY, POZNAN UNIVERSITY OF MEDICAL SCIENCE, SZPITALNA 27/33 STR. 60–572 POZNAN, POLAND

Introduction: Glucocorticoids, standard therapy in idiopathic nephrotic syndrome, are important risk factors for

osteoporosis. Decrease in bone mineral concentration and increased risk for pathological fractures are caused by direct division of steroids at the cellular level by inhibiting the replication of osteoblasts and apoptosis stimulation. Also proven its effects on the inhibition of collagen I synthesis. LRP5 is one of the Wnt signaling pathway proteins coreceptors involved through the RANK-RANKL in regulation of the osteoblasts function. LRP5 is included to the osteoporosis phenotype genes group and its selected single nucleotide polymorphisms can be responsible for bone mass density (BMD) decrease in patients with glucocorticoid therapy. The aim of our study was to analyze twelve single nucleotide polymorphisms (SNIP) of gene LRP5 potentially associated with osteoporosis risk in children with routine steroidotherapy in the course of the idiopathic nephrotic syndrome.

Material and methods: The study group was composed of 29 children with idiopathic nephrotic syndrome under the age of twelve years old, 13 with osteoporosis and 17 with normal bone mass density. The control group consists of 102 healthy individuals at the same age not treated with glucocorticoids. Odds ratio value (OR) was based on frequencies of selected twelve single nucleotide polymorphisms (SNP) potentially associated with osteoporosis risk in analysis of coding regions of gene LRP5.

Results: The results showed not significant differences in OR value among the three groups. However it was found the differences in the gene structure. Based on Gabriel algorithm we proved that the degree of interdependence between pairs of SNP in children with nephrotic syndrome and osteoporosis was higher than in the other two groups. What's more the SNPs interdependence was the lowest in the group of children with nephrotic syndrome and without osteoporosis.

Conclusions: We suggest it is likely a correlation between the selected SNPs and the risk of osteoporosis.

P171 - Changing pattern in the steroid response of idopathic nephrotic syndrome in children

SERPIL SANCAK[1], LALE SEVER[2], SALIM ÇALIŞKAN[2], NUR CANPOLAT[2], MEHMET TAŞDEMIR[2], NIL ARISOY[2]

[1]*ISTANBUL UNIVERSITY, CERRAHPAŞA MEDICAL FACULTY, DEPARTMENT OF PEDIATRICS*

[2]*ISTANBUL UNIVERSITY, CERRAHPAŞA MEDICAL FACULTY, DEPARTMENT OF PEDIATRIC NEPHROLOGY*

Introduction: Recently, reports from many countries underline an increasing incidence of focal segmental glomerulosclerosis and steroid resistance in pediatric patients with nephrotic syndrome (NS). Previously, we did not find any difference between two groups of patients in two consecutive periods (1979–1989 and 1990–2000) regarding steroid response and histopathological findings. The present study aims to investigate our new patients for characteristics at onset of nephrotic syndrome, response to steroid therapy and biopsy findings, and compare the results with our historical data.

Material and methods: Charts of 176 patients with idiopathic NS, who were admitted to our center between May 2001 and May 2011, were retrospectively analyzed. The inclusion criteria comprised: -New-onset (and untreated) NS; -Children older than 1 year of age; - Minimum 6 months' of follow-up; Overall 46 patients fulfilled these criteria (new patient group). Demographic features, blood pressure measurements and biochemical findings during the first hospital admission, and also response to steroids as well as histopathological findings in those who were performed biopsies were recorded. Findings of new patient group were compared with the data of 159 patients (historical control group) who were studied with similar inclusion criteria and followed up between 1979–2000.

Results: Gender distribution was similar between the two groups. Age at onset was higher (5.7±4.4 vs 3.9±2.7 years, $p=0.01$); hypertension was more frequent (18/46 vs. 33/159, $P=0.001$) and the incidence of steroid resistance was higher (8/46 vs. 10/159, $p=0.03$) in the new patients as compared to historical controls. Considering the patients who were performed biopsies, there was not any significant difference in the distribution of histopathological diagnosis between the groups.

Conclusions: Relative increase in steroid resistance and higher mean of age at the onset of the disease were noted during the last decade in patients with NS as compared to the historical controls.

P172 - Early onset and intermediate progression of steroid-resistant nephrotic syndrome associated with non-neutral p.R229Q polymorphism and novel c.1032delT podocin mutation

IRENA BALASZ-CHMIELEWSKA[1], HALINA BORZECKA[2], DOROTA DROZDZ[3], EWA GACKA[4], AGNIESZKA FIRSZT-ADAMCZYK[5], TOMASZ JARMOLINSKI[6], JOANNA KSIAZEK[7], ELZBIETA KUZMA-MROCZKOWSKA[8], ANNA MEDYNSKA[9], MAGDALENA SILSKA[10], MARIA SZCZEPANSKA[11], MARCIN TKACZYK[12], ANNA WASILEWSKA[13], ALEKSANDRA ZUROWSKA[1]

[1]*DEPARTMENT OF PAEDIATRIC NEPHROLOGY AND HYPERTENSION, MEDICAL UNIVERSITY OF GDANSK*

[2]*DEPARTMENT OF PEDIATRIC NEPHROLOGY, MEDICAL UNIVERSITY OF LUBLIN*

[3]*PAEDIATRIC NEPHROLOGY AND DIALYSIS UNIT, JAGIELLONIAN UNIVERSITY MEDICAL COLLEGE, KRAKOW*

[4]DEPARTMENT OF PEDIATRIC NEPHROLOGY, ZABRZE
[5]DEPARTMENT OF PEDIATRICS AND NEPHROLOGY, TORUN
[6]DEPARTMENT OF PEDIATRICS, NEPHROLOGY AND TOXICOLOGY, DISTRICT CHILDREN'S HOSPITAL, SZCZECIN
[7]DEPARTMENT OF NEPHROLOGY AND HYPERTENSION, THE CHILDRENS' MEMORIAL HEALTH INSTITUTE, WARSAW
[8]DEPARTMENT OF PEDIATRICS AND NEPHROLOGY, MEDICAL UNIVERSITY OF WARSAW
[9]DEPARTMENT OF PEDIATRIC NEPHROLOGY, WROCLAW MEDICAL UNIVERSITY, WROCLAW
[10]DEPARTMENT OF PEDIATRIC NEPHROLOGY, POZNAN UNIVERSITY OF MEDICAL SCIENCE, POZNAN
[11]DIALYSIS UNIT, SILESIAN MEDICAL UNIVERSITY, ZABRZE
[12]NEPHROLOGY DIVISION, POLISH MOTHER'S MEMORIAL HOSPITAL RESEARCH INSTITUTE, LODZ
[13]DEPARTAMENT OF PAEDIATRICS AND NEPHROLOGY MEDICAL UNIVERSITY OF BIALYSTOK, BIALYSTOK

Introduction: Mutations in the gene encoding podocin (NPHS2) cause autosomal recessive SRNS. Children with truncating or homozygous R138Q mutations manifest with early onset disease and ESRD (end-stage renal disease) in 1st decade of life. Later onset in children and adult-onset SRNS have been reported if a podocin mutation occurs in a compound heterozygous state with the R229Q genetic variant.

Material and methods: Molecular analysis of NPHS2 was performed in 115 SRNS children recruited from 12 paediatric nephrology referral centres in Poland. 23 patients carrying podocin mutations were identified. The most frequent pathogenic genotype (11/23) was c.1032delT mutation with non-neutral p.R229Q polymorphism. The previously undescribed phenotype of this compound heterozygous podocin mutation is presented.

Results: The 11 children - compound heterozygotes for c.1032delT and p.R229Q came from 7 families. In 8/11 children the disease onset was below 6 yrs of age; in two patients in the 1st, in a further five during the 2nd year of life. Mean age at onset was 4.5 yrs (1 month to 15 yrs). 10/11 patients had received immunosuppressive treatment but none achieved remission. Six children progressed to ESRD in the 2nd decade life (mean age 14.5 yrs), a mean 12,6 yrs from symptom onset. Recurrence of NS post transplantation was not observed.

Conclusions: An early onset of disease was observed in children with c.1032delT and p.R229Q in contrast to previous reports of compound heterozygotes carrying different pathogenic NPHS2 mutations and R229Q genetic variant. Disease progression in children with c.1032delT and p.R229Q is intermediate between that reported for homozygotes with 2 mutations and for previously reported different compound heterozygotes. Specific allele combinations of podocin mutations may be important for both accurate classification and prognosis.

P173 - Mycophenolate mofetil therapy in children with steroid-dependant

ANNA MOCZULSKA, JOANNA KWINTA-RYBICKA, JOANNA WIśNIOWSKA, AGNIESZKA SZEWCZYK, EWA WIERZCHOWSKA-SLOWIACZEK, IWONA OGAREK, KATARZYNA WILKOSZ, JACEK A. PIETRZYK
DPT.OF PEDIATR.NEPHROL. JUMC KRAKOW

Introduction: Steroid-dependant nephrotic syndrome (SDNS) requires long term treatment with high risk of adverse effects. The aim of the study was to evaluate efficacy of mycophenolate mofetil (MMF) treatment in children with SDNS.

Material and methods: The study group consisted of 44 children (15 girls and 29 boys), treated with MMF for SDNS in years 2004–2012. The disease occurred at the age of 2,86 ±2,77 yrs (9 mo to 12 yrs) and MMF was introduced after 5,84±3,85 yrs (0,3 - 15) of therapy with the initial dosage of 984±195 mg/m² BSA/day (486–1283). In 7 pts MMF was the first choice medication. MMF treatment was monitored over period of 26,24±18,44 mo (range 4–86).

Results: Patients were monitored for relapses and remissions of NS one year before and during entire MMF therapy. Number of relapses of NS decreased from 2,45±1,41 (0–5) in preceding year, down to 1,55±1,27 (0–4) in the first year after introducing MMF(p=0,042). The mean length of remission period expressed in months increased from 4,15± 3,58 (0–12) up to 6,29±4,53 (0–12) respectively (p= 0,0081). Evaluation of eGFR (according to Schwartz et al. 2009) alternations before introducing MMF and during treatment showed significant increase from 92,84±27,84 to 109,34±22,26 ml/min/1,73 m² after first 12 months of MMF therapy (p=0,0005). The mean serum albumin concentration raised from 37,78±7,13 g/l up to 41,93±4,9 g/l, respectively (p=0,002). During MMF treatment it was possible to reduce Prednisone dosages from 0,33±0,3 mg/kg/day (0–1,21) to 0,15±0,16 mg/kg/day (0–0,5) at 12th month (p= 0,005). Similar result was observed for CsA with dosage reduction from mean 3,28±1,3 mg/kg/day (0,55-5,92) to 1,83±1,8 mg/kg/day (0–5,19) (p=0,007). MMF treatment was discontinued in 6 patients (13,6 %) due to its inefficacy (n=5) or side effects (n=1). In 2 pts treatment was finished after achieving remission after 11 and 21 months.

Conclusions: Introduction of MMF therapy in children with SDNS allows for dosage reduction of other medications such as GCS and CsA, and while being well tolerated, leads to clinical and biochemical improvement in most of the cases. The risk of fall of eGFR according to primary renal disease may be postponed.

P174 - EARLY DETECTION OF LEFT VENTRICULAR DYSFUNCTION BY TISSUE DOPPLER ECHOCARDIOGRAPHY IN CHILDREN WITH CHRONIC KIDNEY DISEASE

YLVA TRANAEUS LINDBLAD[3], JONAS AXELSSON[1], RITA BALZANO[2], GEORGIOS VAVILIS[2], GIANNI CELSI[3], MILAN CHROMEK[3], PETER BARANY[1]
[1]*DIVISION OF RENAL MEDICINE, CLINTEC, KAROLINSKA INSTITUTET*
[2]*DEPARTMENT OF CLINICAL PHYSIOLOGY, KAROLINSKA UNIVERSITY HOSPITAL HUDDINGE*
[3]*DIVISION OF PEDIATRIC MEDICINE, CLINTEC, KAROLINSKA INSTITUTET*

Introduction: Myocardial dysfunction is common in pediatric chronic kidney disease (CKD). It appears early in the disease progression and persists after renal transplantation. Left ventricular (LV) function has previously been studied by conventional pulse-wave Doppler echocardiography (cPWD), while data from analysis with new tissue Doppler velocity imaging (TDI) are sparse. We studied LV structure and function in pediatric CKD patients comparing cPWD with TDI, and related the data to carotid intima media thickness (cIMT) and known cardiovascular risk factors.
Material and methods: The study included 34 children/adolescents with CKD stages 2–5 (all pre-dialysis), 44 renal transplant patients and a control group of 19 children with normal renal function. The mean age of the study population was 11.4 (range 0.8-18.8) years and 59.8 % were males.
Results: While there was no difference in LV systolic function or cIMT between patients and controls, both patient groups had significantly lower LV diastolic function. The most sensitive parameters were the ratio between early and late diastolic peak filling velocities, TDI E′/A′ and estimate of the filling pressure of the left ventricle cPWD E/TDI E′. Specifically, children with CKD 2–5 had TDI E′/A′ 2.77 (range 1.8-5.8) and transplanted patients 2.4 (range 1.3-4.2) compared to 4.6 (range 2.1-6.0) in the control group ($p< 0.0005$). In a stepwise linear regression analysis high diastolic blood pressure, young age, increased inflammation markers in blood and a low GFR were independent predictors of worsened LV diastolic function.
Conclusions: Our study shows that children with CKD have significantly deteriorated LV diastolic function that persists after renal transplantation. TDI is a more sensitive tool than cPWD in assessing early myocardial dysfunction. Our data advocate preventive measures such as rigorous blood pressure control in further studies.

P175 - ANTHROPOMETRIC MEASURES AND BLOOD PRESSION IN ADOLESCENCE

TERESA PAPALIA, ROSITA GRECO, AGATA MOLLICA, DANILO LOFARO, RENZO BONOFIGLIO
COSENZA HOSPITAL

Introduction: The purpose of this study is to examine wether BMI, WC, WHR, WHtR were related to Blood Pressure (BP) among South Italian schoolchildren.
Material and methods: A total of 872 italian students were examined between 2007 and 2010. The adolescents were enrolled on a voluntary basis and the children's parents gave their informed written consent. Weight, height, BP, WC were measured, BMI, WHR and WHtR were calculated. Based on percentiles of BMI, the subjects were classified as underweight, normalweight, overweight and obese. The students with BP> 95th percentile were considered as hypertensive. Central adiposity was defined as WC >75th or WHR of ≥0.90 in boys and ≥0,85 in girls and abdominal obesity WHtR ≥0.5.
Results: 16.8 % were obese, 31.4 % with WC>75th percentile, 20.6 % with a WHR higher than the WHO cut-off values and 36.2 % with WHtR>0.5. 7.9 % showed high-BP. Logistic regression showed a strong correlation between BMI and high-BP (OR 1.028, $p<0.0001$), between WC and high-BP (OR 1.029, $p<0.0001$). Also WHtR (OR 2.888, $p<0.0001$) and WHR (OR 1.951, $p=0.001$) correlated with high-BP. In the male subgroup all the variables considered showed a good capability to predict high-BP, in particular BMI (AUC 0.830, 0.74-0.92; $p<0.0001$) and WHR (AUC 0.804, 0.72-0.88). In the females only WC (OR 2.790, $p=0.022$) and WHtR (OR 1.923, $p<0.05$) were able to predict "Hypertension".
Conclusions: In this study we found in male and female a different correlation among BMI, WHR and BP. It's probably associated with the different sex hormones status during the transition through puberty. WC and WHtR could be valid indicators of high BP in childhood and the easily measurable anthropometric indices. However further studies are required to confirm our data.

P176 - Markers of systemic inflammation in children with hyperuricemia

ANNA WASILEWSKA, EDYTA TENDERENDA, KATARZYNA TARANTA- JANUSZ, JUSTYNA STYPUŁKOWSKA
DEPARTMENT OF PEDIATRICS AND NEPHROLOGY, MEDICAL UNIVERSITY OF BIAŁYSTOK, POLAND

Introduction: The purpose of the study was to investigate serum concentrations of the monocyte chemoattractant protein-1 (MCP-1) and high-sensitivity CRP (hs-CRP) in children and adolescents with hyperuricemia.
Material and methods: The study involved 52 hyperuricemic patients mean age 15.53±1.7 yrs. Twenty seven healthy individuals with normal serum uric acid (SUA) level were selected as the control group (C). Serum MCP-1 and hs-CRP were measured in all the participants by enzyme-linked immunosorbant assay (ELISA) and immunonephelometry, respectively.
Results: Hyperuricemic patients showed increased sMCP-1 (median: 69.58 pg/ mL), and hs-CRP (median: 0.53 mg/ L) vs. controls (48.39 pg/ mL, 0.24 mg/ L; respectively) ($p<0.01$). The children with obesity also presented significantly higher levels of sMCP-1 and hs-CRP (median: 81.69 pg/ mL and 1.18 mg/ L, respectively) in comparison with non-obese (median: 59.62 pg/ mL and 0.41 mg/ L, respectively; $p<0.01$). We found that only hs-CRP correlated positively with BMI Z - score ($r=0.33$, $p<0.05$). ROC analyses performed to check the sensitivity and specificity of both examined markers for hyperuricemia, revealed the higher AUC for sMCP-1, however the difference between AUC for sMCP-1 and hs-CRP was not statistically significant ($p>0.05$).
Conclusions: Serum MCP-1 and hs-CRP levels are elevated in hyperuricemic patients, but the role of obesity on inflammation markers needs further investigation.

P177 - Adiponectin, leptin and ghrelin in hypertensive children and adolescents

ANDREJA STELCAR[1], EVGENIJA HOMSAK[2], JERNEJ DOLINSEK[1], NATASA MARCUN VARDA[1]
[1]*UNIVERSITY MEDICAL CENTRE MARIBOR, PEDIATRICS*
[2]*UNIVERSITY MEDICAL CENTRE MARIBOR, DEPARTMENT OF LABORATORY DIAGNOSTICS*

Introduction: Hypertension, one of the important cardiovascular risk-factors, is often associated with overweight and obesity, where disturbed release of hormones including adiponectin, leptin and ghrelin has been found. Previous research has also demonstrated that adipokines influence blood pressure. The aim of our study was to determine the mean values of adiponectin, leptin and ghrelin in our hypertensive children and adolescents, and to find out if there are any differences in these values between the normal weight and overweight hypertensive group of children.
Material and methods: 73 children and adolescents diagnosed with hypertension have been included in our study, 41 with normal weight and 32 with overweight (BMI>90 percentile). There were 28 boys and 45 girls included with mean age of 16.8±3.7 years. Plasma concentrations of leptin and adiponectin were measured in all included hypertensives and ghrelin in 35 of them. The mean values of investigated hormones were determined and comparison between the two groups performed.
Results: The mean value of leptin was 126.9±11.3 pg, of adiponectin 74.6±5.3 ng and of ghrelin 912.0±51.9 pg. Women presented higher mean values of all hormones than men (180.5±17.4 vs. 93.7±8. 6 pg for leptin, 82.3±7.9 vs. 69.8±6.9 ng for adiponectin, 949.9±69.2 vs. 871.9±78.9 ng for ghrelin) but only the difference for leptin was statistically significant. Higher mean values of leptin and ghrelin and lower of adiponectin were found in the overweight group of children compared to normal weight group, but only the differences for leptin ($p=0.00$) and adiponectin ($p=0.01$) and not for ghrelin ($p=0.31$) were statistically significant.
Conclusions: Significant differences in the concentration of adiponectin and leptin were found between normal weight and overweight hypertensive children. The difference in the concentration of ghrelin was not of statistical importance, possibly because of the sample size.

P178 - Hypertension secondary to a renal artery aneurysm treated by ex vivo aneurysm repair and autotransplantation

HITESH PRAJAPATI, AMY MCCALLUM, ERIC FINLAY
LEEDS GENERAL INFIRMARY

Introduction: Hypertension is becoming a common problem in childhood and adolescence. 5-10 % of cases of paediatric hypertension can be attributed to renovascular disease (RVD). Renal artery aneurysms (RAAs) are rare but a recognised cause of hypertension.
Material and methods: We describe the case of a 16-year-old boy presenting with frontal headaches and chest pain. On assessment his blood pressure was noted to be 170/ 110 mmHg. Echocardiography showed left ventricular hypertrophy with no cardiac cause for the hypertension. Renal function, renal ultrasound scan with dopplers, urinary catecholamine screen and fundoscopy were normal. He was treated with two antihypertensive agents. Ambulatory blood pressure monitoring (ABPM) demonstrated a good response with a mean systolic blood pressure of 120-130 mmHg (75th centile for height). Dimercaptosuccinic acid (DMSA) scan showed split right:left function of 63 %:37 % with a slender left kidney and cortical loss at the left upper pole raising the suspicion of fibromuscular disease (FMD). Subsequent magnetic resonance angiography revealed a 1.5 cm saccular aneurysm in the right kidney with normal appearances of the left kidney which was at odds with the DMSA report. Notably there was no FMD in the main arteries and no renal artery stenosis. Digital substration angiography

confirmed a 1.88 cm right sided aneurysm from which 4 significant vessels arose.
Results: Endovascular treatment was not felt to be an option because of risk to renal parenchyma. As our patient was a keen contact sports enthusiast, a surgical vascular opinion was sought. After counseling, our patient underwent a right nephrectomy, ex-vivo repair of the aneurysm and autotransplantation. Histological examination of the aneurysm confirmed FMD. Post operative ABPM demonstrated a mean systolic blood pressure of 107 mmHg on no antihypertensive treatment with resolution of symptoms and LVH.
Conclusions: Hypertension secondary to RAAs poses diagnostic and treatment challenges. We propose that in selected cases invasive surgical intervention of RAAs is a viable treatment option.

P179 - Is late preterm bırth a risk factor for hypertension ?
FATIH GUNAY[1], HULYA BILGEN[2], HARIKA ALPAY[1], IBRAHIM GOKCE[1]
[1]*MARMARA UNIVERSITY MEDICAL FACULTY, DIVISION OF PEDIATRIC NEPHROLOGY*
[2]*MARMARA UNIVERSITY MEDICAL FACULTY, DIVISION OF NEONATOLOGY*

Introduction: Late-preterm birth (34–36 weeks' gestation) is associated with higher rates of neonatal morbidity and mortality and higher healthcare utilization, but its impact on later life is not well known. In this study we aimed to evaluate whether late-preterm birth affects blood pressure, renal function and urinary protein excretion in children later in life.
Material and methods: Sixty-five children aged 7 to 11 years born as late-preterm and 65age and sex matched children born full-term were evaluated with 24-h ambulatory blood pressure monitoring (ABPM), urinary microalbumin excretion (UAE) and glomeruler filtration rate (GFR). All subjects underwent ABPM prospectively. For each gender, daytime, nighttime and 24-hour systolic, diastolic and mean blood pressures (SBP, DBP, and MAP) were transformed to standard deviation scores (SDS). Blood pressure profiles (SBP DBP, and MAP) were considered abnormal when the corresponding SDS values exceeded 1.63. Urinary microalbumin excretion was expressed as mg/day, the value between 30–300 mg/day was defined as microalbuminuria (MA).
Results: The mean ages of late-preterm group and control group were 8,9±2,4 and 9,58±2,2 years respectively. There was no significant difference in mean GFR and MA levels between late-preterm and term children. Two late-preterm children and three full-term controls had hypertension in at least one ABPM parameter (systolic, diastolic or night BPs). Microalbuminuria was detected in five late-preterm cases and five controls. 24-h systolic BP SDS, daytime systolic BP SDS, nighttime systolic BP SDS, nighttime diastolic BP SDS, 24-h MAP BP SDS, daytime MAP BP SDS, and nighttime MAP BP SDS were found to be significantly higher in late-preterm children compared to term children.
Conclusions: We conclude that late-preterm children have higher BP levels, so those children should be followed up carefully by the pediatrician regarding probable hypertension in their future life.

P180 - Ambulatory blood pressure monitoring and cardiac hypertrophy in children with metabolic syndrome
MAHMUT CIVILIBAL[1], BERNA KAMACI BOSTANCI[2], MURAT ELEVLI[2], NILGUN SELCUK DURU[2]
[1]*HASEKI EDUCATIONAL AND RESEARCH HOSPITAL, DEPARTMENT OF PEDIATRIC NEPHROLOGY, ISTANBUL, TURKEY*
[2]*HASEKI EDUCATIONAL AND RESEARCH HOSPITAL, DEPARTMENT OF PEDIATRICS, ISTANBUL, TURKEY*

Introduction: The metabolic syndrome (MS), a cluster of potent risk factors for cardiovascular disease, is composed of insulin resistance, obesity, hypertension and hyperlipidemia. The aim of our study was to investigated the relationships between MS and left ventricular mass index (LVMI) in childhood MS.
Material and methods: This study included 50 children and adolescents with MS aged between 7–18 years. Thirty age- and sex-matched healthy children served as a control group. The diagnosis of MS was made according to the criteria adapted from the World Health Organization. They underwent clinical examination with causal blood pressure (BP) measurements, 24-hour ambulatory blood pressure monitoring (ABPM) and echocardiogram. Patients underwent echocardiography to detect LVH. LVMI was calculated as left ventricular mass/height2.7.
Results: The mean age of MS group was 12.0±3.1 years. The mean value of LVMI was 46.5±11.5 g/m2.7 in the MS group and it was significantly higher than those in the healthy children. The prevalence of severe LVH was 12 % using adult criteria (LVM>51 g/m2.7) and 44 % using pediatric criteria (LVM>95th percentile). The mean daytime systolic BP load (β=0.315, p=0.003) and HOMA-IR (β= 0.368, p=0.006) were found as the independent predictors of LVMI.
Conclusions: LVH occurs commonly in pediatric MS and is associated with systolic hypertension and insulin resistance.

LVMI should be measured routinely for the predicting of cardiovascular risks in these patients

P181 - Severe neonatal hypertesion: diagnosis, management and renal outcome

KVETA BLAHOVA[1], FILIP FENCL[1], VERONIKA STARA[1], JANA DJAKOW[1], TOMAS SEEMAN[1], MILOS CERNY[2], ZUZANA MORMANOVA[2], MARTIN KYNCL[3], MARIA VEREBOVA[3], RADEK PADR[3], MILOSLAV ROCEK[3]

[1]*DEPARTMENT OF PEDIATRICS, UNIVERSITY HOSPITAL MOTOL AND 2ND FACULTY OF MEDICINE, CHLARLES UNIVERSITY, PRAGUE, CZECH REPUBLIC*

[2]*DEPARTMENT OF NEONATOLOGY WITH INTENSIVE RESUSCITATION CARE UNIT, UNIVERSITY HOSPITAL MOTOL AND 2ND FACULTY OF MEDICINE, CHLARLES UNIVERSITY, PRAGUE, CZECH REPUBLIC*

[3]*DEPARTMENT OF IMAGING METHODS, UNIVERSITY HOSPITAL MOTOL AND 2ND FACULTY OF MEDICINE, CHLARLES UNIVERSITY, PRAGUE, CZECH REPUBLIC*

Introduction: Hypertension in term or preterm neonates is seen in up to 2 % of all infants at NICU. Over 1 year period 6 infants developed severe hypertension with cardiac dysfunction. Causes of hypertension, different therapeutic modalities and renal outcome are analyzed.

Material and methods: 5 newborns developed severe hypertension at 1 to 14 days of age, 1 infant at the age of 6 months. Hypertension was defined as systolic blood pressure≥95 th percentile for age and sex. All had symptoms of cardiac dysfunction (congestive heart failure, cardiomegaly, left ventricular hypertrophy). Causes of hypertension (clinical, laboratory and radiologic testing): unilateral renal venous thrombosis (RVT) with thrombus extended into inferior vena cava (IVC) (n=2, one with solitary kidney), midaortic syndrome (n=1), renal artery stenosis (RAS)/RAS secondary to fibromuscular dysplasia (FMD) (n=3). Risk factors were identified in both pts with RVT (maternal diabetes mellitus, gestational age of <36 weeks), hereditary prothrombotic risk factors were excluded. PRA/plasma aldosteron were extremelly high in all RAS pts. Three or more antihypertensives controlled hypertension in pts with RAS/FMD/midaortic sy. Angioplasty was made in 1/3 pts with RAS at the age of 7 months. One newborn with RVT was treated with low molecular weight heparin (LMWH), selective thrombolysis and surgical intervention.The second one with solitary kidney and RVT required 2 days peritoneal dialysis followed by LMWH therapy.

Results: 6–12 months later renal functions normalized in all pts (GFR 1.38-2.09 mL/s). Pts with RVT are without therapy, in 1/2 is evidence of renal atrophy (function of 25 % on DMSA). 1/3 pts with RAS/FMD remains on antihypertensive monotherapy, function of affected kidney varied from 10 % to 33 %. Only 1 patient (midaortic sy) still required 2 antihypertesives.

Conclusions: In our experience, neonatal renovascular hypertension is no longer uncommon, responds to early detection, aggressive management, and rarely requires early nephrectomy.

P182 - Overhydration as a determinant of blood pressure in children with renal replacement therapy

SOFIE EERENS[1], J.H. VAN DER LEE[2], MARIJKE YSEBAERT[1], NATALIA ZABEGALINA[1], DOMINIQUE TROUET[1], KOEN VAN HOECK[1]

[1]*UNIVERSITY HOSPITAL ANTWERP*

[2]*EMMA CHILDREN'S HOSPITAL AMC*

Introduction: Hypertension is an important co-morbidity in children with renal replacement therapy (RRT). Control of hydration and antihypertensive drugs are complementary treatments both in dialysed and transplanted children. After transplantation, blood pressure is expected to be under control. In this study we assess the relative importance of both mechanisms.

Material and methods: As part of the RICH-Q project, bio-impedance spectroscopy was performed in158 children, age 2–19 years (74 female) treated with RRT. Blood pressure, the mean of 3 sitting measurements, was expressed as the percentage of the 95th percentile (P95) for age, height and sex. The parameters of interest were hydration (H) and Extracellular Water (ECW) in liters. Overhydration was defined as H more than 7 % of ECW.

Results: Twenty three children were treated with peritoneal dialysis (PD), 39 with hemodialysis (HD) and 96 were followed after transplantation (Tx). Age distribution, sex ratio and systolic blood pressure did not differ between treatment groups. 37, 29, and 6 patients were treated with 1, 2, 3 or more antihypertensive drugs, respectively. 59 % of HD, 43 % of PD and 44 % of Tx patients had a systolic blood pressure above the P95. 66 % of all patients were within normal hydration limits; 48 % of these children had hypertension. 20 % of the patients were overhydrated; 42 % of these had hypertension. No associations were found between H, the number of antihypertensive drugs, and hypertension

Conclusions: Although the majority of RRT patients is not overhydrated, and despite considerable use of antihypertensive drugs, about half of the patients is hypertensive, both on dialysis and after transplantation. The underlying mechanisms need further investigation.

P183 - Efficacy of dexamethasone treatment in child with apparent mineralocorticoid excess syndrome (AMEs)

SVETLANA PAPIZH, LARISA PRIKHODINA, OLGA TURPITKO, VARVARA OBUKHOVA, VLADIMIR DLIN
RESEARCH INSTITUTE OF PEDIATRICS & CHILDREN SURGERY, MOSCOW, RUSSIAN FEDERATION

Introduction: AMEs is a rare, autosomal recessive disease with severe hypertension, low renin and aldosterone levels, high rate of CV complication, high risk of mortality due to mutation in the HSD11B2 gene (16q22).
Material and methods: Case: 4 years old girl, 3rd product of consanguineous marriage. She was born with sings of fetal malnutrition - weight 2600 g (3 pc), height 48 sm (10–25 pc). At the age of 8 months the girl presented with polyuria, polydipsia (2.5 l/d), weakness, degrees muscle tone. At 2 years first measured BP was 130/80-140/85 mmHg (> 99th pc); revealed hypokalemia (1.8-2.3 mmpl/l), metabolic alkalosis (pH 7.6; base excess +23.6; standard bicarbonate 45.2 mmol/l), low rennin – 0.1 ng/ml (N 3.1-16.2), angiotensin −0.14 ng/ml (N 2.4-17.0), aldosterone – 11.9 pg/ml (N 20–1100) levels. GFR 136 ml/min/1,73 m2. Renal US search showed bilateral medullare nephrocalcinosis, grade 1. Echocardiography detected initial sings LVH.
Results: Treatment with high doses of CCB (0.3 mg/kg/d) and BRA (1.5 mg/kg/d) did not led to normalization of BP. The child with severe hypertension, low renin and aldosterone levels with normal ACTH and cortisol levels were excluded monogenic forms of hypertension. Firstly excluded Liddle's syndrome - direct sequencing of the SCNN1B and SCNN1G gene not identified of mutation. Sequencing of all exons of the HSD11B2 gene revealed homozygous nondescript mutation c.991A>G which confirmed AMEs. The girl has been treated with amiloride and hypotiasid, potassium supplements with positive dynamics of blood potassium level and reduction of metabolic alkalosis. On the last follow-up (2 year later) detected higher rates of physical development (50ht pc of weight and height), low-normal blood potassium level (3,8 mmol/l), but BP remained high (130/80 mmHg).
Conclusions: Treatment with low doses of dexamethasone (1.25 mg/d) resulted in a significant reduction of hypertension with normalisation of potassium and acid–base status of blood without the use of potassium supplements and BRA

P184 - Reversible nephrotic proteinuria induced by RAAS activation in a child with renal artery stenosis

P.J. SCHRIEMER, M.J.S. OOSTERVELD, A.H.M. BOUTS, J.W. GROOTHOFF
AMC PEDIATRIC NEPHROLOGY

Introduction: We describe a case of nephrotic proteinuria in a child with failure to thrive caused by renovascular malignant hypertension
Material and methods: case report
Results: A 5-month old boy was admitted with complaints of vomiting and failure to thrive. Blood results only revealed mild hyponatraemia (131 mmol/l) and low-normal serum potassium (3.6 mmol/l). Occasionally, hypertension was detected, reason why he was referred for further evaluation. Further analysis revealed nephrotic proteinuria (3.0 g protein/mmol creatinine), slightly elevated cholesterol, serum albumin of 32 g/l, with normal renal function. Diagnostic tests for mutations consistent with congenital/infantile causes of nephrotic syndrome were performed, which later all turned out to be negative. A kidney biopsy taken from his right kidney showed signs of immature podocytes and mesangial sclerosis, consistent with congentital nephrotic syndrome, but also mediahypertrophy. On day 7, he suffered from an acute episode of fever and poor responsiveness. At that moment his blood pressure was 170/105 mmHg. He was treated with 6 antihypertensives, partly i.v. By lowering the blood pressure to systolic 130 mmHg, clinical symptoms disappeared. Angiography revealed a stenosis of the left renal artery. Plasma renin activity and aldosterone levels were very high. An autotransplantation of his left kidney was performed. Unfortunately, despite treatment with 5 antihypertensives, among them high dose ACE inhibitors and angiotensine II blockers, his hypertension persisted, reason why nephrectomy was performed after 2 months. Within 2 weeks the proteinuria resolved completely and the blood pressure turned normal with oral ACE-inhibitors, a calciumantagonist and beta-blocker. He was discharged with a normal renal function in good clinical health and a rise in body weight
Conclusions: Measurement of blood pressure in infants can be difficult, especially in case of very severe hypertension. Extreme RAAS activation due to malignant renovascular hypertension may mimic infantile nephrotic syndrome with equally abnormal podocytes which is completely reversible by RAAS inhibition

P185 - AMBULATORY BLOOD PRESSURE MONITORING PARAMETERS AND THEIR VARIABILITY IN CHILDREN AND ADOLESCENTS IN RELATION TO BODY MASS INDEX: A SINGLE-CENTER EXPERIENCE

OLEH AKCHURIN[1], JOSEPH MAHGEREFTEH[1], HRIDYA SUMAN[1], ROBERT WORONIECKI[2]
[1]*ALBERT EINSTEIN COLLEGE OF MEDICINE / MONTEFIORE MEDICAL CENTER*
[2]*COLUMBIA UNIVERSITY COLLEGE OF PHYSICIANS & SURGEONS / MORGAN STANLEY CHILDREN'S HOSPITAL OF NEW YORK PRESBYTERIAN*

Introduction: The linkage between hypertension and obesity in pediatric and adolescent population is a well recognized emerging phenomenon. However the evidence regarding the relationship between body mass index (BMI) and parameters of ambulatory blood pressure monitoring (ABPM) among inner-city US youth is limited.
Material and methods: A cross-sectional study. Patients with known renal disorder and/or secondary hypertension were excluded from the study. Only initial ABPMs were analyzed, subsequent follow-up ABPMs were not included into the data analysis.
Results: One hundred twenty six patients (77 % male, 23 % female), referred to our center in 2009–2010, were included. Average age of the patients was 15.9 3.1 years, average BMI 29.3+/−8.8 kg/m2, average BMI z-score 1.4+/−1.2. No significant correlation between BMI and mean 24 hours or daytime systolic blood pressure (SBP), SBP load or SBP variability has been found in the studied cohort, however BMI (but not BMI z-score) correlated positively with nocturnal SBP (r=0.2), and both BMI and BMI z-score with nocturnal SBP load (r=0.2). 24 hours diastolic blood pressure (DBP) and diurnal DBP correlated negatively with BMI z-score (r=−0.17 and r=−0.21 respectively). Pulse pressure (PP) and heart rate (HR) correlated positively with BMI and BMI z-score. PP variability and diurnal DBP variability correlated positively with BMI and BMI z-score (r=0.19 and r=0.3 respectively).
Conclusions: In pediatric and adolescent patients higher BMI was not associated with elevation of 24 hours or daytime SBP, but rather with increase of PP and decrease of DBP, as well as increase of BP variability, especially during the day. This indicates complex nature of relation between BMI and BP regulation in adolescents, possibly related to compensatory cardiohemodynamic changes. Further studies are needed in order to reveal the underlying mechanisms.

P186 - KIDNEY DAMAGE IN PRIMARY HYPERTENSION IN CHILDHOOD

ILKNUR GIRISGEN[1], FERAH SOMEZ[1], CIGDEM YENISEY[2]
[1]*ADNAN MENDERES UNIVERSITY PEDIATRIC NEPHROLOGY DEPARTMENT*
[2]*ADNAN MENDERES UNIVERSITY BIOCHEMISTRY DEPARTMENT*

Introduction: Primary hypertension is the most important risk factor for chronic kidney disease in adulthood. However, the role of hypertension in kidney damage in childhood is not known exactly. The aim of this study was to investigate the effects of primary hypertension on kidney in children.
Material and methods: Patients (with mean age 10,4±3,8 (5–17) years, n=56) who had blood pressure higher than 90 percentile during well child follow up and healthy children (with mean age 10,9±2,6 (7–16) years, n=27) with the normal blood pressure were included to the study. 24 hours blood pressure measurements were recorded for all the patients. Microalbumin and N-Acetyl-β-D-Glucosaminidase levels in the 24 hour urine were investigated in study and control groups. The chi-square, Mann Whitney U, Spearman correlation and t tests test were used for the statistical analysis.
Results: The patients have higher levels of urinary N-Acetyl-β-D-Glucosaminidase (0,4347±0,0058 IU/L) than the control (0,4063±0,402 IU/L) group (p<0,001). No significant difference was found in the levels of urinary microalbumin excretion between primary hypertension and control groups. In the patients with white coat hypertension, higher levels of urinary N-Acetyl-β-D-Glucosaminidase (0,430±0,350 IU/L) than the control group (0,4063± 0,0402 IU/L) were observed.
Conclusions: In conclusion, it was thought that primary hypertension had effects on kidney damage in childhood. It is suggested that urine NAG excretion might be used as an early sign of hypertension induced renal damage.

P187 - FACTORS IN THE PATHOGENESIS OF PRIMARY HYPERTENSION IN CHILDREN

ILKNUR GIRISGEN[1], FERAH SONMEZ[1], CIGDEM YENISEY[2]
[1]*ADNAN MENDERES UNIVERSITY PEDIATRIC NEPHROLOGY DEPARTMENT*
[2]*ADNAN MENDERES UNIVERSITY BIOCHEMISTRY DEPARTMENT*

Introduction: In recent years, primary hypertension increasing parallel with childhood obesity in puberty. Ambulatory blood pressure measurement is the gold standard in the diagnosis of hypertension. Factors in the pathogenesis of primary and white coat hypertension in children are not known exactly. The aim of our study was to evaluate ambulatory blood pressure of the patients diagnosed as hypertension during well child follow up and to investigate the factors causing primary hypertension.
Material and methods: Patients (n=56) who had blood pressure higher than 90 percentile during well child follow up and healthy children (n=27) with the normal blood pressure were included to the study. 24 hours blood pressure measurements with the blood pressure monitor were recorded as the day-night mean blood pressure, the blood pressure loads and the dipper-non-dipper characteristics. Na and K in the 24 hour urine and renin, aldosterone, nitric oxide and endothelin in blood were investigated in all patients and the control group.

Results: The mean daytime systolic and diastolic blood pressure, day-night systolic blood pressure loads of the patients were statistically significant higher than the control group. 52 % of the patients diagnosed as white coat hypertension. According to the tests for evaluation of etiology the patients had statistically significant higher levels of blood renin (92,50±160,80 ng/ml), lower levels of blood endothelin (0,76±0,91 fmol/ml) and urinary Na excretion (106,00±16,80 mEq/L) than the control group respectively (17,80±14,50 ng/ml, 0,88 ±0,44 fmol/ml, 138,00±13,20 mEq/L). In the patients with white coat hypertension, statistically significant higher levels of blood renin and lower level of urinary Na were observed. In the obese children, daytime systolic blood pressure load, blood renin (143,00± 198,00 ng/ml) and nitric oxide (29,90±8,80 μmol/L) levels were found higher than the patients with normal weight (66,00±133,00 ng/ml, 26,40±12,40 μmol/L)) respectively.

Conclusions: In conclusion, it was thought that ambulatory blood pressure measurement was necessary for the true diagnosis of hypertension in children. In the pathogenesis of childhood primary hypertension and white coat hypertension, blood renin and urinary sodium excretion had important roles.

P188 - EVALUATION OF RENAL FUNCTIONS AND BLOOD PRESSURE IN LOW BIRTH WEIGHT CHILDREN

NERGIS OZCAN[3], FERAH SONMEZ[1], ILKNUR GIRISGEN[1], ALPARSLAN UNSAL[4], CIGDEM YENISEY[2]
[1]*ADNAN MENDERES UNIVERSITY PEDIATRIC NEPHROLOGY DEPARTMENT*
[2]*ADNAN MENDERES UNIVERSITY BIOCHEMISTRY DEPARTMENT*
[3]*ADNAN MENDERES UNIVERSITY PEDIATRICS DEPARTMENT*
[4]*ADNAN MENDERES UNIVERSITY RADIOLOGY DEPARTMENT*

Introduction: "Fetal programming" hypothesis has been widely recognized as a possible mechanism for the development of a number of chronic diseases in adulthood. It has been reported marked association between LBW and reduced nephron number. Fewer nephrons, with subsequent hyperfiltration and glomerulosclerosis in the remaining nephrons, could lead to accelerated ageing and early loss of renal function and the development of hypertension and increased susceptibility to renal disease in later life. We aimed to investigate renal functions and blood pressure in healthy children who were born with low birth weight and the effects of low birth weight on renal functions and blood pressure.

Material and methods: This study was carried on 33 children aged 7 to 18 years who admitted to the chidren outpatient clinic and were learned as borned with a birth weight under 2500 gr, without a known disease or use of medication during the study period. The control group included 30 age- and sex-matched healthy children who were born at term with a birth weight appropiate for gestational age. Microalbumin, N-Acetyl-β-D-Glucosaminidase, Na and K in the 24 hour urine and BUN, creatinine and cystatin-C levels in the blood were investigated in the study and the control groups. Size, parenchymal thickness, AP diameter and volume of the kidneys (with using ellipsoid formula) were examined by ultrasound. 24 hours blood pressure measurements were evaluated.

Results: According to the laboratory evaluations the patients had higher levels of blood cystatin-C (2450,03 ±344 ng/ml) and urinary Na (144,6±243,6 mEq/L) and N-Acetyl-β-D-Glucosaminidase excretion (0,44± 0,04 IU/L) than the control group (2216,83±191 ng/ml, 138,86±71,7 mEq/L, 0,41±0,03 IU/L), respectively In the ultrasound evaluation kidney volumes were smaller in the LBW group than in the controls, although all kidneys were anatomically normal. According to the results of ambulatory blood pressure measurements, a small number of children (3,2 % daytime systolic, 12,9 % nighttime systolic, 6,5 % nighttime diastolic) had high blood pressure levels. However, the two groups did not differ in the mean daytime or nighttime systolic and diastolic blood pressure, day-night systolic-diastolic blood pressure loads and the ratio of non-dipper blood pressure.

Conclusions: In conclusion, it was found that children borned with LBW had deterioration of renal function as a result of insufficiency in kidney development due to tubular damage. We suggested that LBW children should be follwed for renal functions and blood pressure.

P189 - Ultrasonographic evaluation of superior mesenteric artery angle and left renal vein in healthy children: effects of positional and respiratory changes on parameters

SUAT FITÖZ[1], ASLI KAVAZ[2], BURCU BULUM ÖZTÜRK[2], BIRSIN ÖZÇAKAR[2], ATILLA ELHAN[3], FATMA ŞEMSA ALTUGAN[2], MESIHA EKIM[2], FATOŞ YALÇINKAYA[2]
[1]*ANKARA UNIVERSITY SCHOOL OF MEDICINE, PEDIATRIC RADIOLOGY, ANKARA, TURKEY*
[2]*ANKARA UNIVERSITY SCHOOL OF MEDICINE, PEDIATRIC NEPHROLOGY, ANKARA, TURKEY*
[3]*ANKARA UNIVERSITY SCHOOL OF MEDICINE, BIOSTATISTICS, ANKARA, TURKEY*

Introduction: To obtain the normal AP diameters and PV values of the LRV and to demonstrate the effects of positional and respiratory changes on superior mesenteric artery (SMA) angle and left renal vein (LRV) in healthy children.
Material and methods: Ninety eight volunteers were enrolled in the study. Twelve of them were excluded because of abdominal gas artifacts, obesity, retroaortic course of the LRV, etc. Doppler ultrasonographic examinations were performed after having fasted for 6 to 8 hours, and, mesenteric angle, LRV diameter and peak velocity (PV) were measured in both the supine and upright positions.
Results: Statistical analyses were based on data of 86 healthy subjects (46 male, 40 female). The ages of the patients were 6 years to 17 years (mean, 10.2 years). The mean AP diameters of the hilar and aortomesenteric portions of the LRV in the supine position were 6,55±1,1 (mean± standard deviation) and 2,3±0,59 mm, respectively. The upright position measurements of the hilar and aortomesenteric portions of the LRV vein were 6.98±1,32 and 1,91± 0,48 mm, respectively. The mean AP diameter ratios of the left renal vein between hilar and aortomesenteric portions were 2,97±0,73 in the supine position, and, 3,86±1,23 in the upright position. The mean PVs in the left renal vein at the hilar and aortomesenteric portions in the supine position were 20,32±6,41 and 70,45±31,11 cm/s, respectively. The mean PVs in the upright position were 19,64±7,68 cm/s at the hilar and 80,83±38,68 cm/s at the aortomesenteric portions. The mean PV ratios of the left renal vein were 3,61± 1,73 in the supine position and 4,66±2,9 in the upright position. The mean angles of the SMA in the supine position were 34°±14,5° during inspiration and 46°±17,8° during expiration. In the upright position the mean angles of the SMA during inspiration and expiration were 18,8°±6,9° and 21,3°±8,5°, respectively.
Conclusions: Normal AP diameters and PV values of the LRV of healthy children were obtained. The respiratory changes of the angles of the SMA in the upright position were found to be smaller compared to supine position.

P190 - Cardiovascular Morbidity in Juvenile-onset Systemic Lupus Erythematosus

CATHERINE QUINLAN, STEPHEN MARKS, KJELL TULLUS
GREAT ORMOND STREET HOSPITAL FOR CHILDREN NHS FOUNDATION TRUST

Introduction: Juvenile-onset Systemic Lupus Erythematosus (JSLE) is a more aggressive disease than adult-onset SLE and data from the UK JSLE Cohort Study has shown that 80 % of patients have renal involvement. There is minimal data on the cardiovascular (CV) risk of patients with JSLE but they are thought to be at increased risk as they age and, as a result, the importance of the prevention of long-term CV complications is becoming increasingly recognised.
Material and methods: We report the preliminary results of our study aiming to characterise early CV disease using well validated, non-invasive studies to demonstrate pre-clinical CVD. We measured cIMT and PWV on a pilot group (n=10) of patients with JSLE. We compared these results to measurements conducted in the control group of a published study from our centre (1), which consisted of healthy children of a similar age group.
Results: Mean cIMT in the control group was 0.38 mm, compared to a mean value of 0.47 mm in our pilot group, a 23.7 % increase. Mean PWV was 5.41 m/sec in our study and 4.8 m/sec in the published "controls", a comparative increase of 12.7 %. This is a highly significant result. Our group is currently too small to permit formal sub-group analysis. However, children with higher cIMT and PWV did not differ from the overall group with respect to hypertension, age or activity scores. They were, however, more likely to have severe disease, a higher BMI and a positive family history of CV disease.
Conclusions: Our preliminary results suggest a potentially significant increase in well-established risk factors for CV morbidity and mortality occurring in children and young adults with lupus despite modern treatment modalities. This study is ongoing and we hope to identify disease specific CV risk factors for patients with JSLE to enable clinicians to better identify those most at risk of developing CV disease and to thus optimise the long-term outcomes for these patients. References 1.Shroff RC, Donald AE, Hiorns MP, Watson A, Feather S, Milford D, et al. Mineral metabolism and vascular damage in children on dialysis. J Am Soc Nephrol 2007 Nov;18(11):2996–3003.

P191 - Birth Weight and Blood Pressure in a High Birth Weight Pediatric Population

SANDRA DIS STEINTHORSD[1], SIGRIDUR BIRNA ELIASD[1], OLAFUR SKULI INDRIDASON[2], RUNOLFUR PALSSON[2], VIDAR ORN EDVARDSSON[3]
[1]*UNIVERSITY OF ICELAND*
[2]*LANDSPITALI – THE NATIONAL UNIVERSITY HOSPITAL OF ICEL*
[3]*CHILDREN´S MEDICAL CENTER, LANDSPITALI – THE NATIONAL UNIVERSITY HOSPITAL OF ICELAND, REYKJAVIK, ICELAND*

Introduction: Low birth weight has been associated with increased risk of hypertension later in life. The aim of the current study was to evaluate the association between birth weight and blood pressure in healthy 9- to 10-year-old Icelandic children.

Material and methods: Each child underwent 4 seated blood pressure measurements and a blood pressure percentile calculation from the average of the 4 measurements. Height and weight were measured and birth weight retrieved from the Icelandic Birth Registry. Pearson´s correlation was used to correlate birth measures and anthropometric data with blood pressure percentiles. Multivariable linear regression was employed to examine the independent association between blood pressure percentiles and birth measures.
Results: Of 887 children with complete data, 452 were female (51 %). Mean blood pressure was 112/64 in males and 111/63 mm Hg in females. Mean birth weight was high, 3718±616 g. A significant negative correlation between birth weight and both systolic (r=−0.09, p=0.005) and diastolic (r=−0.08, p=0.014) blood pressure percentiles was observed. The relationship, which was stronger in females, persisted after controlling for body mass index percentile. The association was similar for the birth length and head circumference while there was no correlation between gestational age and absolute blood pressure values.
Conclusions: Low birth weight seems to be a significant predictor of blood pressure in 9- to 10-year-old Icelandic children. Careful blood pressure follow-up may be indicated in low birth weight children as they may be at an increased risk for future cardiovascular complications.

P192 - Nutcracker syndrome, underestimated cause of haematuria?

MARTIN ĆUK, BERNARDICA VALENT-MORIć, IVA PALčIć, MONIKA KUKURUZOVIć
UNIVERSITY HOSPITAL CENTER "SISTERS OF MERCY"

Introduction: Nutcracker syndrome (NcS) refers to a compression and distension of left renal vein (LRV) most commonly between aorta and superior mesenteric artery producing impaired blood outflow and LRV hypertension that leads to haematuria and sometimes orthostatic proteinuria. There are also other vascular causes of (NcS). It is diagnosed through renal Doppler ultrasound (DU), MR angiography (MRA) or CT angiography (CTA).
Material and methods: We analysed patients with microhaematuria and macrohaematuria that were referred to our Institution from 2010–2011. Inclusion criteria for performing DU, MRA, CTA were normal blood pressure and absence of oedema, significant haematuria, proteinuria <1 g a day, normal renal function according to estimated and calculated creatinine clearance, normal blood clotting tests and calcium excretion, normal values of complement and vasculitis screening tests.
Results: Eight of 27 (26 %) were included in investigation for NcS, 1 female and 7 male; 52.5 % (5) had (NCS) (4 male and 1 female). Their age was between 5 and 16 y, median age 12 y. Eighty percent (4) had classical radiologic findings of NcS and 20 % (1) had LRV compression between two renal arteries. All males also had left varicocoele. During a one year period of surveillance haematuria resolved spontaneously in 80 % (4). There was no need for surgical intervention in any of our patients.
Conclusions: We found NcS to be a benign condition and the important cause of haematuria in children and adolescents. We suggest radiological evaluation in all children with haematuria that fulfil our inclusion criteria. This would reduce further unnecessary investigation. Further investigation is required to establish a protocol for diagnosing NcS in children and adolescents.

P193 - Diastolic Dysfunction in Children with Stage 2 Chronic Kidney Disease

MEHMET TASDEMIR[1], AYSE GULER EROGLU[2], NUR CANPOLAT[1], SALIM CALISKAN[1], AYSE AGBAS[1], MELTEM DONMEZ SEVIM[1], LALE SEVER[1]
[1]*ISTANBUL UNIVERSITY CERRAHPASA MEDICAL FACULTY PEDIATRIC NEPHROLOGY*
[2]*ISTANBUL UNIVERSITY CERRAHPASA MEDICAL FACULTY PEDIATRIC CARDIOLOGY*

Introduction: Cardiovascular abnormalities are common in children with chronic kidney disease (CKD). Diastolic dysfunction begins in the early stages of CKD in adults; however, there is not enough data addressing this issue in children. This study aims to investigate cardiac parameters, especially diastolic function (DF), in the very early stages of CKD in children.
Material and methods: Twenty-four patients (15 boys, 12.5+ 3.5 years) with stage 2 CKD (GFR: 60–89 ml/min/1.73 m2) and 31 healthy children of comparable age, height and sex underwent standard echocardiography and tissue Doppler imaging. To assess DF, early (E) and late (A) diastolic transmitral flow velocities and early (Em) and late (Am) diastolic myocardial velocities were measured. E/A and Em/Am ratios were calculated. Left atrial (LAD) and aortic (AD) diameters and isovolumetric relaxation time (IVRT) were also determined; z scores were calculated. Blood pressure was evaluated by office measurements and ambulatory blood pressure monitoring (ABPM). Hypertension was defined as having a 24-h mean arterial pressure index above 1 and/or the use of antihypertensive drugs.
Results: Patients were found to have worse left ventricular DF compared to controls [(lower E, 84.0±1.9 vs. 93.6±1.4 cm/s, p=0.02), (lower E/A, 1.74±0.5 vs. 2.13±0.4, p=0.01), (lower Em, 22.3±5.6 vs. 27.3±4.4 cm/s, p=0.04), (higher LAD z-score, 0.34±0.82 vs. 0.30±0.89, p=0.02)]. There were no differences in systolic function and myocardial performance between the patients and the controls.

Fourteen patients were hypertensive and 10 were normotensive. There were no differences in regards to cardiac parameters between these two groups. Left ventricular diastolic parameters were worse even in normotensive patients as compared to the healthy controls [(E, 84.0±1.8 vs. 93.6±1.4 cm/s, p=0.004), (Em, 21.3±4.9 vs. 27.3±4.4 cm/s, p=0.02)].
Conclusions: Left ventricular diastolic dysfunction can be seen in children with stage 2 CKD, including those who are normotensive.

P194 - ALTERED GENES PROFILE OF RENIN-ANGIOTENSIN SYSTEM, IMMUNE SYSTEM AND ADIPOKINES RECEPTORS IN LEUCOCYTES OF CHILDREN WITH PRIMARY HYPERTENSION

LITWIN MIECZYSLAW[1], MICHALKIEWICZ JACEK[2], NIEMIRSKA ANNA[1], TROJANEK JOANNA[2]
[1]*DEPARTMENT OF NEPHROLOGY & ARTERIAL HYPERTENSION*
[2]*DEPARTMENT OF MICROBIOLOGY & IMMUNOLOGY, THE CHILDREN'S MEMORIAL HEALTH INSTITUTE, WARSAW, POLAND*

Introduction: Renin-angiotensin system (RAS), metabolic abnormalities and immune activity play important role in the pathogenesis of primary hypertension (PH). The aim of the study was to assess expression of angiotensinogen (AGT), angiotensin 2 type 1 receptor (AGT2R2), angiotensin converting enzyme (ACE), renin (REN), CD14 molecule (CD14) adiponectin type 1 receptor (ADIPOR1) and leptin receptor (LEPR) genes in leucocytes of children with PH before and after 6 months of non-pharmacological treatment based on dietary advice and increased physical activity.
Material and methods: Leucocyte mRNA expression of AGT, AGT2R, ACE, REN, CD14, ADIPOR1, LEPR genes was measured with quantitative RT-PCR in 23 children with PH before and after 6 months of non-pharmacological treatment. 24 h ambulatory blood pressure monitoring, lipids, glucose, insulin, left ventricular mass and carotid intima-media thickness was assessed at start and after 6 months of treatment.
Results: PH children presented with intermediary phenotype of overweight and metabolic syndrome (MS) was present in 9 pts (39,1 %). On average, the expression of AGT, AGT2R1, ACE, REN, LEPR, CD14 and ADIPOR1 was increased. After 6 months of treatment blood pressure, heart rate and prevalence of MS (4 pts/17.9 %) significantly decreased. The expression of AGT, AGT2R1, ACE, REN, LEPR genes decreased following treatment and those of ADIPOR1 and CD14 remained elevated; only REN expression decreased significantly. Changes in blood pressure, left ventricular mass, carotid intima-media thickness, BMI and waist circumference did not correlate with changes in expression of RAS, immune system and adipokines genes.
Conclusions: Expression of genes of the RAS components, CD14, and adipokines receptors in leucocytes was significantly altered in the PH children as compared to the healthy control children. Non-pharmacological antihypertensive treatment led not only to decrease in blood pressure but also to changes in the expression of the RAS system genes in leucocytes, with significant decrease in renin gene expression.

P195 - A rare cause of renovascular hypertension in children: Co-existence of polyarteritis nodosa, antiphospholipid syndrome and MTHFR mutation

NURAN CETIN[1], BILAL YILDIZ[1], NURDAN KURAL[1], TAMER KAYA[2]
[1]*ESKISEHIR OSMANGAZI UNIVERSITY, FACULTY OF MEDICINE DEPARTMENT OF PEDIATRIC NEPHROLOGY*
[2]*ESKISEHIR OSMANGAZI UNIVERSITY, FACULTY OF MEDICINE DEPARTMENT OF RADIOLOGY*

Introduction: Renovascular disease (RVD) causes 5–10 % of all childhood hypertension. Polyarteritis nodosa (PAN) is a vasculitis of small/medium-sized arteries that can result in vascular aneurysms and tissue infarction. Despite intense systemic inflammation, loss of tolerance with cross-reactive or autoreactive antibody formation is not a hallmark of PAN.
Material and methods: We present a child with the co-existence of classic PAN, antiphospholipid antibodies (aPL) and metilen-tetra-hydro-folate reductase (MTHFR) mutation which not previously reported.
Results: A 16-years-old boy was admitted because of fatigue, headache, abdominal pain and nausea. His blood pressure was 180/120 mmHg with grade-II hypertensive retinopathy. When the causes of hypertension were investigated; elevated renin activity (>100 ng/ml/s), aldosteron level (240 pg/ml) and anti-cardiolipin antibodies [IgG 45.3 GPL / IgM 34.1 MPL], decreased bilateral resistance-index and acceleration time in left kidney, multiple microaneurysms, occlussion and thrombosis at left renal artery and thrombosis at posterio-inferior branches of right renal artery, prolonged APTT, normal complement levels, negative HBsAg and ANCA and positive lupus anticoagulant tests were found. He was diagnosed as having PAN and antiphospholipid syndrome. The antihypertensive agents, prednisolone and pulse cyclophosphamide therapy were started and then stent was inserted in left renal artery. Two months later, he was admitted due to dizziness and the right arm and leg numbness-tingling. Brain MRI/MRI angiography showed acute infarct area of the left parietal and frontal lobe and left MCA stenosis. We found peripheral sensory-motor

neuropathy and heterozygous MTHFR A1298C mutation in our patient. IVIG and LMW heparin treatment was added. After 2 weeks, the clinical symptoms improved.

Conclusions: In conclusion, our patient showed that aPL could be contributed to the development of multiple arterial stenosis, aneurysms and thrombotic events in patients with hypertension. If hypertensive patient develop thrombotic events, the doctor should look beyond the RVD such as PAN and consider investigation for aPL and MTHFR mutation.

P196 - The polymorphisms of genes that affect the endothelium in primary hypertension of childhood

BETUL SOZERI[1], YASEMIN OZDEMIR[1], AFIG BERDELI[2], SEVGI MIR[1]

[1]*EGE UNIVERSITY FACULTY OF MEDICINE DEPARTMENT OF PEDIATRIC NEPHROLOGY*

[2]*EGE UNIVERSITY FACULTY OF MEDICINE DEPARTMENT OF MOLECULER MEDICINE*

Introduction: Primary Hypertension(PH) has a complex etiology, and with the availability of information about genetics. Polymorphism of the eNOS gene G894T has been shown to altering the primary structure of the eNOS gene.PH causes atherosclerosis and abnormal regulation of vascular endothelial growth factor(VEGF) is contributing factor Some polymorphisms have been associated to VEGF-A protein production,such as +405 G→C or −460 T→C. Genetic variations of the IL-6 gene may be key regulators of IL-6 production and therefore may predispose an individual to cardiovascular events. G-174 C polymorphism in the promoter region of the IL-6 gene has been shown to be functional and influence IL-6 production both in vitro and in vivo. The aim of this study is to search the frequency these genes polymorphisms and their effects on target organ damage in children with primary hypertension.

Material and methods: 50 pediatric patients(M/F=35/15) with primary hypertension and healthy controls have been studied. We had evaluated microvascular changes(arterial stiffness by pulse vawe velocity and augmentation index) by Vi-corder® and the macrovascular changes(carotid intima thickness-cIMT and left ventricule mass index-LVMI) by ECHO. Four different genetic polymorphisms that are correspondinglyIL-6-174 G>C, eNOS-894 G>T, VEGF+405 G>C and VEGF-460 C>T were studied in patients and controls.

Results: The mean age was 13,1±3,2 years. The existence of IL-6-174 G>C G and VEGF+405 G>C C alleles found more often in hypertensive patients(66 % vs 46 %, OR [1,161(%95CI: 0,869-1,547)]; 58 % vs 31.6 %, OR:1,128 [(%CI: 0,692-1,838)] respectively). In patients with stage 2 HT had IL-6-174 G>C and VEGF+405 G>C polymorphisms than other patients and had more target organ damage. Both microvascular and macrovascular changes were found higher in patients with C alleles in VEGF +405 and patients carrying the GG genotype and G allele in IL-6 gene. Also hypertensive retinopathy were found significantly higher in these patients. There was no significant difference on frequency of alleles in two groups for the presence of eNOS-894 G>T and VEGF 460 C>T. There was no association between eNOS-894 G>T polymorphism and target organ damage (eye,kidney and cardiovascular system)

Conclusions: The carrying IL-6-174 G allele and VEGF+405 C allele polymorphisms were found to be associated with primary hypertension in Turkish population. Also, these patients had increased risks of both microvascular and macrovascular changes. The T 786 G>C transition in ENOS gene may not be a contributing factor to primary hypertension in our population. Further studies are required to verify these findings.

P197 - Clinical Analysis Based on 23 Nutcracker Syndrome in a single center experience

HULYA NALCACIOGLU[1], GURKAN GENC[1], DEMET TEKCAN[1], Y. KAMIL YAKUPOGLU[2], SABAN SARIKAYA[2], OZAN OZKAYA[1]

[1]*ONDOKUZ MAYIS UNIVERSITY FACULTY OF MEDICINE, DEPARTMENT OF PEDIATRIC NEPHROLOGY*

[2]*ONDOKUZ MAYIS UNIVERSITY FACULTY OF MEDICINE, DEPARTMENT OF UROLOGY*

Introduction: Nutcracker syndrome (NS; left renal vein entrapment syndrome) refers to the compression of the left renal vein (LRV) between the aorta and the superior mesenteric artery (SMA), resulting in renal venous hypertension. This syndrome manifests with left flank and abdominal pain, with or without hematuria or with orthostatic proteinuria. The aim of the retrospective study is to analysis of clinical characteristics of patients who were diagnosed as nutcracker syndrome in our institution to raise a awereness of the disease.

Material and methods: The demographic data, clinical findings, left renal vein Doppler ultrasonographic (US) measurements, and the clinical course of 23 cases with Nutcracker syndrome was evaluated retrospectively.

Results: Twenty-three children on NS (F/M:15/8; median age:13; range 5–18 years) were enrolled in the study. Proteinuria was the most common presenting symptom(12 of 23 patients). Of the remaining 11 patients, 4 patient presented only with flank pain, 3 patient, only with macroscopic hematuria and 4 cases with isolated microscobic hematuria. Doppler US was performed all cases and in 8 case the diagnosis was confirmed by renal magnetic resonance

(MR) angiography. Of the 23 patients, 22 with mild and tolerable symptoms were treated conservatively. One female patient who complained of significant recurrent flank pain underwent transposition of the LRV.

Conclusions: In conclusion, nutcracker syndrome should be kept in mind in the differential diagnosis of children presenting with orthostatic proteinuria, haematuria and flank pain. Doppler sonography of LRV is a useful screening tool in patients with these symptoms to diagnose nutcracker syndrome.

P198 - The effects of white coat hypertension in children

BETUL SOZERI[1], YASEMIN OZDEMIR[1], MURAT DEVECI[2], SEVGI MIR[1]

[1]EGE UNIVERSITY FACULTY OF MEDICINE DEPARTMENT OF PEDIATRIC NEPHROLOGY

[2]EGE UNIVERSITY FACULTY OF MEDICINE DEPARTMENT OF PEDIATRIC CARDIOLOGY

Introduction: White coat hypertension (WCH) has been defined as elevated blood pressure (BP) in the office but diagnosed as normal BP by ambulatory blood pressure monitoring (ABPM). The few studies of white coat hypertension in childhood report a prevalence ranging from 16 % to 88 %. The clinical significance of WCH remains uncertain. The goal of this study is to evaluate the target organ damage in childhood with white coat hypertension

Material and methods: 50 pediatric patients (M/F=35/15) who are between 5 and 18 years old and diagnosed as primary hypertension(PH) and healty controls (n=100, M/F=46/54) have been examined.We evaluated microvascular changes (arterial stiffness by pulse wave velocity-PWV) and macrovascular changes (carotid intima media thickness and left ventricular hypertrophy) in cardiovascular system in patients. Also, microalbuminuria analysed for kidney damage and the involvement of eye disease with fundus examination were done.

Results: We determinated that WCH was diagnosed in 8 (%16) patients with PH. 1 of 8 patients had prehypertension, two of them had stage 1HT and 5 of 8 had stage 2HT. PWV was measured as a mean value of 5,6± 0,61 m/s (in control group 5,30±0,70 m/s). According to results, the values of 6 of 8 patients were higher then the control group. cIMT was measured as a mean value of 0,45 ±0,03 mm on left and right in WCH group. In control group, it was measured as 0,405±0,041 mm. One of the patients had left ventricular hypertrophy and two of them had grade 1 hypertensive retinopathy.

Conclusions: Based on the results, all of the patients with WCH from the morphological CVS (cIMT increase), 6 of them from the functional CVS (increase in pulse wave velocity) and 2 of them from the involvement of eye disease were affected. This was the indicator of the fact that WCH is not a benign illness.Therefore these patients should be evalutaed in terms of end organ damage.

P199 - Ambulatory arterial stiffness index in obese children

KATARINA BABINSKA, LASZLO KOVACS, JANUSZ FEBER

2ND DEPARTMENT OF PEDIATRICS, COMENIUS UNIVERSITY MEDICAL SCHOOL, UNIVERSITY CHILDREN'S HOSPITAL, BRATISLAVA, SLOVAKIA (SLOVAK REPUBLIC)

Introduction: As changes in arterial function precede the development of atherosclerotic lesions, an increased arterial stiffness may be an early marker of increased cardiovascular risk, especially in obese and/or hypertensive patients. The aim of our study was to evaluate the severity of arterial stiffness in children with various degrees of obesity in comparison with a control group of non-obese non-hypertensive children.

Material and methods: 144 obese patients (BMI>2.0 SDS; median age=14.7 years) and 66 controls (median age= 15.1 years) underwent anthropometry, biochemical evaluation and ambulatory blood pressure monitoring (ABPM). Obese patients were divided into 3 groups (each n=48) based on their BMI Z scores: >=2.00 to <3.49 (Group1), >=3.50 and <4.49 (Group2) and >4.50 (Group3). Ambulatory arterial stiffness index (AASI) was obtained from ABPM of each patient (1-regression slope of diastolic on systolic blood pressure). Continuous metabolic syndrome score (cMetS) was calculated as sum of Z scores of BMI, 24 h mean arterial pressure (MAP), serum HDL cholesterol, triglycerides and fasting glucose. Relationship between AASI and cMets and their cut-off values were calculated.

Results: AASI was 0.35±0.17 in control group and increased from 0.40±0.16 in Group1 to 0.44±0.14 in Group2 and to 0.47±0.15 in Group3 ($p<0.0001$), regardless of the presence ambulatory hypertension. AASI was increasing with level of cMetS, but on univariate analysis correlated significantly with height SDS ($p=0.009$), serum cholesterol ($p=0.007$) and day/night MAP ($p=0.04$). However, on multivariate analysis only height SDS was a significant predictor of the AASI ($p=0.04$). cMetS increased progressively from 2.4±2.2 to 6.3±2.8 from Group1 to Group3 ($p<0.0001$).

Conclusions: The main findings of our study are a) AASI is elevated in obese normotensive and hypertensive children compared to healthy population; b) obese children with MS have significantly higher AASI regardless of their blood pressure status and severity of ambulatory hypertension.

P200 - Coarctation of thoracic aorta and hypoplasia of renal arteries

JASNA SLAVICEK, DANICA BATINIC, DANKO MILOSEVIC, LJILJANA NIZIC, KRISTINA VRLJICAK, SONJA HODZIC, MAJA LEMAC, HRVOJE KNIEWALD, IVA PALCIC
UHC ZAGREB

Introduction: A case of coarctation of thoracic aorta associated with hypoplasia of renal arteries has not been described in literature. We describe a 17.5-year-old male patient with coarctation of thoracic aorta, hypoplasia of both renal arteries, consequent hypoplasia of both kidneys, and chronic renal insufficiency.

Material and methods: The patient was born after normal pregnancy, BW 2150 g, normal family history. At the age of 28 days patent arterial duct was diagnosed and surgically ligated at the age of 3 months. Patient had no health problems until he was 13.5 years when hypertension (RR 200/100) and renal insufficiency were established due to fatigue, headache, and muscular cramps. Ultrasound (US) showed HLV, LV dilation, normal contractility. LVEF 0.72, normal aortic root, widened ascending aorta and arch followed by a narrow portion (1.2 cm) and the narrowest portion at coarctation site (6 mm). Max. Systolic gradient with turbulence jet up to 4 m/s, i.e. 64 mm Hg. MSCT - Concentric aortic stenosis 11–12 mm long in the distal aortic arch, narrowed short portion 5 mm in diameter. Developed collaterals evident. Pronouncedly narrow, hypoplastic renal arteries present, cca 2 mm in diameter. Hypotrophic kidneys.

Results: Peritoneal dialysis was initiated. After 2.5 months dilation of coarctation and stent placement were performed. Control US: gradient 10 mmHg. RR 130/65. Cadaveric kidney transplantation was performed at the age of 16 years. A year after stent placement restenosis was observed with 20 mm Hg, gradient and blood pressure increase to 130-160/65. Slight elevated creatinine was observed.

Conclusions: We described unique case of coarctation of thoracic aorta with hypoplasia of renal arteries.The patient was treated with balloon dilation and stent implantation. Long-term periodical follow-up is necessary after dilation and stenting due to possible recoarctation and hypertension that could compromise the function of transplanted kidney in our patient.

P201 - Study of the left ventricular mass and cardiac function in children with Chronic Kidney Disease (CKD) with echocardiography (ECHO) and tissue Doppler imaging (TDI)

VALENTINA CORAZZI, FRANCESCA MENCARELLI, RICCARDO MASETTI, MARIANNA FABI, CLAUDIO LA SCOLA, ANDREA PASINI, GIOVANNI MONTINI
S.ORSOLA-MALPIGHI HOSPITAL - DEP. PEDIATRICS

Introduction: Cardiovascular disease (CVD) is a common cause of morbidity and mortality in children with CKD. Left ventricular hypertrophy (LVH) and diastolic dysfunction (LVDD) are known to be early markers. Aim of the study: To evaluate 1. early markers of cardiomyopathy (LVH and diastolic function - DF) with ECHO, cPWD and TDI in a population of children with CKD 2. the correlation between cardiac disease and possible risk factors (hypertension, disturbances of calcium, phosphorus and PTH, anemia, dyslipidemia).

Material and methods: 39 children were studied, median age 10.4 years (3.3-19.8). Underlying renal diseases were: hypo/dysplasia (N=28), nephronophthisis (N=6), Alport (N=2), ARPKD (N=3). Thirty-six percent of patients were on CKD stage 1–2, 38 % on stage 3, 15 % on stage 4. Four patients were on peritoneal dialysis. LVH was defined as a left ventricular mass index (LVMI) higher than the 95th percentile (38.6 g/h2,7). DF was estimated by cPWD and TDI.

Results: LVH was present in 20 patients (51 %). LVMI and DF index valuated with TDI (E'/A'=early over late diastolic myocardial velocity at septal mitral annulus) were significantly related to the glomerular filtration rate (GFR) ($p<0.003$, $p<0.004$). We didn't find correlation between DF valuated with cPWD and GFR. LVMI was correlated with phosphorus and hemoglobin ($p<0.0001$, $p<0.004$) and E'/A' was correlated with phosphorus and PTH ($p=0.04$, $p=0.007$). LVH was present since the first stages of CKD (29 % of patients on stages 1–2 had LVH). E' was reduced in 73 % of our patients. We didn't find any correlation between LVH and systemic hypertension.

Conclusions: LVH is present since the first stages of CKD. TDI is more accurate than cPWD to diagnose LVDD. ECHO evaluation with TDI could be suggested also for children prior to dialysis and with a normal blood pressure. Together with cardiac evaluation, an early and intensive treatment of the modifiable risk factors is recommended.

P202 - Successful surgical treatment of renal artery stenosis due to neonatal aortic thrombosis

AURELIE DAVOURIE-SALANDRE[1], ALAIN RAYNAUD[2], ROBIN AZOULAY[3], ANNABEL PAYE-JAOUEN[4], YVES CASTIER[5], ALAA EL GHONEIMI[4], MARIE-ALICE MACHER[1]
[1]*PEDIATRIC NEPHROLOGY, HOPITAL ROBERT DEBRE, APHP, UNIVERSITY OF PARIS DIDEROT, FRANCE*
[2]*DEPARTEMENT OF VASCULAR RADIOLOGY, LABROUSTE CLINIC, FRANCE*
[3]*DEPARTEMENT OF RADIOLOGY, HOPITAL ROBERT DEBRE, APHP, UNIVERSITY OF PARIS DIDEROT, FRANCE*

[4]DEPARTEMENT OF PEDIATRIC SURGERY AND UROLOGY, HOPITAL ROBERT DEBRE, APHP, UNIVERSITY OF PARIS DIDEROT, FRANCE
[5]DEPARTEMENT OF THORACIC AND VASCULAR SURGERY, HOPITAL BICHAT, APHP, UNIVERSITY OF PARIS DIDEROT, FRANCE

Introduction: Umbilical artery catheters have been associated with thrombotic complications, such as occlusion in the aorta, or renal arteries.
Material and methods: We report a case complicated by renal artery stenosis and subsequent hypertension, successfully treated by aortic surgery.
Results: A newborn boy, without any family medical history of thrombosis, had an arterial umbilical catheterism for neonatal suffering. A severe hypertension led to the diagnosis of occlusion of both renal arteries due to the extensive thrombosis of the distal aorta. Thrombophilic factors were not found and renal function remained normal. Hypertension could be medically managed during the first years. At 8 years of age, hypertension became resistant to medical therapy. CT scan and angiography demonstrated a persistent acquired coarctation of the abdominal aorta and the persistence of ostium stenosis of the right renal artery, while left kidney was hypotrophic. A Tc-99 m DMSA scintigraphy confirmed the low left renal function (14 %) and he underwent left nephrectomy without effect on blood pressure. A surgery of the right renal artery was then performed and peroperatory findings were a collateral circulation from the gastroduodenal and diaphragmatic arteries. Ostium of the renal artery could not be found and has probably been incorporated during the vascular reconstruction. A transaortic endarterectomy with release of the renal artery ostium led to the successful recovery of blood flow through the ostium. An angiography performed 1 month after surgery showed a persistent ostial gradient of 20 mmHg and a percutaneous transluminal angioplasty was then performed with good results. Arterial blood pressure is now within normal range with minimal anti hypertensive treatment.
Conclusions: This case report, underlines the difficult management of renovascular hypertension in children, and the successful surgical treatment in this unusual case of occlusion of the renal artery.

P203 - MIDDLE AORTIC SYNDROME IN CHILDREN – SINGLE CENTRE EXPERIENCE

JOLANTA ANTONIEWICZ[1], GRAŻYNA BRZEZIńSKA-RAJSZYS[2], PIOTR KALICIńSKI[3], ANDRZEJ KOśCIESZA[4], MAREK PęDICH[4], JADWIGA DASZKOWSKA[2], RYSZARD GRENDA[1]
[1]DEPARTMENT OF NEPHROLOGY, KIDNEY TRANSPLANTATION AND ARTERIAL HYPERTENSION, THE CHILDREN'S MEMORIAL HEALTH INSTITUTE
[2]DEPARTMENT OF CARDIOLOGY
[3]DEPARTMENT OF SURGERY
[4]DEPARTMENT OF RADIOLOGY

Introduction: Middle aortic syndrome (MAS) is an uncommon condition characterized by segmental narrowing of the distal thoracic and/or abdominal aorta, commonly involving the visceral and renal arteries, with poorly controlled arterial hypertension. OBJECTIVE: Course of disease and treatment efficacy assessment in children with middle aortic syndrome with abdominal aorta involvement.
Material and methods: 23 children (13 girls, 10 boys) aged from 3,5 to 14,8 (mean 9,5±3,6): 6 with neurofibromatosis, 3 with Williams syndrome, 3 with Takayasu disease, 1 with telangiectasis. Renal artery stenosis and visceral arteries stenosis were diagnosed in 22 and 14 patients respectively, in 2 cases thoracic aorta was also involved. All children were observed from 0,8 to 14,5 years (mean 4,9±3,6). 20 patients underwent individualised surgical treatment (vascular surgery, angioplasty, stenting), while 3 were treated conservatively. Final outcome assessment was based on blood pressure index (BPi) analysis, control of target organ damage (left ventricular hypertrophy - LVH) and pharmacotherapy regimen.
Results: 12 children (52 %) were accidentally diagnosed with hypertension. In 2 (9 %) hypertensive emergencies occurred. In all patients BP values were significantly reduced (systolic BPi 1,28 vs. 1,1 $p<0.05$; diastolic Bpi 0,96 vs. 0,82 $p<0.05$) and in 12 (52 %) finally normalised. In all cases LVH reduction was observed (left ventricular mass index deSimone: 51,4 v 34,2 g/m2.7; $p<0.05$), although in 5 (22 %) LVH persists. Drug intake was decreased from 3,3 in baseline to 3,1 (n.s).
Conclusions: Complex treatment of MAS (surgery and pharmacotherapy) leads to successful clinical outcome.

P204 - HIGH SENSİTİVE CRP VALUE IN THE DIAGNOSIS OF CHILDHOOD NONDIPPER HYPERTENSİON

SEÇİL CONKAR, NİDA DİNÇEL, SEVGİ MİR
EGE UNIVERSITY PEDIATRIC NEPHROLOGY

Introduction: Pediatricians have increasingly used ambulatory blood pressure monitoring (ABPM). ABPM is superior to casual measurements for predicting cardiovascular morbidity and mortality and association with target-organ damage (TOD).The aim of this study is to evaluate the relationship between ABPM results and TOD
Material and methods: We had both casual and ABPM measurements of 39 children.Blood pressure(BP) levels of 90th percentile and above,were accepted hypertension.The sum of the 95th percentile above levels were noted as

systolic/diastolic load. BP load of more than 25 % has been determined as significant.Average fall of more than 10 % in both daily and night values were called as dipper hypertension.In terms of TOD, retinal,renal and cardiac evaluation was performed.

Results: Among 39 patients,27were hypertensive by ABPM.There were no statistically differencies between the parameters of birth weight, age, gender, body mass index and lipids in the hypertensive and normotensive cases. There were 27 hypertensive cases detected by ABPM, whereas 23 were by casually.12 of 27 cases found by ABPM were dipper, last 15 were non-dipper. Ratio of TOD were 33 % and 60 %,in dipper and non-dipper cases, respectively.5 of non dipper cases were also having hsCRP. 11 patients were white-coat hypertensive without any TOD.among the 23 cases detected hypertensive, 12 of them were correlated with ABPM results. Microalbuminuria,uric acid and high sensitive CRP(hs CRP) values were statistically higher in non-dipper cases than in dipper ones ($p < 0.05$).Among the 16 casually normal patients,15(38.4 %) were hypertensive by ABPM; masked hypertension. In 6/15(%40) cases had alsoTOD.

Conclusions: Masked hypertension incidence was found as 38.4 %,with a rate of 40 % TOD.In patients with family history of hypertension and TOD, ABPM has to be needed.Also,hsCRP can be considered as an indicator of non-dipper hypertension and TOD.

P205 - ROLE OF PROTEINURIA and HYPERTENSION IN REFLUX NEPHROPATHY

SEVGI YAVUZ, ALI ANARAT, AYSUN KARABAY BAYAZIT
CUKUROVA UNIVERSITY

Introduction: In this prospective study we aimed to determine the patients with vesicoureteral reflux (VUR) carrying risk for development of reflux nehropathy (RN).

Material and methods: Seventy-six children (27 boys and 49 girls) longer than 120 cm with primary VUR were enrolled into the study. Microalbuminuria (urinary microalbumin≥30 mg/g creatinine) was regarded as the major indicator of reflux nephropathy and patients were divided into two groups according to the presence of microalbuminuria (MA). Ambulatory blood pressure monitorization (ABPM) was applied to all patients. ABPM measurements were standardized to age and height with LMS method. MA (+) and MA(−) groups were compared according to z scores.

Results: Systolic (24 hour and night), diastolic (24 hour) and mean arterial pressure (day, night and 24 hour) measurements were significantly higher in MA(+) group ($p<0,05$).

Conclusions: Microalbuminuria and hypertension are valuable predictors of RN in VUR. Follow-up of children with serial ABPM and urine microalbumin tests seems to be reasonable in order to identify the high risk group.

P206 - IMPACT OF ENDOTHELIAL DYSFUNCTION ON LEFT VENTRICULAR HYPERTROPHY IN CHILDREN WITH CHRONIC KIDNEY DISEASE

DROZDZ DOROTA[1], KORDON ZBIGNIEW[2], KWINTA PRZEMKO[3], BERSKA JOANNA[4], ZACHWIEJA KATARZYNA[1], MIKLASZEWSKA MONIKA[1], RUDZINSKI ANDRZEJ[2], SZTEFKO KRYSTYNA[4], PIETRZYK JACEK A.[1]
[1]*DIALYSIS UNIT JAGIELLONIAN UNIVERSITY MEDICAL COLLEGE, KRAKOW*
[2]*DEPT. OF PEDIATRIC CARDIOLOGY, JUMC*
[3]*DEPT. OF PEDIATRICS, JUMC*
[4]*DEPT. OF CLIN. BIOCHEMISTRY, JUMC*

Introduction: Cardiovascular diseases are the most common cause of morbidity and mortality among patients with chronic kidney disease (CKD). Endothelial cells play a key role in vascular homeostasis, so theirs dysfunction represents an early step in atherosclerosis and predicts cardiovascular complications. Left ventricular hypertrophy (LVH) is also an important cardiovascular risk factor. The aim of the study was to evaluate the relation of selected endothelial dysfunction biomarkers to the impairment of renal function as well as to LVH in children with CKD stage 2–5.

Material and methods: Study covered 71 children (44 M, 27 F) with CKD stage 1–5 at mean age of 11 yrs (SD=5), and eGFR 32 ml/min/1,73 m2 (SD=27). Serum creatinine, cystatin C, thrombomodulin, ADMA, oxy LDL and carbonyl levels were measured. LVM and LVMI were evaluated echocardiographically using HP 5500 device. Patients were divided into 4 groups according to CKD stage 1–2; 3; 4 and 5.

Results: Significant correlation between cystatin C and thrombomodulin ($r=0.775$; $p<0.001$), ADMA ($r=0.42$; $p=0.002$), oxy LDL ($r=0.4076$; $p=0.002$) and carbonyl level ($r=0.37$; $p=0.01$) were found. Serum creatinine correlated significantly with thrombomodulin ($r=0.74$; $p<0.001$), ADMA ($r=0.4$; $p=0.001$), oxy LDL ($r=0.41$; $p<0.001$) and carbonyl level ($r=0.27$; $p=0.045$). GFR correlated inversely with thrombomodulin ($r=-0.65$; $p<0.001$) and ADMA level ($r=-0.25$; $p=0.046$). 34 patients showed LVH (3 - CKD stage 1–2; 7 - stage 3; 10 - stage 4; 14 - stage 5). LVM (SD) correlated significantly with oxy LDL level ($r=0.299$; $p=0.016$). In children with LVH significantly higher oxy LDL level (93.3 vs. 77.6 U/L; $p=0.025$) and thrombomodulin (12.94 vs. 8.91 ng/ml; $p<0.001$) were noted.

Conclusions: The study showed the contribution of progressive endothelial dysfunction, expressed as elevated

levels of thrombomodulin and ADMA in children with CKD stage 2 to 5, to left ventricular hypertrophy.

P207 - Urinary α- glycosidase and β2-microglobulin as markers of renal damage in patients with vesicoureteral reflux and renal parenchymal damage

NATALIA ZAICOVA, JANA BERNIC, VICTORIA CIOLAC, ELENA CRUSHENITSKAIA, OLGA IVANCENCO
INSTITUTION OF SCIENTIFIC RESEARCH, MOTHER AND CHILD CARE

Introduction: To investigate whether urinary excretion of α-gl and β2m may help to assess the degree of tubular damage and of tubulointerstitial dysfunction in patients with vesicoureteral reflux (VUR).
Material and methods: 71 patients aged 1 to 14 years (52 females) with VUR were enrolled in the study. All patients had standard clinical and laboratory examination, ultrasound, X-ray and renal DMSA scan. Children were divided into 3 groups depending on the degree of renal scars and reflux nephropathy (RN): I (n=9): VUR without scars, II (n=41): VUR with mild RN (scars 1–3), and III (n=21): VUR with severe RN (> 3 scars). Ten healthy children served as controls. Urinary excretion and ratios over creatinine of neutral α-gl and β2m were measured by ELISA.
Results: All patients with VUR demonstrated significantly elevated urinary excretion of α-gl and β2m as compared to controls ($p<0.05$). We found an association between the level of α-gl and β2m in the urine and severity of kidney damage and RN: the levels of α-gl and β2m in the urine of children with severe RN were 2 times higher than in the control group ($p<0.05$). In patients with mild RN the urinary levels of α-gl and of β2m were lower than in the group of children with severe kidney damage ($p>0.05$). In the group of children with no signs of RN the levels of α-gl and of β2m were lower than in the patients with severe RN and mild RN ($p <0.05$).
Conclusions: Excretion of α-gl and of β2m in patients with VUR depends on the degree of RN. These proteins can therefore be considered as easily available and early markers of pathological changes of the basement membrane and of tubular function, thus of renal tissue damage. We therefore recommend determination of α-gl and of β2m for initial work up of children with VUR.

P208 - ACUTE PYELONEPHRITIS AND THE INCIDENCE OF THE SYMPTOMS

VALBONA STAVILECI
PEDIATRIC CLINIC, UCC OF KOSOVA

Introduction: Differentiation of non-complicated urinary tract infections versus complicated infections like pyelonephritis is not always simple. Diagnosis and the right time management are extremely important especially if we consider the risk of permanent kidney damage.
Material and methods: To analyze the clinical and laboratory signs also radiological presentation of the disease in children diagnosed with acute pyelonephritits Methods. Among cases admitted to Nephrology Unit diagnosed as pyelonephritis acuta, during 2010, we analyzed presentation symptoms by age, inflammatory laboratory results, protein degradation products, urine and kidney ultrasound findings.
Results: Among of 83 cases with urinary tract infections, 27 (32.5 %) were diagnosed as pyelonephritis acuta. Duration of infection before hospitalization was the same regardless of age or gender. Repeated urinary tract infections were more frequent in the preschool age. Acute pyelonephritis by gender was more frequent in infants and preschool age in males and school age of the female gender. 29.6 % of the cases were male and 70.3 % of the cases were female. Inflammatory parameters (SE) were high in 88.8 % of cases and the value of above 100 mm/h was in 20.8 % of cases. Dominated presentation symptoms were high temperature in 66.6 % (all ages), abdominal pain in 29.6 % (age school), nausea 14.8 % (preschool ages), burn during urination in 18.5 % (ages school), frequent urination 11.1 %, swelling (school age) 7.4 %, back pain in the 7.4 % of cases. Dominated casts in the sediment of urine were leukocytes, proteins were positive, while bacteria and erythrocytes were positive only to preschool age. Degradation products of protein were increased 44.4 % of cases that explains deteriorated function of the affected kidney. Ultrasound examination of the kidneys resulted normal in 18.5 % of cases, 37 % had pyelonephritic changes. While the sign of urinary stasis was found in 51.8 % cases and from these 40.7 % of cases were up to the school age and 11.1 % were among school age.
Conclusions: In cases with high temperature should be planned examination of urine sediment and an ultrasound examination of abdominal organs, before we plan any other examination.

P209 - Use of urinalysis as a screening tool for asymptomatic infants

GAMZE BEREKET, GÜNSELI BOZDOĞAN, EBRU TUĞRUL SARIBEYOĞLU, MÜJDE ARAPOGLU, ALPAY ÇELIKER
ACIBADEM UNIVERSITY

Introduction: The utility of screening urinalysis in asymptomatic children has been questioned based on studies done in school age children or adolescents showing that it is not

cost effective and generates unnecessary discomfort on family. AAP recommended to abandone this screening in 2007 but many pediatricians perform screening urinalysis at some point during childhood. There is no data evaluating the utility of screening urinalysis during infancy.
Material and methods: Thus, we retrospectively reviewed results of screening urinalysis done in infants at 6–18 months of age who had regular medical care since birth at our center. Infants with a ICD-10 diagnostic code for routine pediatric exam (Z00.1) and a urinalysis which was requested with this code on the same date were included. Patients with a prior history of urinary tract infection, stone disease, prenatal or postnatal hydronephrosis were excluded. A total of 683 patients met the inclusion criteria.
Results: 44 (6 %) babies had an abnormal urinalysis. The most common abnormality (n: 39, 5,7 %) was pyuria with or without bacteriuria on microscopic exam. Of these 39 babies, 5 had a repeat urinalysis only, 18 had a repeat urinalysis with urine culture, and 16 had a urine culture alone. Only 6 (0,87 % of total) patients were given antibiotic treatment after these tests. All 6 babies who received treatment had an ultrasound which was normal and 2 patients had a VCUG which were also normal. 85 % of babies who had pyuria were female. The other abnormalities detected were microscopic hematuria and proteinuria. All of these 5 patients had a repeat urinalysis which were normal.
Conclusions: In summary, screening urinalysis results were abnormal in 6 % of the babies, but in 86 % of those, abnormalities were transient. These data constitute a new evidence that screening urinalysis during infancy also is unjustified supporting the AAP 2007 recommendations to discontinue screening.

P210 - OUTPATIENT PELVIC FLOOR THERAPY (BIOFEEDBACK) COMPARED TO ANTICHOLINERGIC TREATMENT IN GIRLS WITH OVERACTIVE BLADDER DYSFUNCTION.

CHEBL MOURANI, NEHME NEHME, BERNARD GERBAKA
HOTEL DIEU DE FRANCE (HDF)

Introduction: We compared in a prospective and randomized study the treatment of girls with overactive bladder dysfunction. The first group (A) was treated by using an outpatient pelvic floor therapy program consisting of voiding and drinking schedule, pelvic floor relaxation biofeedback, instruction and toilet behavior. The second group (B) was treated with a more conventional treatment using anticholinergic drugs only.
Material and methods: The files of 52 girls (age between 4 and 12 years) with high suspicion of overactive bladder (OBA) were analyzed. OBA was suspected on clinical symptoms (voiding Score) and after radiological investigations including bladder evaluation by ultrasound (pre and post voiding volume, thickness of the bladder) and voiding cystogram. Patients with high grade reflux IV and V were excluded from this study. Twenty six girls in group (A) received conventional treatment while 26 girls in group (B) were treated with a conservative treatment (Biofeedback and toilet behavior). No significant difference was noted between both groups neither in the percentage and degree of reflux, nor in the number of previous episodes of UTI.
Results: After six months of treatment and follow-up in both groups, the data was collected and analyzed. That same data was validated and completed in only 18 patients from group (A) and 17 patients from group (B). Two UTI episodes were reported in Group (A) compared to 3 episodes in group (B). Bladder capacity and day-time incontinence improved in 16 patients from group (A) compared to 15 patients from group (B). Four patients receiving anticholinergics were excluded from the study due to drowsiness, blurred vision and impairment of cognitive function
Conclusions: This study demonstrated that biofeedback therapy alone was as efficient as classical treatment on improvement of voiding dysfunction (VD) and number of UTT. Pelvic-floor exercise is a physiotherapeutic, noninvasive treatment. Biofeedback should be included in the treatment of girls with OAB and UTI. Finally, Biofeedback treatment avoids using anticholinergic treatment which may be responsible for serious neurological side effects.

P211 - Prevalence and quality of life of Slovenian children with primary nocturnal enuresis

KATJA KARNIčNIK, NASTJA KOS, ALENKA KOREN, NATAšA MARčUN VARDA
UNIVERSITY CLINICAL CENTRE MARIBOR

Introduction: The purpose of our study was to get epidemiologic data about enuresis and influence of enuresis on the quality of life of Slovenian children and adolescents.
Material and methods: Prospective epidemiologic study was performed in Slovenia in 2011 and was supported with two questionnaires. The first questionnaire was distributed among primary school population that included 1248 children from 6 to 15 years. The second questionnaire included 44 children, who have been treated for enuresis in Nephrology Unit of our Department of Paediatrics.
Results: Enuresis was diagnosed in 12.4 % of all children, 11.8 % in girls and 13.0 % in boys. There was evident linkage between the appearance of enuresis in children and their relatives ($\chi 2=124{,}933$, $p=0{,}0$). The study also showed that enuresis influences the quality of life in nearly half of the children questioned who mentioned disorder. Disorder restricts them mostly in relations with coevals. 52.4 % of

them confessed that none of their friends knew about their bedwetting problem and 40.9 % of children with enuresis have already tried to hide bedwetting problem. Answers about some psychosocial characteristics have shown that enuresis is not as impeding as expected. We have also found out that enuresis is not well-known in general population of children.

Conclusions: We found out that the prevalence of enuresis in Slovenia is comparable to prevalence in other countries. General lack of knowledge about enuresis is still a big problem. Despite the data about worse quality of life of children with enuresis, more than a half of children questioned in a survey think that enuresis does not affect their lives.

P212 - the effects of desmopressin treatment on urine and blood electrolytes in children with primary enuresis nocturna

NESRIN TAŞ, KIBRIYA FIDAN, YAŞAR KANDUR, OĞUZ SÖYLEMEZOĞLU
GAZI UNIVERSITY FACULTY OF MEDICINE

Introduction: Electrolyte disturbances after desmopressin treatment has been reported in children with various disease including diabetes insipidus and nocturnal polyuria.. However data on the effects of desmopressin on water/electrolyte disturbances about children with primary monosymtomatic nocturnal enuresis (PMEN) is rare. In the present study we aimed to evaluate the effect and tolerability of desmopressin on blood and urine electrolytes and osmalality in primary monosymptomatic enuresis nocturna.

Material and methods: Thirty five children with PMEN between the ages of 5 and 15 years were included in the study. The patients were asked for collecting daytime urine volume and informed about the night time fluid restriction before starting the desmopressin melt tablet. Urinary and blood osmolalities, urinary and blood sodium, potassium, calcium and spot urine sodium/creatinine, calcium/creatinine values were determined before and on the third and seventh days after begining the treatment.

Results: 35 patients were included in the study. 21 patients (%60) were boys, and 14 (%40) were girls. The mean age was 9,6±2,7. Blood sodium values were 137 (135–141) mEq/L before the treatment, 138 (133–141) mEq/L on the third, 137 (134–141) mEq/L on the seventh days of treatment respectively. No significant changes were determined on blood sodium values. Blood osmolality values were 266,5 (231–328) mOsml/kg H2O at the beginning, 260,5 (235–368) mOsml/kg H2O on the third, 265,5 (244–342) mOsml/kg H2O on the seventh days respectively. No significant changes were determined on blood and urine osmolality values. Urine calcium/creatinine values were 0,03 (0,01-0,24) mg/mg at the beginning, 0,06 (0,01-0,24) mg/mg on the third, 0,04 (0,01-0,17) mg/mg on the seventh days respectively. No significant changes were determined on urine calcium/creatinine values.

Conclusions: Desmopressin was well tolereted, safe and effective treatment in children who were matching of fluid intake restriction proposal with PMEN.

P213 - LONG-TERM FOLLOW-UP OF CHILDREN WITH NOCTURNAL ENURESIS

AN-SOFIE GOESSAERT[1], BENTE SCHOENAERS[2], KAREL EVERAERT[1], JOHAN VANDE WALLE[3]
[1]*UROLOGY, UNIVERSITY HOSPITAL GHENT, BELGIUM*
[2]*GHENT UNIVERSITY, BELGIUM*
[3]*PEDIATRIC NEPHROLOGY, UNIVERSITY HOSPITAL GHENT, BELGIUM*

Introduction: There seem to be several similarities between nocturnal enuresis and nocturia. In both conditions, bladder dysfunction and nocturnal polyuria are important underlying pathogenetic mechanisms; also an important impact on cognitive functioning and quality of life is observed. Since this overlap in pathogenesis and comorbidities and the lack of research on the occurrence of both conditions in one patient, this study aims to investigate the prevalence of nocturia and other urinary symptoms in patients who have suffered from nocturnal enuresis.

Material and methods: A questionnaire was sent to 1265 patients treated between 3 and 15 years ago in the University Hospital of Ghent for nocturnal enuresis evaluating past treatment for and current status of enuresis and validated questionnaires on urinary incontinence (ICIQ-UI) and overactive bladder symptoms (ICIQ-OAB). Participants were asked to send back the completed questionnaire with the informed consent.

Results: A completed questionnaire was sent back by 364 subjects (28,8 %). Nocturia is reported by 130 of 362 subjects (35,7 %). Comparing the nocturic group to the non-nocturic group, mean age is 18,11 (SD 3,713) and 16,74 (SD 2,771) ($p<0,000$), sex distribution (male/female) is 1,13 and 2,00 ($p<0,008$) and nocturia frequency in the nocturic group is 1,16 (SD 0,404). Voiding frequency in daytime, urge and urinary incontinence have a significantly higher prevalence in patients with nocturia compared to those without nocturia. The associated bother is systematically scored higher in the nocturic group. No correlation can be found between the presence of nocturia and type of treatment received for nocturnal enuresis. Logistic regression analysis shows a higher odds for nocturia in male enuretics ($p<0,007$) and with increasing age ($p<0,000$).

Conclusions: Over one out of 3 former enuretic patients develops nocturia, often accompanied by other urinary symptoms and with significant bother. Some of these

patients might benefit from continuous treatment, even after resolution of nocturnal enuresis.

P214 - Prevalence of vesicoureteral reflux in pyelonephritis and changes of sensitivity to antibacterial therapy

BIRUTE PUNDZIENE[1], JURGITA ANUZIENE[1], VIDAS DRUSKIS[2], AUGUSTINA JANKAUSKIENE[2]
[1]*HOSPITAL OF LITHUANIAN UNIVERSITY OF HEALTH SCIENCES, KAUNAS, LITHUANIA*
[2]*VILNIUS UNIVERSITY, VILNIUS UNIVERSITY CHILDRENS HOSPITAL, VILNIUS, LITHUANIA*

Introduction: Objective: To identify prevalence of vesicoureteral reflux in pyelonephritis; to determine, whether the range of germs and sensitivity to antibacterial preparations have changed.
Material and methods: We investigated 239 children, aged from 1 month to 7 years, with acute pyelonephritis, treated in two University hospitals of children in 2009. Acute pyelonephritis was diagnosed according fever>380 C, bacteriuria≥105 colony-forming units/ml, leukocytosis, CRP> 20 mg/l and ultrasound changes.
Results: Pyelonephritis was diagnosed in girls more often comparing with boys, 71.1 % and 28.9 %, respectively. Boys had pyelonephritis more often than girls only under age of six months (52.2 % and 12.9 %, χ^2 0,00). Micturating cystourethrogram was performed in 50 % (55/110) of children under age of one year and in 58.6 % (34/58) of children under the age of six months. Vesicoureteral refluxes were diagnosed in 29.7 % of all cases. Vesicoureteral refluxes commonly diagnosed in children under 6 months of age were 35.3 % (12/34). Vesicoureteral refluxes were diagnosed in 42.9 % (9/21) of boys at the same age. The most frequently diagnosed II0 36,8 % (χ^2 0,00), while the III0 10,5 % and high degree (IV-V0) vesicoureteral refluxes were 13.2, 2.6 % of children respectively. The main cause of the pyelonephritis remained E. Coli (83.3 %), Klebsiella (2.3 %), Enteroccocus (1.7 %), Pseudomona (1.7 %) etc. E. Coli sensitivity to ampicillin was only 51 %, gentamicin 91.8 %, cefuroxime 92.5 %, nitrofurantoin 93.2 % and trimethoprim 74.8 %.
Conclusions: One-third of children, who have undergone micturating cystourethrogram, identify vesicoureteral refluxes. This corresponds to many authors. The II0 vesicoureteral refluxes are the most frequently diagnosed. E. Coli remains the main germ of pyelonephritis in our country for several decades. As E. colli is insufficiently sensitive to ampicillin, it is not suitable for initial treatment of pyelonephritis.

P215 - What antibiotic should be used to start the treatment of acute pyelonephritis in children? The study of regional resistance of microbes in the Czech Republic, Olomouc region.

HANA FLÖGELOVA[1], MARIE ROHANOVA[1], MILAN KOLAR[2], JANA ZAPLETALOVA[3]
[1]*DEPT. OF PAEDIATRICS, UNIVERSITY HOSPITAL AND FACULTY OF MEDICINE AND DENTISTRY, PALACKÝ UNIVERSITY OLOMOUC, CZECH REPUBLIC*
[2]*DEPT. OF MICROBIOLOGY, UNIVERSITY HOSPITAL AND FACULTY OF MEDICINE AND DENTISTRY, PALACKÝ UNIVERSITY OLOMOUC, CZECH REPUBLIC*
[3]*DEPT. OF MEDICAL BIOPHYSICS, UNIVERSITY HOSPITAL AND FACULTY OF MEDICINE AND DENTISTRY, PALACKÝ UNIVERSITY OLOMOUC, CZECH REPUBLIC*

Introduction: Initial antibiotic therapy for acute pyelonephritis (APN) should be based on regional resistance of the most common agents causing urinary tract infections (UTIs). In the Czech Republic, the most commonly administered agents are combined aminopenicillins (AINs) or second-generation cephalosporins. The aim of the study was to compare the resistance of microbes causing APN to cefuroxime (CRX) and combined AIN. In addition, resistance of pathogens to co-trimoxazole (COT) and nitrofurantoin (FURA), used for prophylaxis of UTIs, was compared.
Material and methods: A retrospective study of medical records of children hospitalized for the first and/or second attack of APN in 2009–2011. Complete data were obtained for 121 attacks of APN (of which 45 were in boys) in children aged 0.5 month to 18 years and 10 months (a median of 11 months).
Results: The most common initial antibiotics were CRX (98x, 81 %) and combined AIN (17x, 14 %). The pathogens causing APN were Escherichia coli (106x), Enterococcus spp. (6x), Klebsiella pneumoniae (4x), Pseudomonas aeruginosa (2x) and Klebsiella oxytoca, Serratia marcescens and Enterobacter spp. Resistance to CRX was in 16 attacks (13.2 %) and to AIN in 32 attacks (26.4 %); resistance to both CRX and AIN in 10 attacks of APN. McNemar's test showed significantly higher prevalence of resistance to AIN as compared with CRX ($p=0.004$). Resistance of microbes to COT was found in 30 attacks and to FURA in 8 attacks; resistance to both COT and FURA was observed in 4 attacks of APN. Resistance to COT was significantly more prevalent than resistance to FURA ($p<0.0001$).
Conclusions: For initial therapy of APN in children from the Region of Olomouc, cefuroxime is more suitable than combined aminopenicillin, for the significantly lower resistance rates. For prophylaxis of UTIs, nitrofurantoin is more suitable than co-trimoxazole if susceptibility of the particular etiological agent is unknown.

P216 - Relationship of sleep and life quality with children monosymptomatic enuresis nocturna by using actigraphy

SENEM ALKAN[1], PELIN ERTAN[2], GÖKHAN TEKIN[1], HASAN YÜKSEL[3], ÖZGE YILMAZ[3], HIKMET YILMAZ[4]
[1]*CELAL BAYAR UNIVERCITY SCHOOL OF MEDICINE DEPARTMENT OF PEDIATRICS*
[2]*CELAL BAYAR UNIVERCITY SCHOOL OF MEDICINE DEPARTMENT OF PEDIATRIC NEPHROLOGY*
[3]*CELAL BAYAR UNIVERCITY SCHOOL OF MEDICINE DEPARTMENT OF PEDIATRIC ALLERGY*
[4]*CELAL BAYAR UNIVERCITY SCHOOL OF MEDICINE DEPARTMENT OF NEUROLOGY*

Introduction: Monosymptomatic enuresis nocturna (MNE) is a condition of reccurent incontinence on the bed or clothes while sleeping. Actigraph is a device which can detect activity through measuring sleep and wake patterns by motion-sensitive microsensors. The aim of the study is; to expose the general quality of life and sleep disturbance of children with enuresis using subjective methods and investigate the effects of sleep disorders with an actigraphic values for MNE.

Material and methods: 40 children who attended Celal Bayar university school of medicine department of pediatric nephrology with MNE and 20 healthy children were included to study. Quality of life (KINDL) and Pittsburg Sleep Quality Index (PSQI) surveys have been filled out for all children. Families have filled-out sleep diaries .For seven consecutive days actigraphic sleep analysis has been applied in conjunction with sleep diaries.

Results: 'Self-esteem', 'Family', 'School' and 'Friends' relationships of MNE were statistically significantly lower ($p<0.05$) than healthy children. No significant difference was determined for 'physical and emotional well-being' between two groups ($p>0.05$). All the parameters related to PSQI were significantly lower in children with MNE ($p<0.05$). 'Actual Wake Time', 'Number of Gap' and 'Sleep Fragmantation Index' were found significantly higher in MNE group ($p<0.05$). 'Sleep efficiency' and 'Actual Sleep Time' were found statistically significantly lower in enuresis group ($p<0.05$). 'Total Activation Score' parameter did not show reasonable difference ($p>0.05$).

Conclusions: Actigraph analysis, an easily applied, non-invasive and objective sleep evaluation method indicates that children with MNE cannot have a continuous, high quality sleep and hence they need to rest during the day due to their insufficient and divided sleeps at nights. All of these factors affecting the sleep of enuretic children reduce their life and sleep quality. Practical usage of actigraphic analysis which doesn't require hospitalization with its low cost makes it a popular candidate to be used as an alternative to polysomnography which is the gold standard of sleep disorders.

P217 - Sleep pattern and cognitive dysfunction in patients with nocturnal enuresis associated with nocturnal polyuria?

CHARLOTTE VAN HERZEELE[1], KARLIEN DHONDT[2], ANN RAES[1], PIET HOEBEKE[3], JOHAN VANDE WALLE[1]
[1]*PEDIATRIC NEPHROLOGY, UNIVERSITY HOSPITAL GHENT, BELGIUM*
[2]*CENTRE FOR NEUROPHYSIOLOGICAL MONITORING, UINIVERSITY HOSPITAL GHENT, BELGIUM*
[3]*PEDIATRIC UROLOGY, UNIVERSITY HOSPITAL GHENT, BELGIUM*

Introduction: There is a comorbidity and a possible causality between nocturnal enuresis (NE), sleepdisorders and attention deficit-hyperactivity disorder (ADHD), as suggested by CK Yeung, a theory that has not yet been confirmed, although we found some correlation in an extremely therapy resistant population. If the mismatch between nocturnal diuresis/functional bladdervolume, resulting in enuresis has a negative effect on cognitive function and sleep characteristics, then an effective anti-enuretic therapy should ameliorate these comorbid symptoms. This prospective study evaluates the beneficial impact of desmopressin melt on sleep, ADHD-symptoms, cognition, quality of life and self-esteem in a random enuresis-population.

Material and methods: 33 patients aged 6–16 years with MNE according to the ICCS criteria, who experience at least 4/7 wet days with proven nocturnal polyuria(NP), defined as nocturnal diuresis >100 % bladder volume for age. Patients are tested before the start of desmopressin melt and 6 months later. It is a multi-informant multi-method study, using polysomnography, questionnaires, interviews and neuropsychological testing. Results at screening visit are now available.

Results: Patients have a significantly disrupted sleep, 29 of 33 (87,88 %) children had greater than 5 periodic limb movements per sleep hour (normal PLMS index). The PLMS index ranged between 3.6 and 23.3, mean 10.82 +/− 4.83. 9.1 % were diagnosed with the full syndrome of ADHD, 3 % with the ADHD hyperactive/impulsive subtype and 18.2 % met the criteria of the ADHD inattentive subtype. In total 10 of the 33 (30.3 %) children were diagnosed with ADHD.

Conclusions: The preliminary results of the screening data reveal increased prevalences of both PLMS index and ADHD in children with NP in a population of nocturnal enuresis. Although there might be a selection bias of the recruitment in a tertiary study-population, patients did not have the clinical history of therapy resistance as in previous reports.

P218 - Reliability of the Flemish Version of the Pediatric Incontinence Questionnaire (PinQ)

ELKE DE BRUYNE[1], CHARLOTTE VAN HERZEELE[1], ELINE VAN HOECKE[1], JETTY BORCHERTS[2], ALEXANDER MINNAERT[1], JOHAN VANDE WALLE[1]
[1]*PEDIATRIC NEPHROLOGY, UNIVERSITY HOSPITAL GHENT, BELGIUM*
[2]*EDUCATIONAL SCIENCES, UNIVERSITY OF GRONINGEN, THE NETHERLANDS*

Introduction: The Pediatric Incontinence Questionnaire (PinQ) is a reliable and valid cross-cultural tool to assess and measure the health related quality of life (HRQoL) in children and adolescents with urinary incontinence. The primary aim was to adapt the Dutch version of the PinQ and to test the reliability of the Flemish version. A secondary aim was to compare the self-reported (child) version with the proxy (parent) version.

Material and methods: This cross-sectional study was conducted at the Department of Pediatric Nephrology from the University Hospital of Ghent, a tertiary referral center for childhood urinary incontinence. From September 2009 to April 2011 a total of 64 children (46 M / 18 F, M=9.6 y, SD=2.89 with an age range of 5 – 17 year) with (non-) monosymptomatic enuresis and their parents participated in this study, by completing a self-reported or proxy Flemish version of the PinQ twice with an interval of 2 weeks.

Results: Internal consistency reliability showed a Cronbach's α of 0.93 for the self-reported versions and 0.83 for the proxy versions. Reproducability using a test-retest interval of 2 weeks was satisfactory for the self-reported and proxy versions (ICC 0.88, 95 % CI 0.78-0.93 and 0.70, 95 % CI 0.51-0.83, respectively). The ICC for interrater convergence between the self-reported and proxy versions was 0.63, which shows a moderate agreement. There was no significant difference between girls and boys in mean total scores.

Conclusions: The Flemish version of the PinQ proved to be reliable to assess HRQoL in children and adolescents with (non-)monosymptomatic enuresis. The results revealed a moderate agreement between children and parents on their perception of the influence of incontinence on HRQoL.

P219 - A SUCCESSFUL STRATEGY FOR CHILDREN WITH REFRACTORY OVERACTIVE BLADDER SYNDROME: AN INPATIENT BLADDER REHABILITATION PROGRAM

SNAUWAERT EVELIEN[2], VANDE WALLE JOHAN[1], CATHERIN RENSON[3], VANDAELE JOHAN[1], RAES ANNE[1], VAN LAECKE ERIK[3], DEBRUYNE ELKE[1], ROELS SANNE[4], DEGUCHTENAERE ANNE[1], HOEBEKE PIET[3]
[1]*GHENT UNIVERSITY - PEDIATRIC NEPHROLOGY*
[2]*GHENT UNIVERSITY - ASSISTANT PEDIATRICS*
[3]*GHENT UNIVERSITY - PEDIATRIC UROLOGY*
[4]*GHENT UNIVERSITY - DEPARTMENT OF DATA ANALYSIS - FACULTY OF PSYCHOLOGY*

Introduction: Despite empiric management, a group of children with overactive bladder syndrome (OAB) fails to improve bladder and voiding functions. To approach the need for new strategies for children with refractory OAB, the Ghent University hospital set up an inpatient bladder rehabilitation program (RBP). In this study, we aims to evaluate the outcome of this RBP for children with refractory OAB.

Material and methods: The charts of all children (N=357) with refractory OAB who followed RBP between 2000 and 2010 were reviewed at 6 periods of time: at 1st consultation, at entry and completion of RBP and 3, 6 and 12 months after RBP. To evaluate the outcome of RBP, continence, enuresis (eVS, score of 1 to 9; 1=dry, 9=7/week) and daytime incontinence voiding scores (dVS, score of 1–10; 1=dry, 10= >7/week) and maximal voiding volume (maxV) were registered at each time period. Linear mixed models (through proc mixed, Statistical Analysis Software, SAS®) were used to account for the longitudinal character of the data.

Results: RBP in children with refractory OAB resulted in a spectacular increase of dryness (<1 % at entry RBP to 26.6 % 1 year after RBP). A decline in the proportion of children (68.2 % to 22.9 %) with combined daytime & night incontinence was found. RBP resulted in a decline of the severity of the incontinence problems: a significantly improvemend in eVS and dVS of 3.8 and 3.6, respectively, was found. Children who are younger, are boys, have nocturnal polyuria, have dysfunctional voiding or encorpresis had a significantly unfavorable results.

Conclusions: RBP is a successful treatment modality and resulted in an spectacularly increase of dryness. An important shift from combined and severe to isolated and mild forms of incontinence was found. In contrast to the other new strategies, this is a 100 % safe therapy with good long-term effects.

P220 - LOWER URINARY TRACT DYSFUNCTION IN YOUNG ADULTS. PRELIMINARY RESULTS

MARTA FERNáNDEZ FERNáNDEZ, LIZBELY DAYANA MORENO DUQUE, JORGE MARTíNEZ SáENZ DE JUBERA, VANESSA FERNáNDEZ IGLESIA, ELENA HIERRO DELGADO, ESTíBALIZ GARRIDO GARCíA, PABLO LOBO MARTíNEZ, LUIS MIGUEL RODRíGUEZ FERNáNDEZ
COMPLEJO ASISTENCIAL UNIVERSITARIO DE LEóN

Introduction: Voiding disorders are relatively frequent among children. There is limited information about the prevalence of these conditions at the onset of adulthood. The goal of this study is to determine the prevalence of lower urinary tract (LUT) dysfunction symptoms in a group of young adults in our context.
Material and methods: 85 students (10 males) enrolled at the College of Nursing of the University of León (age range: 19–39; median: 20 years), responded to an anonymous survey about LUT symptoms (ICCS terminology) that included information about the existence of: - voiding frequency - Day-time / nocturnal incontinence - Urgency, holding manoeuvres and/or nocturia - Hesitancy, alterations of stream - LUT pain, bladder tenesmus - Post-micturition dribble - Constipation and encopresis - Treatment in case they had suffered any kind of urinary disorder.
Results: 34 out of the 85 students admitted having some form of LUT symptoms (40 % overall, 42.6 % of women). Among males, only one reported decreased voiding frequency and straining during urination; a second reported nocturia. Most common LUT symptom was nocturia (23/75 females, 1/10 males). 10 of the 75 females (13.3 %) suffered urgency; in 7 of them it was accompanied by holding manoeuvres. None showed nocturnal enuresis. Only one woman reported day-time incontinence. More infrequent symptoms were: increased (3/73 females) or, decreased (1/73 females and 1/10 males) voiding frequency, straining (3/85) or genital pain and/or bladder tenesmus (2/85). None reported alterations of the stream or encopresis. Four students reported suffering constipation. None of the 34 students with LUT symptoms had undergone treatment.
Conclusions: The results indicate a high frequency of LUT symptoms among the participants, as well as the complete absence of therapeutic intervention. More than 10 % of the young women reported urgency, which probably correlates with overactive bladder. Nocturnal enuresis seems to be an unusual disorder in our context.

P221 - CAN WE USE NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN AS A KIDNEY DAMAGE MARKER IN CHILDREN WITH VESICOURETERAL REFLUX?

SELİM BATMAZ[1], ALİ DELİBAŞ[1], NECATİ MUŞLU[2], FATMA KARAZİNDİYANOĞLU[2], BAHAR TAŞDELEN[3]
[1]MERSIN UNIVERSITY MEDICAL FACULTY DEPARTMENT OF PEDIATRIC NEPHROLOGY, MERSIN, TURKEY
[2]MERSIN UNIVERSITY MEDICAL FACULTY DEPARTMENT OF BIOCHEMISTRY, MERSIN, TURKEY
[3]MERSIN UNIVERSITY MEDICAL FACULTY DEPARTMENT OF BIOSTATISTICS, MERSIN, TURKEY

Introduction: In this study urinary and plasma Neutrophil Gelatinase-Associated Lipocalin (NGAL) were evaluated as two potential biomarkers for determining the kidney damage in patients with primary vesicoureteral reflux (VUR).
Material and methods: A total of 49 patients aged between 3 months-17 years (21 male, 28 female) with VUR were enrolled in the study. The patients who had urinary tract infection (UTI) in the last 3 months were excluded from the analysis. The control group was consisted of 34 patients who experienced previous UTI without VUR and renal scarring. Plasma and urine NGAL, plasma Cystatin C levels, blood and urine samples were analized. Glomerular filtration rate (GFR) and proteinuria levels were measured.
Results: The patients having VUR with renal damage had shown significantly elevated levels of plasma and urine NGAL, urine NGAL/creatinine and Cystatin C variables when compared to the group having VUR without renal damage ($p<0.001$, $p<0.001$, $p<0.001$, $p<0.001$) and also the levels of all these parameters were increasing with the increment in degree of VUR. The GFR levels of the patients having VUR with renal damage were also decreased significantly ($p<0.001$). Predicting value of probable renal damage of plasma NGAL was 77.4 %, 76 %, 88.1 %, urine NGAL was 76.9 %, 86.9 %, 91.5 %, urine NGAL/creatinine rate was 78.7 %, 86 %, 92.8 %, Cystatin C was 80.3 %, 75.8 %, 84.5 % for the right, left and both kidneys respectively ($p<0.001$). It was shown that plasma NGAL had 90.5 %, urine NGAL had 91.9 %, urine NGAL/creatinine rate had 93.1 %, plasma Cystatin C had 94 % true prediction value for proteinuri ($p<0.001$).
Conclusions: As plasma and urine NGAL levels of the patients having VUR with kidney damage were found to be significantly increased, plasma and urine NGAL levels could be used as noninvasive markers on diagnosing and the follow ups of VUR patients with renal damage.

P222 - COMPARATIVE STUDY OF PEDIATRIC URINARY TRACT INFECTIONS CAUSED BY EXTENDED-SPECTRUM BETA-LACTAMASE-PRODUCING AND NON-PRODUCING BACTERIA

JOHN DOTIS, NIKOLETA PRINTZA, ALEXANDRA MARNERI, CHRYSA GKOGKA, FOTIOS PAPACHRISTOU
1ST DEPARTMENT OF PEDIATRICS, ARISTOTLE UNIVERSITY OF THESSALONIKI, HIPPOKRATIO HOSPITAL

Introduction: In Gram-negative pathogens, beta-lactamase production remains the most important contributing factor to beta-lactam resistance. Extended-spectrum beta-lactamase-producing bacteria (ESBL) are emerging as a cause of urinary tract infections (UTI) worldwide. However, risk factors and clinical parameters have not been defined for

children with ESBL UTI. The aim of the study was to evaluate clinical characteristics and associated risk factors for UTI due to ESBL.

Material and methods: A retrospective analysis of files from children hospitalized with UTI due to ESBL between 01/01/2009 and 31/12/2011 was evaluated. Data were compared with a randomly-selected control group of children, matched by age and sex, with non-ESBL UTI.

Results: In a total of 347 positive urine cultures, 36 (10.4 %) were phenotypically ESBL-producing bacteria, coming from 29 patients (17 boys). Two patients had 3 episodes and three patients had 2 episodes. Although the most frequently isolated microorganism was Escherichia coli in both groups, Klebsiella spp. and Enterobacter cloacae were found to be more frequent in those diagnosed with ESBL UTI (p=0.043 and p=0.047, respectively). There were no significant differences between the groups in demographics, presenting symptoms, underlying disease and laboratory findings. Children with ESBL UTI were hospitalized for a longer duration (9.8 vs. 7.4, days, p=0.004), had higher rates of urinary tract anomalies (48 % vs. 14 %, p=0.0005), UTI prophylaxis (21 % vs. 5 %, p=0.015) and abnormal DMSA findings (45 % vs. 17 %, p=0.03) compared with children suffering from non-ESBL UTI (n=87). There were 2 bacteremias cases each for both groups (p=ns). However, all patients progressed well clinically.

Conclusions: Children with urinary tract anomalies, previous hospitalization and those receiving antimicrobial prophylaxis appear to be at higher risk for ESBL UTI. The recognition of risk factors for UTI, caused by ESBL bacteria in children, may aid in the identification of high-risk cases and may enable proper management of these patients.

P223 - CRANBERRY IN CHILDREN WITH RECURRENT URINARY TRACT INFECTIONS

ANNA COSTA, GIOVANNI PAVONE, CIRO CORRADO, ROSA CUSUMANO, SILVIO MARINGHINI
PEDIATRIC NEPHROLOGY

Introduction: Urinary tract infections (UTI) are frequent in children and often recur. Prolonged antibiotic treatment may produce side-effects and microbial resistance. It has been documented that Cranberry products reduce the number of UTI in adult women. Aim of our study is to determine the efficacy and safety of Cranberry (IVUMIR®) to prevent recurrency of UTI in children

Material and methods: We enrolled 44 children (33 F, 11 M), median age 5.2 years (range 0.6-14 years), with at least two documented episodes of UTI during the six months prior to enrollment. Children with vesicoureteral reflux (VUR) grade III or above, neurogenic bladder and urinary malformation were not included. All patients received IVUMIR ® for six months and were observed for further 6 months without therapy. All children received a renal ultrasonography; and cystography according to the recommendations of the Italian Society of Pediatric Nephrology. An urine analysis and colture were done every 30 days or in case of symptoms suggestive of UTI. We divided our population in two groups according to age: group A (8 F, 8 M from 6 months to 3 years old) and group B (25 F, 3 M from 4 to 14 years old).

Results: In group A no UTI was observed during or after treatment with IVUMIR ® compared to 0.29 episodes/month/pt before it. In group B the number of UTI was 0.27/month/pt before IVUMIR ® and 0.09/month during treatment. Patients with recurrence of UTI were all girls (median age 7.8 years) with high prevalence (89 %) of voiding disorders (VD). No side effects during treatment with IVUMIR ® were detected.

Conclusions: In our study IVUMIR ® was associated with a significant reduction in the number of IVU. In older females, the effectiveness of cranberry is reduced because of high prevalence of VD.

P224 - UNCOMMON CAUSES OF HEMORRHAGIC CYSTITIS

SARA CHOCRON, JOSE MARIA VALLE, PATRICIA MORERA, MARINA MUñOZ, ALVARO MADRID, ENRIQUE LARA, RAMON VILALTA, JL NIETO
HOSPITAL UNIVERSITARI VALL D'HEBRON

Introduction: Macroscopic haematuria is an unusual finding in general population, with 0.13 to 0.41 % of prevalence. In healthy chilhood, urinary tract infections are the most common etiology. In these cases, the pathogens of hemorrhagic cystitis correspond to germs which colonize periurethral area and frequently are enteric bacteria. On the other hand, among the viral causes, the adenovirus is predominantly found. However, other causes must to be studied if the common one were excluded.

Material and methods: We performed a retrospective review of our patients affected by hemorrhagic cystitis secondary a polyomavirus and parasites

Results: We present a series of five clinical cases with special interest for being patients with hemorrhagic cystitis owing to uncommon etiological agents. We analyze the onset, diagnose, treatment and evolution of these five patients who presented with macroscopic heamaturia. The cause of haematuria was an urinary tract infection, 3 of them due to poliomavirus infection (BK and JC) and the rest secondary to parasitic infection (schistosomiasis).

Conclusions: After being excluded the main causes of macroscopic haematuria, uncommon etiology as viral and parasitic urinary tract infeccion have to be studied. The

complete background of the patient, specially epidemiologic aspects, have to be taken into account. Thinking in these etiologies of hemorrhagic cystitis, we will be able to focus the diagnose and offer the specific treatment to our patients.

P225 - EVALUATION OF THE RATE OF TLR-4 ASP299GLY AND THRE399ILE POLYMORPHISIMS AND LEUKOCYTE TLR-4 EXPRESSION LEVELS IN PATIENTS WITH AND WITHOUT POSTPYELONEPHRITIC RENAL SCARRING

MERAL TORUN BAYRAM[1], ALPER SOYLU[1], HALIL ATEŞ[3], SEFA KIZILDAĞ[2], MEHMET ATILLA TÜRKMEN[1], SALIH KAVUKÇU[1]
[1]*DOKUZ EYLUL UNIVERSITY MEDICAL FACULTY, DEPARTMENT OF PEDIATRICS, IZMIR, TURKEY*
[2]*DOKUZ EYLUL UNIVERSITY MEDICAL FACULTY, DEPARTMENT OF MEDICAL BIOLOGY, IZMIR, TURKEY*
[3]*DOKUZ EYLUL UNIVERSITY MEDICAL FACULTY, DEPARTMENT OF INTERNAL MEDICINE, IZMIR, TURKEY*

Introduction: In this study, we aimed to determine the rate of TLR-4 Asp299Gly and Thr399Ile polymorphisms and leukocyte TLR-4 expression level in children with acute pyelonephritis in order to evaluate the association of those parameters with renal scar development.
Material and methods: The study was performed in children with pyelonephritis. Patients with and without renal scarring and control cases were classified as Group 1, Group 2 and Group 3, respectively. All three groups were compared for the rate of TLR-4 Asp299Gly and Thr399Ile polymorphisms determined in genomic DNA obtained from periperal blood samples, and for basal and lipopolysaccharide (LPS) stimulated periperal blood myeloid cell TLR-4 expression levels.
Results: There were 168 patients (86 in Group 1, 82 in Group 2) and 120 control cases. Myeloid cell TLR-4 expression levels were similar in Groups 1 and 2. However, both groups had lower basal and LPS stimulated TLR-4 expression levels than Group 3. While the rate of TLR-4 Asp299Gly polymorphism was not different among the three groups, the rate of TLR-4 Thr399Ile polymorphism was higher in Groups 1 and 2 than in Group 3. Group 1 and Group 2 were not different. Moreover, myeloid cell TLR-4 expression levels were lower in children with TLR-4 Thr399Ile polymorphism than in children without this polymorphism.
Conclusions: Children carrying TLR-4 Thre399Ile polymorphism and/or having low level of leukocyte TLR-4 expression have a tendency to develop pyelonephritis, probably due to difficulty in eradication of bacteria from the urinary system. However, presence of TLR-4 polymorphism or level of TLR-4 expression were not associated with postpyelonephritic renal scarring.

P226 - VOIDING DYSFUNCTION IN PATIENTS WITH URINARY TRACT INFECTION

BURCU BULUM ÖZTÜRK, BIRSIN ÖZÇAKAR, ASLI KAVAZ, MESIHA EKIM, FATOŞ YALÇINKAYA
ANKARA UNIVERSITY SCHOOL OF MEDICINE PEDIATRIC NEPHROLOGY, ANKARA, TURKEY

Introduction: Voiding dysfunction is common in children and the relationship between urinary incontinence and urinary tract infections (UTIs) are well known. Symptom scoring systems have been used for clinical assessment of children presenting with dysfunctional voiding and incontinence symptoms. The aim of this study is to evaluate voiding dysfunction and response to treatment in patients with UTI.
Material and methods: A total of 191 (182 girls, 9 boys) patients who were ≥4 years with the history of at least one UTI were enrolled to the study. All children were evaluated with dysfunctional voiding and incontinence scoring system which composed of 13 symptom questions and 1 quality of life question with a total score ranging from 0 to 35. The patients who had a score of ≥9 (quality of life score is excluded) were considered to have voiding dysfunction. Behavioral therapy (voiding training, timed voiding and toilet posture) were given to all patients with voiding dysfunction and after therapy patients were assessed for the second time with symptom scores.
Results: The mean age of the patients was 8.2±3.1 years (4–17.1). Voiding dysfunction was seen in 111 (58 %) patients and 61 (55 %) were evaluated for the second time after 5.7±2.6 months. 72 % of patients' voiding dysfunction was ameliorated and 23 % was improved. These 61 patients' mean voiding dysfunction symptom score was 16.7±5.5 (9–27) and 78 % of the patients had poor quality of life at the first admission, but in the follow-up score was declined to 5.9±5.5 (0–22) and the percent of patients who had poor quality of life was 34 % at the second control.
Conclusions: This study indicates once more that voiding dysfunction is often accompanied by UTIs, especially in girls. Behavioral therapy is very worthwhile in correcting voiding dysfunction. Symptom scoring systems not only would allow diagnosis of dysfunctional voiding and incontinence symptoms, but also would make monitoring the response to treatment more objective.

P227 - First time Urinary Tract Infection in children. Age, reflux and chemoprophylaxis in relation to renal scars formation.

DESPOINA TRAMMA, GEORGE GERASIMOU, ANGELIKI KLISSARHAKI
ARISTOTLE UNIVERSITY OF THESSALONIKI

Introduction: The aim of our prospective study was to evaluate the clinical and laboratory characteristics of children presented with first urinary tract infection (UTI) and developed renal scars.
Material and methods: Inclusion criteria : a) first incident of febrile UTI, b) two of the following findings : fever> 38.5 ° C, WBC>10.000 cells/mm3, ESR>20 mm/h, CRP> 20 mg/dl, c) absence of congenital urinary abnormalities, except of vescicoureteral reflux (VUR) e) no UTI relapses between the two scintigraphies. 99mTc-Dimercaptosuccinic acid renal scintigraphy (DMSA) was performed within 3 days after admission and if abnormal, then follow-up DMSA was performed after 6–8 months. Cystourethrography was performed 1 month after UTI.
Results: A total of 70 children were enrolled in the study. The main pathogen was E.coli. VUR was found in 21.5 % of the children. 75 % of the children had findings of acute pyelonephritis (APN) in DMSA and there was a complete recovery in 68 % of them. Scars were observed more frequently in older children, with VUR grade>III and not taking chemoprophylaxis.
Conclusions: : 1) first episode of APN in children occurs in more than 50 % during the first year of life. Boys are mostly affected, 2) VUR does not appear to be associated with first episode of APN, 3) children>1 year of age had a higher risk of renal scarring, 4) chemoprophylaxis may serve as a protective agent to renal scars formation.

P228 - ANALYSIS OF KIDNEY STATIC AND DYNAMIC SCINTIGRAPHY AFTER DEFLUX TREATMENT OD VESICOURETERAL REFLUX

MIRJANA POROPAT[1], MARTINA CIGLAR[2], DANICA BATINIć[3], DAMIR DODIG[1], STANKO TEžAK[1], MARIJA TOPALOVIć-GRKOVIć[4]
[1]*DEPARTMENT OF NUCLEAR MEDICINE AND RADIATION PROTECTION, UNIVERSITY HOSPITAL CENTRE ZAGREB AND MEDICAL SCHOOL OF THE UNIVERSITY OF ZAGREB, CROATIA*
[2]*DEPARTMENT OF NUCLEAR MEDICINE AND RADIATION PROTECTION, UNIVERSITY HOSPITAL CENTRE ZAGREB, CROATIA*
[3]*DEPARTMENT OF PAEDIATRICS, UNIVERSITY HOSPITAL CENTRE ZAGREB AND MEDICAL SCHOOL OF THE UNIVERSITY OF ZAGREB, CROATIA*
[4]*DEPARTMENT OF ANAESTHESIOLOGY AND INTENSIVE CARE, UNIVERSITY HOSPITAL CENTRE ZAGREB, CROATIA*

Introduction: The primary goal for the treatment of vesicoureteral reflux (VUR) in children is to reduce the incidence of recurrent urinary tract infections (UTIs) and possible renal damage. The aim of the study was to evaluate renal damage with DMSA static scintigraphy and possible disturbances of urinary tract with MAG3 dynamic scintigraphy in children treated with Deflux because of VUR.
Material and methods: The 99 m Tc-DMSA was performed in 19 children (25 kidneys treated with Deflux therapy) and scans were graded as normal, pathologic with scars or equivocal. Dynamic renal scintigraphy was performed with 99mTc-MAG3 in 16 children (21 kidneys treated with Deflux) and in 5 children because of delayed elimination diuretic was injected. Scintigrams were performed 2 or more months after endoscopic treatment.
Results: DMSA scintigraphy in 11 out of 25 treated kidneys was normal. In 8 kidneys we found renal damage with defect of parenchyma and in 6 equivocal findings were noticed. In 13 kidneys without deflux treatment (with or without reflux) 6 kidneys were normal, 2 had parenchymal defect and 5 kidneys had equivocal findings. MAG3 dynamic scintigraphy was good in 16 out of 21 treated kidneys. In 5 treated kidneys because of delayed elimination diuretic was injected with good respond and complete elimination of activity. Those 5 kidneys with disturbed elimination before endoscopic treatment had VUR grade III or more. In 11 untreated kidneys 2 kidneys had slower elimination of activity with good diuretic respond.
Conclusions: After Deflux treatment DMSA scintigraphy had equal kidney damage in treated or untreated kidneys. The similar findings we found on MAG3 dynamic scintigraphy with slightly more delayed elimination in treated kidneys but with good diuretic respond. Further examination is still necessary to establish the proper timing for endoscopic treatment and its impact on renal damage and function because of similar result of damage in untreated kidneys

P229 - DMSA SCINTIGRAPHY AFTER FIRST URINARY TRACT INFECTION IN CHILDREN WITHOUT VESICOURETERAL REFLUX

MARTINA CIGLAR[1], MIRJANA POROPAT[2], DANICA BATINIć[3], DAMIR DODIG[2], STANKO TEžAK[2]
[1]*DEPARTMENT OF NUCLEAR MEDICINE AND RADIATION PROTECTION, UNIVERSITY HOSPITAL CENTRE ZAGREB, CROATIA*
[2]*DEPARTMENT OF NUCLEAR MEDICINE AND RADIATION PROTECTION, UNIVERSITY HOSPITAL CENTRE ZAGREB AND MEDICAL SCHOOL OF THE UNIVERSITY OF ZAGREB, CROATIA*
[3]*DEPARTMENT OF PAEDIATRICS, UNIVERSITY HOSPITAL CENTRE ZAGREB AND MEDICAL SCHOOL OF THE UNIVERSITY OF ZAGREB, CROATIA*

Introduction: Urinary tract infection (UTI) is the most common infection in children and the 99mTc DMSA

scintigraphy is the golden standard for detection of parenchymal damage. The aim of this study is to determine the necessity and value of the DMSA scintigraphy after the first UTI in kidneys without vesicoureteral reflux (VUR).

Material and methods: In 52 patients (104 renal units) after first UTI and without reflux on VCUG DMSA scans were performed 2 months or more after the first UTI. The scans were graded as normal, pathological with cortical defects and equivocal. Ultrasound (US) was also performed in all patients and parenchyma thickness was assessed as normal or diminished, and findings were compared with DMSA scan

Results: DMSA scans showed pathological findings in 33 out of 104 (32 %) kidneys. Cortical defects were found in 10 (10 %) kidneys and suspected damage in 23 (22 %) kidneys. US detected diminished parenchymal thickness in 11 out of 104 (10, 5 %) kidneys . In 7 out of 11 kidneys DMSA scans had pathological findings too. On DMSA scans cortical defects were found in 1 and suspected damage in 6 out of 11 kidneys.

Conclusions: Our study confirms DMSA scintigraphy as a valuable method in detection of renal damage and identifies the children for more careful medical attention. In contrary US cannot be used as a single study for evaluation of parenchymal damage after the first UTI. We suggest DMSA scinitigraphy in all children after the first UTI because of over 30 % of pathological findings after the first UTI even in those without VUR.

P230 - HEAT SHOCK PROTEIN 70 IN URINARY TRACT INFECTION

ALEV YILMAZ[1], SEVINC EMRE[1], ASUMAN GEDIKBASI[2], EVREN ONAY UCAR[3]

[1]*ISTANBUL UNIVERSITY ISTANBUL MEDICAL FACULTY PEDAITRIC NEPHROLOGY DEPARTMENT*

[2]*BAKIRKOY DR. SADI KONUK TRAINING AND RESEARCH HOSPITAL BIOCHEMISTRY DEPARTMENT*

[3]*ISTANBUL UNIVERSITY FACULTY OF SCIENCE DEPARTMENT OF MOLECULAR BIOLOGY AND GENETICS*

Introduction: Heat shock protein (HSP) 70 is a member of HSP families which regulate the response to any hazardous factors including infectious agents to prevent protein structure. The aim of our study was to assess whether urine levels of Hsp70 increase in children with UTI and to determine the optimal cut-off level for urine Hsp70 to predict UTI in children.

Material and methods: Thirty patients with UTI [median age: 7.28 years (5.9-10.1)] and 30 healthy children [median age: 4.65 years (3.73-8.93)] were enrolled the study. Eleven of the patients with UTI had pyelonephritis. Random urine samples were obtained for measurement of Hsp70 and creatinine from the control and collection of urine samples were done prior to treatment of UTI at the time of presentation (pt) and after treatment (at). Urine level of Hsp70 was measured by ELISA.

Results: Mean urine Hsp70 level prior to treatment were significantly higher in the UTI group than in the control group (347.5±181.48 pg/ml and 18.58±3.46 pg/ml, respectively; p=0.0001). Using a cut-off 28.7 pg/ml for prediction of UTI, sensitivity and specificity were 100 % and 96.6 %, respectively (AUC: 0.99). Mean urine Hsp70 level after treatment decreased to 35.84±40.68 pg/ml in UTI group (p=0 .0001). Mean urine Hsp70/creatinine prior to treatment were also significantly higher in the UTI group than in the control group (393.77±112.02 pg/ml and 39.93± 47.61 pg/ml, respectively; p=0.0001). Using a cut-off 179.5 pg/ml for prediction of UTI, sensitivity and specificity were 100 % and 96.6 %, respectively (AUC: 0.99). Urine Hsp70/creatinine was higher in the patients with pyelonephritis (p=0.048). Mean urine Hsp70 level after treatment decreased to 60.68±51.11 pg/ml in UTI group (p=0 .0001).

Conclusions: Our findings suggest that urine Hsp70 level increase in children with UTI and Hsp70/creatinine may be useful for prediction of pyelonephritis in children with high sensitivity, specificity.

P231 - Resistance to oral antibiotics in small children at recurrent urinary tract infection

SVANTE SWERKERSSON, ULF JODAL, SVERKER HANSSON

THE PEDIATRIC URONEPHROLOGICAL CENTER, THE QUEEN SILVIA CHILDREN´S HOSPITAL, GÖTEBORG, SWEDEN

Introduction: The aim of the study was to analyse the resistance pattern at recurrent urinary tract infection (UTI) and its relation to vesicoureteral reflux (VUR) and prophylaxis.

Material and methods: Retrospective analysis of 1015 children below 2 years of age with first-time community acquired UTI, diagnosed 1994–2003. Recurrent UTI occurred in 48 boys and 67 girls. Long-term prophylaxis was given to 124 children, 80 with dilating VUR. The drugs used were trimethoprim (n=100), cefadroxil (n=12) or nitrofurantoin (n=12).

Results: Recurrence occurred in 69/735 (9 %) children without VUR, 14/92 (15 %) in non-dilating VUR and 32/88 (40 %) in dilating VUR. Recurrent UTI with non-E. coli bacteria was found in 1 (1 %) children without VUR, in 4 (29 %) with non-dilating VUR and 14 (44 %) with dilating VUR (p<0.0001). Of the recurrences, 91 had no prophylaxis and 24 occurred during prophylaxis. In the non-prophylaxis group E. coli was isolated in 81 children and

non E. coli in 10. In the prophylaxis group 15 had E. coli and 9 had non-E. coli. Overall antibacterial resistance at the recurrence in the non-prophylaxis group was 19 % to trimethoprim, 7 % to cefadroxil, 9 % to nitrofurantoin, and in the prophylaxis group 82 %, 26 % and 17 %, respectively. Resistance to trimethoprim for E. coli increased from 14 % at the index UTI to 29 % at the first recurrence (p=0.0005). No significant increase was found for cefadroxil or nitrofurantoin. There was no relation between the treatment at the index UTI and the resistance pattern at recurrent infection.
Conclusions: Despite the fact that most children with dilating VUR were given antibacterial prophylaxis, they had a high frequency of recurrent UTI. At the recurrent infection non-E. Coli bacteria and resistant strains were more prevalent. The use of antibacterial prophylaxis had great impact on the development of resistance, while isolated antibacterial courses seemed to be of less importance.

P232 - Prevalence of vesicoureteral reflux after the first episode of acute pyelonephritis in children aged 0–36 months

ALEKSANDRA PARIPOVIC, NATASA STAJIC, JOVANA PUTNIK, RADOVAN BOGDANOVIC
INSTITUTE OF MOTHER AND CHILD HEALTHCARE OF SERBIA, BELGRADE, SERBIA

Introduction: Aim was to assess the prevalence of vesicoureteral reflux (VUR) after the first episode of acute pyelonephritis (APN) in children aged 0–36 months. Another aim was to investigate if ultrasonography (US) could point to the detection of VUR.
Material and methods: We retrospectively analyzed 764 pediatric patients who had voiding cystourethrography (VCUG) after the first APN between 1.1.2008. and 31.1.2009. Detailed history including data about previous APN was collected. Renal US and serum concentrations of urea and creatinin were checked in each patient. Other investigations were performed according to the indications.
Results: Mean age was 9.3±7.8 months, with 52 % of female patients. VUR was detected in 29 % (221/764): grade I in 7 %, II - 72 %, III - 15 %, IV - 5 %, and V - 1 %. Intravenous urography was performed in 2 % (15/764) of patients who had significant dilatation on US without signs of VUR on VCUG. Pathologic findings on US were present in 19 % of patients: 31 % had enlarged kidney, 52 % pyelon/ureter dilatation, 13 % enlarged kidney with dilatation of pyelon/ureter, and 4 % renal hypoplasia.
Conclusions: VUR was detected in a one-third of pediatric patients after the first APN. Since majority of patients (80 %) had VUR without urinary tact dilatation, a more selective and restrictive approach to VCUG should be adopted. VUR could not be predicted on the merit of US exam.

P233 - CHILDREN URINARY TRACT INFECTION PATHOGENS' CHANGES DURING LAST YEARS IN TERTIARY CARE HOSPITAL

KRISTINA STEPONENAITE-JANOVICIENE, GENOVAITE BERNATONIENE, AUGUSTINA JANKAUSKIENE
VILNIUS UNIVERSITY, CHILDREN HOSPITAL, AFFILIATE OF SANTARISKIU KLINIKOS

Introduction: Urinary tract infection (UTI) is one of the most common pediatric infections. It may cause permanent kidney damage. The aim of this study was to determine uropathogen frequency and its changes in children during several decades.
Material and methods: Results of urinary cultures performed from patients admitted to Children's Hospital during last several decades were analyzed.
Results: E.coli is still the most common uropathogen in children, though its frequency is decreasing, but statistically unreliable (1997–74.7 %, 2002–63.1 %, 2003–60.3 %, 2007–51.6 %, 2010–63.2 %, p-value between 2010 and 1997> 0.05). Enterococcus is on the second place and its frequently is growing up (1997 – 4.6 %, 2002 – 5.6 %, 2003 – 6.6 %, 2007 – 15.2 %, 2010 – 11.5 %, p-value between 2010 and 1997<0,001). E.coli susceptibility to antibiotics doesn't change during last years and nitrofurantoin remains the first choice for treatment of UTIs (ciprofloxacin 2003 – 99 %, 2010 – 97 %, ceftazidime 2003 – 98 %, 2010 – 97 %, cefuroxime 2003 – 97 %, 2010 – 97 %, nitrofurantoin 2003 – 97 %, 2010 – 99 %, gentamicin 2003 – 94 %, 2010 – 90 %, amoxicillin/clavulanic acid 2003 – 78 %, 2010 – 75 %, trimethoprim/sulphamethoxazole 2003 – 78 %, 2010 – 75 %, trimethoprim 2003 – 78 %, 2010 – 78 %, ampicillin 2003 – 54 %, 2010 – 49 %).
Conclusions: The decrease of E.coli may be associated to this microorganism suppression in the gastrointestinal tract due to frequent use of antibiotics and more resistant bacteria pass to the urinary tract.

P234 - FREQUENCY OF URINARY TRACT INFECTIONS IN PATIENTS WITH NEONATAL INDIRECT HYPERBILIRUBINEMIA

ELIF BAHAT ÖZDOĞAN[1], MEHMET MUTLU[2], MUKADDES KALYONCU[1], GÜLAY KARAGÜZEL[3], YAKUP ASLAN[2]
[1]*KARADENIZ TECHNICAL UNIVERSITY FACULTY OF MEDICINE, DEPARTMENT OF PEDIATRIC NEPHROLOGY*
[2]*KARADENIZ TECHNICAL UNIVERSITY FACULTY OF MEDICINE, DEPARTMENT OF NEONATOLOGY*
[3]*KARADENIZ TECHNICAL UNIVERSITY FACULTY OF MEDICINE, DEPARTMENT OF ENDOCRINOLOGY AND METABOLISM*

Introduction: Urinary infections are an important cause of prolonged jaundice. But there is conflict about the role of the urinary infections on the pathological jaundice in the first 14 days of the life. Some infants have etiological reasons for hyperbilirubinemia. This study aims to determine the frequency of urinary tract infections in neonates presenting with jaundice in the first 2 weeks of life with bilirubin levels that require phototherapy, and were not found to have any abnormalities in routine etiologic studies.
Material and methods: This study was done with neonates 2–14 days old that have indirect bilirubin levels above the phototherapy limit but were not found to have any condition that would lead to elevated bilirubin levels, e.g. systemic infection, isoimmunization, erythrocyte enzyme defect, erythrocyte structural defect, hypothyroidism, sequestrated blood, polycythemia, or metabolic disease. Urine samples for urinalysis and urine culture were obtained using catheterization. . In patients with a positive urine culture, blood cultures and confirmatory urine culture from a catheter were obtained before initiating antibiotic therapy.
Results: During the study, 482 neonates presented to with jaundice and 262 of these fulfilled our criteria.. UTI rate was 12 % and bacteriemia/urosepsis rate was 6 %. Mean bilirubin level on admission was found 20.9 +6.1 mg/dl. Thirty-five (13 %) of these patients were treated with blood exchange and phototherapy; the rest were treated with phototherapy only. Weight loss in terms of percentage of birth weight (p: 0.02) was higher on uninfected patients and rebound bilirubin levels (p: 0.01) was higher on UTI group.
Conclusions: UTIs may present with isolated jaundice and may cause urosepsis, renal scarring, hypertension and chronic renal failure if they are not treated. In the neonatal period, infections lead to hyperbilirubinemia via hemolysis, inadequate conjugation, decreased excretion and oxidant stres. The findings of this study show the benefits of obtaining urine cultures for the diagnosis of UTI in neonatal patients with hyperibilirubinemia requiring phototherapy who have unexplained hyperbilirubinemia.

P235 - ASSOCIATION OF URINARY TRACT INFECTION AND VESICOURETERIC REFLUX IN CHILDHOOD

PINAR TABANLI, BANU ACAR, NERMIN UNCU, F. ŞEMSA ÇAYCI, GÖKÇE GÜR, NILGÜN ÇAKAR
ANKARA CHILDREN'S HEMATOLOGY AND ONCOLOGY HOSPITAL

Introduction: To evaluate the frequency of urinary tract infection (UTI), grade of vesicoureteric reflux (VUR) and whether spontaneous resolution or type of operation for correction of VUR.
Material and methods: 108 children with VUR, followed between 2009–2011 are included in the study. VUR was graded as mild (Gr I-II), moderate (Gr III) and severe (Gr IV-V).
Results: 81 female (75 %), 27 male (25 %) children (age: 1 month-131 months; median: 45,25±34,75 month) are evaluated. One patient (0,9 %) had GrI, 7,4 % had GrII, 44,4 % had GrIII, 32,4 % had GrIV and 14,8 % had GrV VUR. Four groups are formed according to spontaneous resolution, resolution after STING, after UNC or UNC following STING. Type of resolution was evaluated in two groups as mild VUR (GrI-II) and severe VUR. Spontaneous resolution was observed in 55,5 % of mild and in 12 % of severe VUR groups (p=0,01). No relapse was observed in spontaneous resolution group, while 48 of 91 patients (52,7 %) surgical correction (STING or UNC) had relapses. STING was performed in 71 and UNC in 20. Among 71 STING patients 46 (64,7 %) had relapses and, among 37 UNC patients 2 (5,4 %) had relapses. The frequency of UTI decreased significantly in all groups. The frequency of UTI in STING and UNC groups were similar (24,1 % and 24,3 %). Voiding dysfunction or residual urine was observed in 22 patients without resolution of VUR.
Conclusions: All VUR patients should be evaluated for dysfunctional voiding and the patients UNC and STING were performed should be monitored for UTI even after the operation.

P236 - THE EFFECT OF CIRCUMCISION ON THE FREQUENCY OF URINARY TRACT INFECTION AND RENAL PARENCHYMAL DAMAGE IN PATIENTS WITH ANTENATAL HYDRONEPHROSIS

ENGIN KOSE[1], CANER ALPARSLAN[1], OZLEM TURAN[1], MURAT KANGIN[2], ALKAN BAL[1], PINAR KUYUM[1], FULYA KAMIT[1], NIL CEFA ARSLAN[1], CEVRIYE KUBRA CENKCI[1], ONDER YAVASCAN[1], NEJAT AKSU[1]
[1]*TEPECIK TRAINING AND RESEARCH HOSPITAL, PEDIATRIC NEPHROLOGY, IZMIR, TURKEY*
[2]*DIYARBAKIR NATIONAL HOSPITAL, DIYARBAKIR, TURKEY*

Introduction: The objective of this study was to determine the effect of circumcision on the frequency of urinary tract infection (UTI) and renal parenchymal damage in infants with antenatal hydronephrosis (AH).
Material and methods: The data were collected prospectively between 1998–2009. Infants with a fetal pelvis diameter of ≥5 mm identified with antenatal ultrasound (US) were followed-up. All patients were evaluated in terms of UTI frequency, and renal scarring on Technetium 99 m-dimercaptosuccinic acid scan (DMSA). The chi-square and

student's t were used for statistical analysis. A P value <0.05 was considered significant.

Results: The study included 178 (134 males, 44 females) patients. Of these, 29 were diagnosed by vesicoureteral reflux (VUR), 87 by obstructive uropathy and 54 by non-obstructive uropathy. Of 134 males, 111 infants were circumcised. The mean monitoring time was 45±24.9 months and mean age of circumcision was 14±16.06 months. The pre-circumcision UTI frequency (2.97±1.14/y) was significantly higher than post-circumcision period (0.25±0.67/y) ($p<0.005$). Also, pre-circumcision UTI frequency (2.97±1.14/y) was significantly higher than the UTI frequency observed in female cases (0.85±0.91/y) and in overall study group (0.73±0.79/y) ($p<0.05$). In circumcised patients the rate of renal damage (7.3 %) was lower than females (16 %) and overall study group (10.6 %) ($p<0.05$).

Conclusions: In conclusion, early circumcision of infants with AH will aid to prevent UTI and consequently renal parenchymal damage.

P237 - THE EFFECT OF CIRCUMCISION ON GROWTH AND NUTRITION STATUS IN INFANTS WITH ANTENATAL HYDRONEPHROSIS

ENGIN KOSE[1], CANER ALPARSLAN[1], OZLEM TURAN[1], MURAT KANGIN[2], ALKAN BAL[1], PINAR KUYUM[1], FULYA KAMIT[1], NIL CEFA ARSLAN[1], CEVRIYE KUBRA CENKCI[1], ONDER YAVASCAN[1], NEJAT AKSU[1]

[1]TEPECIK TRAINING AND RESEARCH HOSPITAL, PEDIATRIC NEPHROLOGY, IZMIR, TURKEY

[2]DIYARBAKIR NATIONAL HOSPITAL, DIYARBAKIR, TURKEY

Introduction: The objective of this study was to determine the effect of circumcision on the growth and nutrition status in infants with antenatal hydronephrosis (AH).

Material and methods: The data were collected prospectively between 1998–2009. Infants with a fetal pelvis diameter of ≥5 mm identified with antenatal ultrasound (US) were followed-up. Body height (HZ) and weight (WZ) Z scores as well as weight-for-height index (WHI) were calculated. Turkish reference curves for age and gender were taken with in all scores. The HZ and WZ scores or WHI were calculated for each patient at the first and last visits. The chi-square and student's t were used for statistical analysis. A P value <0.05 was considered significant.

Results: The study included 178 (134 males, 44 females) patients. Of these, 29 were diagnosed by vesicoureteral reflux (VUR), 87 by obstructive uropathy and 54 by non-obstructive uropathy. Of 134 males, 111 infants were circumcised. The mean monitoring time was 45±24.9 months and mean age of circumcision was 14±16.06 months. In all patients, the HZ of the circumcised subjects (0.18±1.01) was statistically higher than uncircumcised subjects (−0.26±0.92) ($p<0.05$). Although insignificant, the HZ of the circumcised males (0.13±1.24) with VUR was higher than the uncircumcised patients (0.03±0.55) ($p>0.05$). The HZ of the circumcised males (−0.13±0.54) with obstructive uropathy was also higher than uncircumcised males (−0.49±0.66) and females (−0.13±0.87) ($p<0.05$). The HZ of the circumcised males (0.19±1.12) without urinary tract abnormality was higher than uncircumcised subjects (−0.56±0.79) ($p<0.05$). Although nutrition scores were better in the circumcised males, no statistically significant effect of circumcision on the nutrition status was detected.

Conclusions: In conclusion, circumcision in children with urinary system pathology will decrease the frequency of UTI, hence, it will prevent the catabolism, tubulointerstitial dysfunction and lack of appetite which are created by UTI and the normal course of development is obtained.

P238 - ANGIOTENSIN 2 TYPE 1/TYPE 2 GENE POLYMORPHISMS IN TURKISH CHILDREN WITH VESICOURETERAL REFLUX AND RECURRENT URINARY TRACT INFECTIONS

ŞEBNEM ŞAHIN[1], PELIN ERTAN[2], HAVVA EVRENGÜL[3], BAHADIR DEDE[4], AFIG BERDELI[5]

[1]DR, CELAL BAYAR UNIVERSITY, SCHOOL OF MEDICINE, DEPARTMENT OF PEDIATRICS

[2]PROF, CELAL BAYAR UNIVERSITY, SCHOOL OF MEDICINE, DEPARTMENT OF PEDIATRIC NEPHROLOGY

[3]SPECIALIST, CELAL BAYAR UNIVERSITY, SCHOOL OF MEDICINE, DEPARTMENT OF PEDIATRIC NEPHROLOGY

[4]DR, CELAL BAYAR UNIVERSITY, SCHOOL OF MEDICINE, DEPARTMENT OF PUBLIC HEALTH

[5]PROF, DEPARTMENT OF MOLECULER GENETICS EGE UNIVERSITY FACULTY OF MEDICINE

Introduction: Vesicoureteral reflux (VUR) and subsequently developing reflux nephropathy is the most important cause of end stage renal disease. Early diagnosis and treatment of VUR is important in order to prevent renal scarring and reflux nephropathy. Genetic factors have been evaluated as risk factors for the development of renal scar and reflux nephropathy in recent years. The aim of this study was to investigate the role of Angiotensin 2 (ATR 2) Type1 and Type 2 receptor gene polimorphisms in children with VUR and recurrent urinary tract infection (UTI).

Material and methods: The study included 100 patients (25 patients who have recurrent UTI without renal scar and 25 patients who have recurrent UTI with renal scar. 25 patients who have VUR without renal scar and 25 patients who have VUR with renal scar) Blood was drawn and

analysed for genetic polymorphisms of ATR 2 Type1 and Type 2 genes by the PCR_RFLP method.
Results: The distribution of ATR 2 Type 1gene polymorphism was different between patients and healthy controls (p=0.05) but ATR 2 Type 2 was similar (p>0.05) . There was an association with distribution of ATR 2 Type 1 receptor gene polymorphism and renal scar (p=0.05) but there was no difference with ATR 2 Type 2 (p>0.05). In the present study we compared urinary tract infection group with control group for ATR 2 Type 1 gene polymorphism, and we found significantly difference (p<0,05). There was no significant difference between vesicouretral reflux group with control group for ATR 2 Type 1/ Type 2 gene polymorphism.
Conclusions: The association of ATR 2 Type 2 gene polymorphism and recurrent UTI with renal scar might be useful for early diagnosis of end stage renal disease.

P239 - Voiding disturbances in chuildren with a history of urinary tract infections

AUGUSTINA JANKAUSKIENE, INDRE CICENAITE, DAIVA VAICIUNIENE
VILNIUS UNIVERSITY, CHILDREN HOSPITAL AFFILIATE OF SANTARISKIU KLINIKOS

Introduction: The association between voiding disturbances and urinary tract infection (UTI) has been established, but it is still unclear whether there is a causal relationship. Our aim was to compare voiding disturbances between children with and without a history of UTI.
Material and methods: A cross-sectional study was undertaken from April till July 2011 in children aged 5–18 years at Children's Hospital, Affiliate of Vilnius University Hospital Santariskiu Klinikos. Data were obtained by using a self-administered anonymous questionnaire. The study comprised 261 children: 129 with a history of UTI and 131 without it. The data were compared between these two groups and between age groups (5-11 years and 12-18 years).
Results: There were more girls in a group with a history of UTI (70.5 % vs 54.5 %, p=0.01). The median age was 11 years with no difference between groups with and without UTI. Nocturia (57.4 % vs 41.7 %, p=0.013), urinary urgency (51.9 % vs 42 %, p=0,01) and wetting pants (45 % vs 24 %, p=0.00) were more common in a group with a history of UTI, whereas there was no significant difference of nocturnal enuresis and hesitancy (p>0.05).While voiding disturbances between age groups : 5–11 y (n=132) and 12–18 (n=129) were statistically significant for nocturnal enuresis (20.5 % vs 0.8 %, p=0.000); urgency(49.2 % vs 34.1 %, p<0.017) and wetting pants (40.2 % vs 22.5 %, p=0.002)
Conclusions: Urgency and wetting pants were more common in younger children and in a group with a history of UTI. Nocturnal enuresis was more common in younger children and nocturia – in children with UTI in the past.

P240 - Efficacy of antibioprophylaxis for children with UTI and/or VUR: a systematic methodological review of the published meta-analyses

ESPINDOL REYNALDO[1], COCHAT PIERRE[2], LEROY SANDRINE[1]
[1]*INSTITUT PASTEUR*
[2]*CHU LYON, FRANCE*

Introduction: Antibiotic prophylaxis appeared is though to be a useful intervention to prevent children with UTI and/or VUR from infectious recurrence and scaring. Because of the absence of solid evidence, this recommendation is nowadays debated. Randomized trials comparing antimicrobial prophylaxis with no intervention or placebo have been conducted with contradictory conclusions, summarized by several meta-analyses (MA) also with conflicting results. We aim to perform a systematic review of systematic reviews (SR) and meta-analyses published to clarify their strengths and weaknesses and tempt to draw a conclusion.
Material and methods: All SR +/− MA on antimicrobial prophylaxis vs. placebo or nothing in children with UTI and/or VUR were identified by a systematic electronic search in databases until 2012.
Results: From the 116 abstracts identified, 2 SR (w/o MA) and 7 MA were included, all published since 2000. This represented 15 original trials published since 1968, and 6240 children. Two MA included children with VUR, 5 included children with UTI w and w/o VUR. MA included 6 to 11 trials mostly because on different inclusion criteria (UTI or VUR only). The search methodology quality was good, however the MA methods quality was intermediate: 86 % searched for heterogeneity but without further exploring variability between trials; only 43 % searched for publication bias. All MA found non-significant RR for recurrent UTI or renal scarring, 2 MA showed significant RR for recurrent positive urine culture. Their conclusions varied between antibiotics efficacy (1), non-significant results (4), and evidence of no efficacy (2), which resulted from confusion between efficacy and equivalence trials.
Conclusions: MA experimented difficulties to raw a definitive conclusion about antimicrobial prophylaxis because of varied inclusion criteria, and because of variability between trials. MA on individual patients data would help in analyzing data regarding VUR grade, and other patients

characteristics to make deifinitive conclusion for some patients' groups.

P241 - Efficacy of antimicrobial prophylaxis in children with UTI or VUR: systematic review and meta-analysis

ESPINDOLA REYNALDO[1], COCHAT PIERRE[2], LEROY SANDRINE[1]
[1]*INSTITUT PASTEUR*
[2]*HôPITAL FEMME MèRE ENFANT & UNIVERSITé DE LYON, LYON, FRANCE*

Introduction: Antibiotic prophylaxis is though as one of the few useful interventions to prevent infectious recurrence in children after UTI and/or with VUR. Although this recommendation has been applied for many years, several recent randomized trials comparing antimicrobial prophylaxis vs. not intervention or placebo failed to demonstrate benefits to prevent recurrent symptomatic UTI. However, meta-analyses results remained non definitive and sometimes conflicting. We aim to perform an updated systematic reviews and meta-analysis to study whether antibiotic prophylaxis is effective to reduce recurrent UTI in children after UTI and/or with VUR.
Material and methods: A systematic review identified all randomized trials including children with UTI and/or with VUR, and treated with antimicrobial prophylaxis vs. placebo/nothing. A meta-analysis estimated pooled RR using random-effects model.
Results: From the 536 potentially relevant articles, 10 were included, representing 1756 children; 3 (30 %) were placebo controlled trial, co-trimoxazol was the antibiotic used as prophylaxis in most of studies and the follow-up ranged varied from 1 to 4 years. Antibiotic prophylaxis was significantly associated to the reduction in recurrence of symptomatic UTI (pooled RR: 0.7; 95 % CI: 0.6-0.8) when data from all trials were gathered. When pooling only data from trials that had included children UTI regardless VUR, prophylaxis significantly prevented from infectious recurrence (pooled RR: 0.7; 95 % CI: 0.5-0.9). However the association turned non significant in the sub-group of patients with VUR (w or w/o UTI): pooled RR: 0.8; 95 % CI: 0.6-1.0). There was no evidence of heterogeneity in all analysis ($p > 0.1$).
Conclusions: We found conflicting results between the global analysis and the sub-group analysis of patients with VUR: meta-analysis on individual data be warranted to better characterize in which patients prophylaxis may prevent from infectious recurrences, or not. Lastly, none of the included trials were equivalence trials whereas such design are required to draw a conclusion on non therapeutic efficacy.

P242 - Etiological profile of acute pyelonephritis and antimicrobial susceptibility of urinary pathogens in hospitalized patients in a level III centre (a 18 years comparative study)

TâNIA MARTINS, FILIPA FLOR DE LIMA, FRANCISCA CAETANO, ANA TEXEIRA, HELENA PINTO, CALDAS AFONSO
HOSPITAL SãO JOãO

Introduction: Changes in antimicrobial resistance in acute pyelonephritis (APN) is a growing problem. The initial treatment is often empirical and should always be determined by updated knowledge of etiological profile and antimicrobial susceptibility in each centre.
Material and methods: Retrospective study of clinical reports of patients admitted to Pediatric Department with the diagnosis of APN (proven by positive urinary culture) from January 2010 to December 2011. Comparative study of etiological agents and their antimicrobial susceptibility profile from 1994 to 2011 (previous studies performed on 1994–97, 2002 and 2007).
Results: During the last 2 years (01/2010-12/2011) 137 patients were admitted due to APN (75 F/62 M; median age 6 months (4 days-17 years)). It was the first episode in 108 (78.8 %) patients. Escherichia coli was the most common etiological agent (n=111; 81 %) followed by Proteus mirabilis (n=6), Pseudomonas aeruginosa (n=5), Klebsiella pneumoniae (n=3) and Enterococcus spp (n=3). The second most frequent agent in patients without nephro-uropathy was K. pneumoniae and in patients with nephro-uropathy was P. mirabilis ($p<0.001$). The antimicrobial susceptibility profile of E. coli in the four studies (1994–97, 2002, and 2007, 2010–11) was: 100/99/100/97.3 % to 3 G cephalosporins, -/91.3/87.2/96.3 % to 2 G cephalosporins and 71/74.7/77.8/81.5 % to amoxicillin+clavulanate, 98.6/100/99.1/95.3 % to nitrofurantoin, and 89.8/77.7/78.6/73.8 % to cotrimoxazole. In patients under prophylaxis (n=20; 14.6 %) etiological agents had higher resistance, namely to 1 G cephalosporins ($p=0.03$) and nitrofurantoin ($p=0.006$). P. mirabilis had 66.7 % in vitro sensitivity to amoxicillin+clavulanate. There was empirical treatment failure in four cases (2.9 %).
Conclusions: This study showed no significant change in antimicrobial susceptibility of the most frequent urinary pathogens during the last 18 years. Urinary tract malformation and previous prophylaxis were responsible for different etiological and resistance patterns. Amoxicillin+clavulanate remain a good first choice for empirical treatment of APN in our inpatient care. 2 G and 3 G cephalosporins use should be restricted to selected cases.

P243 - The development of renal scarring in patients with febrile urinary tract infections does not correlate with vesicoureteral reflux

IVONA BUTORAC-AHEL[1], SANJA FLAJSMAN-RASPOR[2], IVANA GRGIC[1], MIRNA SUBAT-DEZULOVIC[2]

[1]CLINICAL MEDICAL CENTRE RIJEKA, DEPT.OF PEDIATRIC NEPHROLOGY
[2]UNIVERSITY SCHOOL OF MEDICINE RIJEKA, DEPT. OF PEDIATR NEPHROLOGY

Introduction: Febrile urinary tract infection (UTI) during childhood with or without vesicoureteral reflux (VUR) can be a predisposition factor for renal scarring. Aims: to evaluate the frequency of VUR in patients with abnormal ultrasound and abnormal dynamic scintigraphy with technetium-99 m mercaptoacetyltriglycine scans (MAG3) performed after the first febrile UTI. Secondly, to evaluate the frequency of renal scarring due to the late scintigraphy in followed-up patients with or without VUR.
Material and methods: Retrospective analysis of consecutively selected 49 children with bacteriologically proven first febrile UTI who underwent renal and bladder ultrasound (RUS) within 3 days and technetium-99 m mercaptoacetyltriglycine scans (MAG3) performed within 7 days after initiation of antibiotic therapy. All selected patients had control MAG3 scintigraphy undertaken after median 16 months (range 6 to 18 months).
Results: of 49 selected pts (36 F,13 M), median age 24 months (range 0.2 to 17 years), abnormal RUS defined by pyelon and/or ureter dilation, asymetry in renal lenght and/or changed parenchymal thikness had 30 (61 %) pts. Abnormal acute MAG3 scintigraphy defined by focal or diffuse parenphymal defects had 39 (80 %) pts, including 12 pts with differential function <45 %. VUR was diagnosed in 20 pts (6 M/12 F, VUR grade III-V in 15 pts) including 10 pts with abnormal RUS and 14 pts with abnormal acute MAG3 scintigraphy. 25 (64 %) pts with abnormal acute scintigraphy were without VUR. Late MAG3 scintigraphy revealed parenphymal changes suggestive of renal scarring in 28 (57 %) pts, in 10 with VUR (35 %) and 18 pts without VUR (65 %).The difference regarding development of renal scarring in pts with or without VUR was insignificant (p=0.79)
Conclusions: Febrile UTI and acute renal parenchymal changes detected by scintigraphy does not necessarily correlate with VUR. In addition, the progression to renal scaring did not differe comparing patients with and without VUR denoting that children with VUR are not more prone to renal scarring.

P244 - Back to the future: a systematic methodological review of emerging approaches for detecting renal scarring in pediatric UTI

LEROY SANDRINE[1], BACCHETTA JUSTINE[2], STEFANIDIS CONSTANTINOS[3], COCHAT PIERRE[1]
[1]INSTITUT PASTEUR, PARIS, FRANCE
[2]HôPITAL FEMME-MèRE-ENFANT, UNIVERSITé DE LYON, BRON, FRANCE
[3]"P. AND A. KYRIAKOU" CHILDREN'S HOSPITAL, ATHENS, GREECE

Introduction: Despite continuing debate, attention is moving from VUR to renal scarring, the most clinically relevant end-point is probably renal scarring, the presence of which is associated with worse renal outcomes in early adulthood. Selective approaches for UTI investigations reduce cost and distress, but misdiagnosis of the fewest possible patients with significant conditions remains the fundamental objective. We aimed to systematically review decision algorithms available.
Material and methods: All decision algorithms dealing with investigations work-up in children after UTI were systematically were identified by a systematic electronic search in databases until 2012.
Results: The top-down approach yielded a 75–96 % sensitivity (Se) and a 52-60 % specificity (Sp) for dilating VUR depending on the validation studies. Renal US was not very sensitive for acute pyelonephritis (APN), dilating VUR, neither scarring (Se: 46-63 %), but offered a better Sp (62–93). Interestingly, ureteral dilation yielded a higher Se (75 %) with a 60 % Sp. CRP yielded a 53-82 % Se for APN, VUR or scarring, with a 62-75 % Sp for APN but a much lower Sp for VUR and scarring (28-56 %). Oostenbrink risk score, Wang's rule and Preda's algorithm combined Renal US with CRP in different manner: Oostenbrink yielded a 100 % Se for dilating VUR but with a validation 3 % Sp, Wang's rule better predicted VUR (Se: 86 %, Sp: 79 %), Preda's algorithm offered 85 % Se and 59-65 % Sp for VUR and scarring. Procalcitonin offered a 65-92 % Se with 30-85 % Sp for all three outcomes, which was not improved when combining with renal US.
Conclusions: Renal US and VCUG alone are not reliable in evaluating UTI. Scores often failed to confirm promising predictive value. Biomarkers provide an interesting alternative, endorsing translational proteomic strategies. Future algorithms may therefore focus more on scarring, with less emphasis on VUR, and possible incorporation of proteomic tools, to provide optimal individualized management and nephroprotection.

P245 - TRANSCUTANEOUS NEUROMODULATION IN CHILDREN WITH NON-NEUROGENIC LOWER URINARY TRACT DYSFUNCTIONS

GROEN LUITZEN-ALBERT[1], PERSYN BENEDICTE[2], RENSON CATHERINE[1], RAES ANN[1], DEHOORNE JOKE[1], VAN LAECKE ERIK[1], HOEBEKE PIET[1], VANDE WALLE JOHAN[1]
[1]GHENT UNIVERSITY HOSPITAL
[2]GHENT UNIVERSITY

Introduction: Transcutaneous electrical nerve stimulation (TENS) is used for more than 10 years to treat children with lower urinary tract dysfunctions. Some retrospective and prospective studies have been published reporting different results. However, all studies have low patient numbers. We evaluated the results of a larger group of 139 consecutively treated patients to determine the influence of TENS on non-neurogenic lower urinary tract dysfunctions.
Material and methods: Between August 1, 2006 and December 31, 2010, 60 girls (mean age 7.3 year) and 79 boys (mean age 7.2 year) were treated with transcutaneous electrical nerve stimulation (TENS). Surface electrodes were placed at the level of sacral root S3. Stimulation of 2 Hz. was applied for 2 hours every day. 104 children had overactive bladder, 13 dysfunctional elimination syndrome, 15 small bladder capacity, 4 underactive bladder and 3 dysfunctional voiding.
Results: Diurnal incontinence and enuresis improved significantly with 54.2 % and 27.3 % respectively. Maximum voided volume improved on bladder diary and and follow-up uroflow. After 1 year, 33 % of the children remained cured of diurnal incontinence and 10 % remained cured of enuresis. 0.02 % of the children needed to stop the therapy because of allergic reaction to the self-adhesive pads.
Conclusions: Transcutaneous electrical nerve stimulation is feasible in a home setting. It is an effective non-invasive therapy which can be used for the treatment of non-neurogenic lower urinary tract dysfunctions.

P246 - EVALUATION OF BURCH COLPOSUSPENSION IN GIRLS WITH SEVERE THERAPY RESISTANT INCONTINENCE DUE TO BLADDER NECK INSUFFICIENCY

GROEN LUITZEN-ALBERT[2], CHRZAN RAFAL[1], DE KORT LAETITIA M.O.[1], KLIJN AART J.[1], DIK PIETER[1], RAES ANN[3], DE JONG TOM P.V.M.[1]
[1]*UNIVERSITY CHILDREN'S HOSPITALS UMC UTRECHT AND AMC AMSTERDAM*
[2]*UNIVERSITY CHILDREN'S HOSPITALS UMC UTRECHT AND UZ GHENT*
[3]*UNIVERSITY CHILDREN'S HOSPITAL UZ GHENT*

Introduction: In a small subgroup of girls with therapy resistant incontinence, bladder neck insufficiency/hypermobile urethra can be diagnosed. This condition is very difficult to treat and might benefit from colposuspension. The results of Burch colposupension for this indication were retrospectively evaluated.
Material and methods: Between September 12, 1990 and December 31, 2010, 109 Burch colposuspensions were performed. 36 girls (mean age 12.9 years) underwent colpospuspension alone for the indication of idiopathic bladder neck insufficiency/hypermobile urethra and were eligible for inclusion. Patients with other diagnoses were excluded (e.g. ectopic ureterocoele, neurogenic bladder, post-urethrotomy). 7/36 patients were excluded because of insufficient follow-up data. 29 patients were included; all received at least 3 years treatment with intensive urotherapy, physical therapy and medical treatment in an outpatient and inpatient setting. Diagnosis of bladder neck insufficiency/hypermobile urethra was confirmed with dynamic ultrasonography, video-urodynamics, Jump-test and Ephedrine-treatment.
Results: Of all patients, 48 % were cured, 28 % showed significant improvement and for 24 % the treatment failed. Complications were local wound infection/heamatoma for one patient without the need for surgical revision and retention requiring CIC, long term in one patient and temporary in another patient.
Conclusions: In a highly selected patient population according to the degree of therapy resistance and aetiology of incontinence, a success rate of 76 % could be achieved (28 % improvement and 48 % cure). This can be considered as an encouraging result for a patient population without other treatment options left. Burch colposuspension is an option for patients with severe therapy resistant incontinence and bladder neck insufficiency if maximal conservative treatment with intensive urotherapy, physical therapy and medical treatment failed. Extensive pre-operative workout with video-urodynamics, cystoscopic evaluation, evaluation of the pelvic floor by a paediatric physical therapist and multi-disciplinary case discussion is highly recommended to achieve correct patient selection.

P247 - BLADDER DYSFUNCTION / RECURRENT URINARY TRACT INFECTION: WHICH IS THE CAUSE?

NİDA DİNÇEL[1], KADRİYE ÖZDEMİR[1], BETÜL SÖZERİ[1], SEVGİ MİR[1]
[1]*EGE UNIVERSITY PEDIATRIC NEPHROLOGY*
[2]*EGE UNIVERSITY PEDIATRİCS NEPHROLOGY*

Introduction: Lower urinary tract function (LUTF) disorders are frequently seen urological problem in children.It can only be presented by recurrent urinary tract infection (R.UTI).Urodynamic studies are important role in the diagnosis and also deterioration of treatment responce. The aim of this study is to ascertain the frequency of LUTF disorders without any symptom/complaint except for R.UTI.
Material and methods: The records of 594 patients had cystometric measurement and uroflowmetry were reviwed retrospectively.264 of them hadn't bladder dysfunction symptoms. All radiographic imagings were normal.Patients were diagnosed with 1 of 4 conditions.The conditions

included 1) dysfunctional voiding(DV): active pelvic floor electromyography during voiding 2) idiopathic detrusor overactivity disorder(IDOD): quiet pelvic floor during voiding, overactive detrusor during filling phase 3) detrusor underutilization disorder(DUD): voiding with expanded bladder capacity but a quiet pelvic floor, and 4) primary bladder neck dysfunction(PBND): right shifted uroflowmetry curve with a quiet pelvic flor and intermittency.

Results: Fourty-four percentage of all patients (264/594) were underwent to urodynamic study, were having normal anatomy and neurology.Although they all haven't any bladder dysfunction symptom or complaint, in order to explain cause of R.UTI,urodynamy was performed.-Mean age of the 264 patients was 8.3 years (range 4.1 to 16.0).Among the 264, 222 of them (84 %) had urodynamical pathology.The pathologic findings were as follows:, 33 (%12.5) had PBND, 99(37.5 %) had IDOD, 66(25 %) had DV and 24(9 %) had DUD,only the last 42(15.9 %) were normal

Conclusions: We supported the need for urodynamic tests, even in anatomycially normal-R.UTIs children, as if they had no any clues of bladder dysfunction.Therefore, we advocate the requirement of urodynamy in these patients asymtomatic for bladder dysfunction were having pathologic urodynamic findings that can be resulted by chronic renal damage

P248 - Nitrofurantoin-induced interstitial pneumonitis and lupoid hepatitis

HAGEN STAUDE, ULRIKE JACOBY, HEIMKE VON OSTEN, KATJA BREUEL, MARIANNE WIGGER
DEPARTMENT OF PEDIATRICS, UNIVERSITY HOSPITAL OF ROSTOCK

Introduction: Nitrofurantoin is experiencing a renaissance in therapy and prevention of urinary tract infections despite a broad spectrum of adverse reactions. These are often related to the gastrointestinal system, whereas fatal inflammatory and fibrotic pulmonary reactions were only occasionally seen.

Material and methods: Here we report on an 8 year old girl with frequent urinary tract infections due to complex neurogenic bladder dysfunction.

Results: Antimicrobial prophylaxis was necessary since infancy. Nitrofurantoin was prescribed for several courses due to intolerance and allergic reactions against numerous antibiotics, i.e. betalactam antibiotics, fluorchinolones, glycopeptides and trimethoprime. After 2 years of continuous administration (1 mg/kg/d) elevated liver enzymes with positive autoantibodies (ANA 1:5120, ASMA 1:320) closely resembling lupoid autoimmune hepatitis were noted. Nitrofurantoin was discontinued and liver function recovered rapidly. One year later nitrofurantoin was reintroduced due to recurrence of urinary tract infections. After one year an interstitial pneumonitis with severe reduction in functional lung volumes developed. Cessation of nitrofurantoin and initiation of glucocorticoid therapy induced a remission. Symptoms resolved completely and pulmonary function was nearly normal 6 weeks later. No further antibiotic prophylaxis was given and urinary tract infections were treated according to resistogram.

Conclusions: Nitrofurantoin is still a therapeutic option to prevent urinary tract infections but requires careful monitoring as multiple and occasionally severe adverse reactions have to be considered.

P249 - Assessments of adults MDRD and CKD-EPI formulas for estimating glomerular filtration rate in children

CHEHADE HASSIB, GIRARDIN ERIC, IGLESIAS KATIA, RAMSEYER PASCAL, FREY PETER, MOSIG DOLORES, CACHAT FRANCOIS
LAUSANNE UNIVERSITY HOSPITAL

Introduction: Glomerular filtration rate (GFR) is a critical indicator of renal function. The optimal measurement of GFR (mGFR) is invasive, costly and difficult to realize. Several formulas for estimated GFR (eGFR) have been developed to replace mGFR, but with no proven effectiveness in being universally applicable across all patients' ages. The NKF-KDOQI guidelines recommend against the usage of adults formulas in pediatric population but with no study to confirm it. We aim to evaluate the accuracy of the two recently used adults' formulas (MDRD and CKD-EPI) in children with various stages of chronic kidney disease (CKD).

Material and methods: 550 inulin clearances (iGFR) for 391 children were analyzed. We divided our cohort into 3 groups: group 1 with an iGFR>90 ml/min x 1.73 m2, group 2 with an iGFR between 60–90 ml/min x 1.73 m2 and group 3 with an iGFR<60 ml/min x 1.73 m2.

Results: Both formulas significantly overestimate the mGFR with a significant bias ($p<0.001$) and present poor accuracies and poor spearman correlations in all CKD groups. For the MDRD and CKD-EPI formulas: with an accuracy of 10 %, only 11 % and 6 % of the eGFR are accurate, respectively. With an accuracy of 50 %, only 38 % and 46 % of the value of eGFR reaches this level of accuracy, respectively.

Conclusions: The predictive performance of these two formulas was suboptimal for eGFR in children with all CKD stages, and cannot therefore be applied in this population group. Our study supports the NKF-KDOQI guidelines.

P250 - Acute kidney injury in pediatric patients: experience of a single center during an 11-year period

BIRUTE PUNDZIENE[1], DIANA DOBILIENE[1], SARUNAS RUDAITIS[1]
[1]*HOSPITAL OF LITHUANIAN UNIVERSITY OF HEALTH SCIENCES KAUNO KLINIKOS*
[2]*CLINIC OF CHILDREN´S DISEASES*

Introduction: The aim of our study was to determine the causes of acute kidney injury (AKI) in children, to compare outcomes between two periods and to evaluate the influence of new methods of renal replacement therapy (RRT) on mortality.
Material and methods: A retrospective analysis of medical record data of all children treated for AKI at the Clinic of Children Diseases, during the period of 1998–2008 (I period 1998–2003 and II period 2004–2008) was made. Age, primary disease, indications for RRT, methods of RRT used, outcomes, causes of mortality rate were evaluated.
Results: Of the 179 children with AKI, 75 (41.9 %) were treated during 1998–2003 and 104 (58.1 %) during 2004–2008. Primary glomerular disease and sepsis were the leading causes of AKI in both the periods. AKI without involvement of other organs was diagnosed: for 42 (56.0 %) children in the first period and 64 (61.5 %) in the second. A total of 124 (69.3 %) children were treated in a pediatric intensive care unit. Multiple organ dysfunction syndrome with AKI was diagnosed for 33 (44 %) patients in the first period and for 40 (38.5 %) in the second. A significant decrease in mortality among patients with MODS during the second period was observed (78.8 % vs. 37.5 %).
Conclusions: More than half of patients had secondary acute kidney injury of nonrenal origin. More than two-thirds of patients with AKI were treated in the pediatric intensive care unit. Multiple organ dysfunction syndrome was diagnosed for 40.8 % of children with AKI. Renal replacement therapy was indicated for one-third of patients with AKI. A 2.5-fold decrease in mortality was observed in the second period as compared to the first one.

P251 - JAFFE CREATININE CENTILES IMPROVE PREDICTION OF RENAL DRUG CLEARANCE IN ELBW NEONATES

ANNE SMITS, ISABEL GEORGE, DJALILA MEKAHLI, MAISSA RAYYAN, GUNNAR NAULAERS, ELENA LEVTCHENKO, KAREL ALLEGAERT
UNIVERSITY HOSPITALS LEUVEN, BELGIUM

Introduction: Birth weight and postnatal age but not creatinine were covariates of amikacin (Ak) clearance in neonates (1), while there is similarity between amikacin clearance and glomerular filtration rate (GFR). We suggest that estimation of GFR in individual cases based on postnatal age dependent threshold (P75) creatinine values for extreme low birth weight (ELBW<1000 g) infants (2) can be used as additional biomarker of amikacin clearance.
Material and methods: Individual Ak pharmacokinetics were calculated (3,4) in ELBW cases admitted between 1999–2006. Individual creatinine values (Jaffe), were classified based on reference values for postnatal age (P75) in ELBW cases (2). Data were reported by median and range, covariates of Ak clearance (ml/kg/min) were analysed (Spearman-Rank, Mann Whitney U).
Results: Ak pharmacokinetics were available in 175 ELBW neonates. Median creatinine was 1.01, 0.47-1.89 mg/dl, (equal to 89, 41.5-167 μmol/l). Median Ak clearance was 0.37 (range 0.05-2.33) ml/kg/min. There was a significant correlation with gestational age ($r=0.325$), postnatal age ($r=0.21$) and birth weight ($r=0.16$). There was a significant higher Ak clearance when creaP75 ($p<0.001$). Similar differences were documented when limited to early (< 8 days) or late neonatal (day 8–28) life.
Conclusions: Further individualisation in amikacin clearance in ELBW neonates based on creatinine reference values (P75) should be considered. This likely reflects non-ontogeny related (disease, co-medication) GFR differences.
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P252 - POSTNATAL CREATININE PATTERNS IN NEONATES: JAFFE COMPARED TO ENZYMATIC QUANTIFICATION

ANNE SMITS, JELTE KELCHTERMANS, SARAH HENDRICKX, DJALILA MEKAHLI, FLORENT VANSTAPEL, ELENA LEVTCHENKO, KAREL ALLEGAERT
UNIVERSITY HOSPITALS LEUVEN, BELGIUM

Introduction: Serum creatinine (Scr) reflects to a certain extent GFR in neonates, but postnatal observations also depends on the technique used (Jaffe colorimetry or enzymatic quantification) as recently quantified in ELBW neonates (1,2). We aimed to assess the impact of enzymatic versus Jaffe quantification method and describe postnatal patterns for both techniques in neonates of higher birth weight (3).
Material and methods: Scr values quantified by Jaffe in 1140 neonates were compared to values obtained by using enzymatic quantification in 1023 neonates in one NICU. All Scr values collected in the first 42 days of postnatal life were collected and postnatal trends for cohorts (< 1 kg, 1–2 kg, 2–3 kg and>3 kg) were compared.

Results: Postnatal patterns were similar between both techniques, with an initial increase in early postnatal life, highest and last in the smallest neonates and a subsequent decrease, most delayed in the smallest neonates. For all consecutive postnatal observations, Jaffe was always higher compared to enzymatic techniques, but the differences in median values between both techniques (0.1-0.26) mg/dl, equal to 8.8-23 μmol/l, were not a fixed value.
Conclusions: When using Scr to estimate renal function in neonates, clinicians should in addition to the postnatal changes and other covariates of renal function, also consider the technique applied. There is no fixed conversion factor to correct for differences between both techniques. References: (1) Allegaert K et al, J Matern Fetal Neonatal Med DOI 10.3109/14767058.2012.657277 (2) Kuppens M et al, J Matern Fetal Neonatal Med DOI 10.3109/14767058.2011.602144 (3) Bueva A et al. Pediatr Res 1994

P253 - Type 1 pseudo-hypoaldosteronism: report on one patient.

KRUG PAULINE, POMMELET VIRGINIE, BOYER OLIVIA, BOUCHIREB KARIM, SALOMON REMI
NECKER HOSPITAL

Introduction: Type 1 pseudo-hypoaldosteronism (PHA1) is a rare genetic disorder of mineralocorticoid resistance, associating salt wasting and hyperkaliemia with high plasma levels of renin and aldosterone. Two genetic forms are described: an autosomal dominant form, also called renal form, associated with a mutation in the mineralocorticoid receptor (MR), and an autosomal recessive PHA1, called multiple organ form, due to mutations in the subunits of the epithelial sodium channel (EnaC).
Material and methods: We report the case of a newborn, issue from consanguinous parents, hospitalized at ten days for hypovolemic chock and ventricular rhythm disorders. Biological tests revealed hyponatremia (119 mmol/l) with unadapted natriuresis (86 mmol/l), major hyperkaliemia (10 mmol/l), low ACTH with normal 17OH progesterone, and high plasma concentrations of renin and aldosterone. Chloride sweat test showed high sodium level (128 mmol/l). Diagnosis of multisystemic form of PHA1 was then established, confirmed by genetic study, which highlighted an homozygous mutation of SCNN1G, coding for γ subunit of EnaC.
Results: During the three first months of life, many hydroelectrolytic decompensations occured, often due to gastrointestinal or respiratory infections. Sodium substitution was progressively rised up to 45 meq/kg/day, associated with a low-potassium diet and cation exchange resin. He presented with a multisystemic disease. First of all, he had an acute respiratory distress needing oxygen therapy, with normal chest X-ray, improved by daily kinesitherapy. This lung impairment was explained by thick and viscous mucus, as seen in cystic fibrosis. Moreover, he had a diarrhea, increased by oral sodium intakes. Fludrocortisone 100 μg per day allowed us to progressively tapered sodium intake down to 30 meq/kg/day and to reduce the frequency of hydrolectrolytic decompensations. The patient went back home at 3 months of life with oral sodium intake 30 meq/kg/day, divided in three daily doses and a nocturnal continuous infusion.
Conclusions: As a conclusion, we report here a severe systemic PHA1, associating renal, cutaneous, gastrointestinal and respiratory involvements. A substitutive therapy with mineralocorticoids allowed us to tapered sodium intake and to reduce the frequency of decompensations, although physiopathology is not clear.

P254 - NGAL in children after complex cardiac surgery - does the postoperative period matter?

MICHAŁ MARKIEWICZ, WOJCIECH KRAJEWSKI, ANNA JANDER, JOLANTA LUKAMOWICZ, JOLANTA ROMAK, MARCIN TKACZYK
POLISH MOTHER'S MEMORIAL HOSPITAL RESEARCH INSTITUTE

Introduction: Acute Kidney Injury (AKI) occurs up to 80 % children after CPB. Neutrophil gelatinase associated lipocain (NGAL) proved its value in detection of subclinical kidney injury after CPB The question of additional risk factors of poor prognosis remains still open. Aim of the study was to assess changes in NGAL concentration in serum in children with very severe congenital cardiac malformations (RACHS 1 – 3,37) after CPB and describe additional risk factors attributed to prolonged kidney injury.
Material and methods: The study group comprised 41 children (M:26 F:15, aged 0–14 y.) after cardiac surgery with CPB with high scoring in RACHS-1 and ARISTOTLE (complexity of cardiac surgery). Clinical parameter of the patient and procedure were analyzed. Blood for NGAL, creatinine, NT-proBNP, lactate was tested before and 2, 4, 12, 24, 48, 72 h after CPB.
Results: 68 % of patients presented with AKI by pRIFLE. We performed further analysis in three subgroups AKI I/F (13) AKI R (20) and non-AKI. NGAL concentration in non-AKI was highest in 2nd hour whereas in AKI I/F in 4th hour and AKI-F in 48 hour from CPB. The rise in NGAL was significant in all three groups of patients. NGAL in AKI-F group was significantly higher than in the rest in 24 h from cardiac surgery. NT-proBNP concentration rose significantly in first 2 groups in 12 h with subsequent decrease, but in AKI-F the peak is detected in 24 h and reached plateau in 48 h. Patients from AKI-F group had longer time of lactate

acidemia, higher VIS score, lower diuresis after operation, longer time of mechanical ventilation and longer stay in ICU.

Conclusions: The study showed that the incidence of AKI is high (68 %) in children after complex cardiac surgery. NGAL serum concentration proved its value in prediction of AKI, but suggested that the AKI in failure stage is not only a result of initial injury but also a consequence of low cardiac output in first several hours after CPB.

P255 - Neonatal presentation of Lesch-Nyhan syndrome with acute kidney injury

ALISON LT MA, RUKSHANA SHROFF, STEPHEN D MARKS

DEPARTMENT OF PAEDIATRIC NEPHROLOGY, GREAT ORMOND STREET HOSPITAL FOR CHILDREN

Introduction: Lesch-Nyhan syndrome is a rare inherited disorder caused by a deficiency of the enzyme hypoxanthine-guanine phosphoribosyl-transferase (HRPT). It is an uncommon cause and easily missed diagnosis of neonatal acute kidney injury and we report the early diagnosis and management of a patient.

Material and methods: Retrospective review of an 18-day old first born baby of non-consanguineous parents who presented with poor feeding and 13 % weight loss from birth. Clinical examination showed depressed fontanelle and dry mucous membranes. Blood tests revealed hyponatramia (110 mmol/l), hyperkalaemia(8.1 mmol/l) with renal failure (urea of 38.2 mmol/l and creatinine of 448umol/l) and metabolic acidosis (pH of 7.26, bicarbonate of 14.8 mmol/l).He was managed with intravenous rehydration, sodium bicarbonate and calcium resonium. Despite adequate hydration, the recovery of his renal function was very slow. The baby was noted to have swollen left index finger at the proximal interphalangeal joint. X-ray of the finger showed soft tissue swelling without fracture or dislocation which led us to test for hyperuricaemia.

Results: He had hyperuricaemia with serum urate of 1440umol/l(normal 80–310) with hyperuricosuria (urine urate : creatinine ratio of 5.31 mmol/mmol (normal 0.42-1.53). Renal ultrasound showed bilateral echogenic kidneys with multiple twinkle artefacts within the medullary pyramids. Endocrine screening for congenital adrenal hyperplasia was normal. No HPRT activity was detected in the red cell lysate assay or in the intact cell study (0 % with normal >20 %) with radiolabelled hypoxanthine. The red cell nucleotide profile showed a high level of nicotinamide adenine dinucleotide so together with hyperuricaemia, these findings wereconsistent with HPRT deficiency, which was confirmed on mutational analysis. The coding region and flaking introns of the HPRT gene were sequenced and the patient is homozygous for the deletion HPRT c.400delG; this mutation is predicted to result in a frame shift and is consistent with complete HPRT deficiency. He was commenced on oral allopurinol and three month follow up has shown a plasma creatinine of 50umol/l, serum and urine urate of 671umol/l and 2.44 mmol/mmol respectively.

Conclusions: Lesch-Nyhan syndrome is an uncommon cause of neonatal acute kidney injury. Clinicians should be alerted to children who present with renal failure, urate crystals seen in nappies (orange tinge may be confused with macroscopic haematuria) and twinkle artefacts on renal ultrasound scans. Early detection and prompt management with allopurinol to reduce hyperuricaemia is of clinical importance.

P256 - Is Serum Cystatin C a Better Marker than Serum Creatinine for Monitoring Renal Function in Pediatric Intensive Care Unit?

NAZIK AŞILIOĞLU[1], YONCA AÇIKGÖZ[2], MUHAMMED ŞÜKRÜ PAKSU[1], MURAT GÜNAYDIN[3], OZAN ÖZKAYA[2]

[1]*ONDOKUZ MAYIS UNIVERSITY SCHOOL OF MEDICINE, DIVISION OF PEDIATRIC CRITICAL CARE, SAMSUN, TURKEY*

[2]*ONDOKUZ MAYIS UNIVERSITY SCHOOL OF MEDICINE, DEPARTMENTS OF PEDIATRIC NEPHROLOGY, SAMSUN, TURKEY*

[3]*ONDOKUZ MAYIS UNIVERSITY SCHOOL OF MEDICINE,DEPARTMENT OF CLINICAL MICROBIOLOGY, SAMSUN, TURKEY*

Introduction: In critically ill patients mild to moderate reductions in glomerular filtration rate are not instantly followed by parallel changes in serum creatinine (SCr). The aim of this study was to identify a value of serum cystatin C (cys-C) level as a marker for monitoring renal function in critically ill pediatric patients in intensive care.

Material and methods: Using an observational cross-sectional design, 98 patients who had been admitted to the pediatric intensive care unit were included in the study. Creatinine clearance was used to estimate Glomeruler Filtration Rate (eGFR). The diagnostic value of serun SCr and cys-C to identify renal impairement (eGFR<80 ml/minute per 1.73 m2) was evaluated using receiver operating characteristic curve analysis.

Results: Impaired renal function was determined in 43 (43.9 %) of 98 patients. The correlation between the inverse of serum cys-C and eGFR ($r=-0.70$, $p<0.0001$) was better than the correlation between the inverse of SCr and eGFR ($r=-0.27$, $p=0.008$). The sensitivity rates for cys-C were higher than for SCr (81 % vs 24 %), and Cys-C showed better negative predictive value and

accuracy than SCr. Serum Cys-C was found to be superior to SCr to predict renal impairment (AUC for cys-C, 0.932 and for SCr, 0.658). Renal impairment was determined in 17 (43.9 %) of 41 critically ill patients younger then one year old. There was no significant correlation between eGFR and SCr (r=−0.27, p=0.08). Cys- C also had a higher diagnostic value than SCr in identifying the impaired renal function of critically ill patients younger than 1-year old (AUC, 0.615 for SCr and 0.929 for cysC).

Conclusions: It can be concluded that cys-C is superior to SCr for the detection of renal impairment in critically ill children.

P257 - Changes in mean arterial pressure/heart rate rhythmicity, target organ damage and visceral obesity in hypertrensive boys on antihypertensive therapy

ANNA NIEMIRSKA[1], MIECZYSŁAW LITWIN[1], JANUSZ FEBER[2]

[1]*CHILDREN`S MEMORIAL HEALTH INSTITUTE, DEPARTMENT OF NEPHROLOGY, KIDNEY TRANPLANTATION @ ARTERIAL HYPERTENSION*

[2]*DIVISION OF NEPHROLOGY, DEPARTMENT OF PEDIATRICS, CHILDREN'S HOSPITAL OF EASTERN ONTARIO, UNIVERSITY OF OTTAWA*

Introduction: Primary hypertension (PH) is associated with disturbed blood pressure rhythmicity (BPR), which may, in turn, worsen the cardiovascular morbidity and mortality. The goal of our study was to analyze changes in BPR over 12-month period in adolescent boys with PH. We hypothesized that management of PH would improve BPR in addition to the improvement of blood pressure (BP) and regression of left ventricular mass (LVM)/carotid intima-media thickness (CIMT).

Material and methods: Fifty boys aged 5 to 17 years (median=14) were prospectively evaluated with ambulatory blood pressure monitoring (ABPM), echocardiography (LVM), ultrasonography (CIMT) and magnetic resonance imaging for visceral adipose tissue (VAT) before and after 12-month of antihypertensive non-pharmacologic (diet, exercise) and pharmacologic treatment. Mean arterial pressure (MAP) and heart rate (HR) rhythmicity was analyzed using Fourier analysis (Chronos-Fit software). Amplitudes and acrophases of MAP/HR rhythms were obtained for 24 h, 12 h and 8 h periods before and after treatment.

Results: Changes in BPR were then correlated with changes in body mass index (BMI), waist circumference (WC), VAT, BP, LVM and CIMT. After one year of antihypertensive therapy 68 % of patients reached normotension on ABPM and LVM/CIMT decreased in 60 %/62 % of patients. No correlation was noted between changes in MAP/HR rhythmicity and changes in BMI, BP and LVM/CIMT, but a significant correlation was noted between the change in 24 h MAP amplitude and the change in WC (p=0.035). Moreover, the decrease of VAT correlated significantly with the decrease of 24 h MAP and 24 h HR acrophases (both p<0.05). There were no differences in changes of MAP/HR rhythms between pts who achieved or not achieved normotension and/or regression of LVM and CIMT.

Conclusions: We conclude that abnormal MAP and HR rhythmicity persists despite effective antihypertensive therapy and regression of target organ damage. Changes in MAP/HR rhythmicity correlate with the decrease of visceral obesity suggesting that visceral fat plays an important role in abnormalities of sympathetic activity in hypertensive adolescents

P258 - URINARY CREATININE MEASUREMENTS IN NEONATES: JAFFE COMPARED TO ENZYMATIC QUANTIFICATION

ANNE SMITS, PIETER VERMEERSCH, MIEKE VAN DYCK, ELENA LEVTCHENKO, SOPHIE VANHAESEBROUCK, DJALILA MEKAHLI, FLORENT VANSTAPEL, KAREL ALLEGAERT

UNIVERSITY HOSPITALS LEUVEN

Introduction: Creatinine can be quantified by Jaffe or enzymatic techniques. However, paired analysis in urine samples collected in neonates to document the extent and the covariates of the difference in urinary creatinine values between both techniques are unreported.

Material and methods: Creatinine in 84 urine samples collected in a study on propylene glycol elimination and tolerance in neonates was quantified by both Jaffe and enzymatic method (Cobas 8000 modular analyser) (1). Jaffe versus enzymatic results were compared (Wilcoxon, Blant Altman) and the impact of clinical characteristics on the individual differences between both techniques were explored (Rank correlation).

Results: Median Jaffe and enzymatic creatinine in urine were 9.25 (3.7-42.2) and 9.15 (3.8-42.9) mg/dl (p<0.05). The mean difference was 0.17 (SD 0.6) mg/dl and there was a significant correlation of this difference with gestational age (r=−0.22), postnatal age (r=0.59) and crea enzymatic in urine (−0.64).

Conclusions: The difference between both techniques is 0.17 (SD 0.6) mg/dl. The absolute difference and its variability is of similar extent when compared to the difference in serum creatinine values recently reported in neonates (2). However, because of the overall higher creatinine values in urine, this only results in about 2 % difference in absolute values and is of limited clinical relevance. References: (1) Kulo A et al., Chromatographia 2011;73:463–470; (2) Allegaert K et al., J Matern Fetal Neonatal Med DOI 10.3109/14767058.2012.657277

P259 - RENAL VEINS THROMBOSIS RESULTING IN ACUTE RENAL FAILURE IN NEWBORN

KHADIJA EMIROVA[1], EVGENIYA TOLSTOVA[1], ELENA OLKHOVA[1], TATIANA PANKRATENKO[2], TATIANA ABASEEVA[2], GALINA GENERALOVA[2], ANASTASIYA MAKULOVA[2]
[1]*MOSCOW STATE MEDICAL STOMATOLOGICAL UNIVERCITY*
[2]*MOSCOW REGIONAL RESEARCH CLINICAL INSTITUTE*

Introduction: Bilateral renal veins thrombosis may be one of the causes of acute renal failure (ARF) in children. Thrombosis in newborns may be due to inherited thrombophilia - genetic polymorphism in coagulation system and coagulation inhibitors deficiency. Antithrombin III (ATIII) is a potent inhibitor of the coagulation cascade, which can be used in treating such patients.
Material and methods: We observed a patient whose condition has sharply deteriorated at the age of 3.5 hours due to gastro-intestinal, pulmonary hemorrhage and gross hematuria. Acute renal failure developed by the end of the first day of life. We revealed low levels of AT III, increase of fibrinolysis, high fibrin degradation products (FDPs), decrease platelet aggregation, prolongation of ACT. Ultrasound revealed multiple thrombosis: main renal veins, vena cava inferior, the left branch of portal vein and adrenal hemorrhage.
Results: We use heparin via continuous infusion in a dose of 600 IU/kg/day with fresh frozen plasma. AT III was administered every 3 days for 300 IU. ARF resolved on the 7th day. Level of AT III and fibrinolysis became normal. The restoration of blood flow in the main renal veins, the left branch of portal vein, vena cava inferior visualized by ultrasound, the adrenal hematoma were lysed. Nephrosclerosis of right kidney was formed. Later we found thrombophilia: reduction of protein C, S, multiple hemostatic system genetic polymorphisms.
Conclusions: Newborns have high risk of developing thrombosis. Ultrasound can confirm pathological thrombus formation. Combined treatment with AT III promotes more rapid recanalization of thrombosed veins. To evaluate the prognosis is necessary to investigate thrombophilic markers.

P260 - SWITCH FROM PROTEASOME TO IMMUNOPROTEASOME IN CHILDREN WITH IDIOPATHIC NEPHROTIC SYNDROME.

ROBERTA CAMILLA, ELISA LOIACONO, LICIA PERUZZI, RACHELE GALLO, MARIA ELENA DONADIO, LUCA VERGANO, FEDERICA CAMPOLO, LAURA MORANDO, ALESSANDRO AMORE, ROSANNA COPPO
NEPHROLOGY, DIALYSIS, TRANSPLANTATION, REGINA MARGHERITA HOSPITAL, TURIN, ITALY

Introduction: In the development of idiopathic nephrotic syndrome (NS) a role of innate immunity has been suggested through viral infections and the interferon pathway. The proteasome (PS) mutisubunit proteases degrade ubiquitinilates proteins and are converted into immunoproteasome (iPS), under the effect of interferons, by replacing β1, β2 and β5 PS subunits with LMP2, MECL-1 and LMP7 iPS subunits. The switch to iPS improves the catalytic proteasomal activities with production of optimal MHC-I ligands, shaping T cell response. In peripheral mononuclear cells (PBMC) of 28 children (2–18 years) with NS we investigated the innate immunity focusing on Toll-like receptor (TLR) expression and the switch from proteasome to immuneproteasome.
Material and methods: Real time PRC (Taqman) was used to measure mRNA expression of TLR3, TLR4, TLR9 and of PS (ß1, ß2, ß5) and iPS (LMP2, MECL-1, LMP7) subunits. The iPS/PS switch was expressed as ratio between iPS and corresponding PS mRNAs.
Results: iPS/PS mRNA subunits ratio of MECL-1/β2 was significantly increased in PBMC from NS patients in comparison to healthy controls (1.26±0.61 versus 1.02±29, P= 0.04) while LMP2/β1 and LMP7/β5 in NS patients were not different from controls (respectively 1.00±0.51 vs 0.91 ±0.42 and 0.91±0.5 vs 1.07±0.33; p ns). The switch MECL-1/β2 was significantly correlated with TLR3 mRNA (P=0.02). This switch remained unchanged in different phases of clinical activity. However, in 3 patients treated with a protease inhibitor provided with anti-PS activity, saquinavir, a reversal to normal values of MECL-1/β2 mRNA ratio was observed (2.02 before treatment vs 0.86 after). No difference was detected in levels of TLR3-4-9 in patients and healthy controls.
Conclusions: We report an a switch from proteasome to immunoproteasome in children with NS which was correlated with TLR3 activation. These results suggest an involvement of the interferon pathway of innate immunity in this disease.

P261 - Typical Hemolytic Uremic Syndrome can be associated with an abdominal compartment syndrome: a case report and review of the literature

MCHIRGUI LEILA, CLEMENT DE CLETY STEPHANE, HOUTEKIE LAURENT, DE MAGNEE CATHERINE, GODEFROID NATHALIE
UNIVERSITY HOSPITAL ST LUC

Introduction: We report the case of a five-years-old boy who presented with typical Hemolytic Uremic Syndrome (HUS) caused by E.Coli 0157:H7. He fulfilled all criteria for a severe form of the disease and developped a lethal abdominal compartment syndrome (ACS).

Material and methods: This boy was admitted for bloody diarrhea and vomitings. Bloodchemistry showed hemolytic anemia, thrombocytopenia, very high WBC count and acute renal failure. He developped anuria, severe colitis and epileptic encephalopathy. Despite continuous veno-venous hemofiltration and plasmapheresis, his condition worsened and intra-abdominal pressure increased from 12 to 22 mmHg. Laparotomy was performed but the child died in the operating room from cardiac arrest.
Results: HUS mortality is reported to be between 1 and 5 % and is nearly always due to severe extrarenal disease, including central nervous system involvement. Long-term sequelae such as chronic renal insufficiency or arterial hypertension are seen in one third of children with HUS. Intestinal complications including severe colitis and bowel necrosis are less frequent but are likely to lead to the development of ACS. ACS is defined by an increased intra-abdominal pressure leading to circulatory troubles and multiorganic defects. It is a rare but severe complication observed in children with a spontaneous evolution to death in 80 to 100 % of the cases. Lack of guidelines makes ACS management in children difficult
Conclusions: Based on this Case report, we suggest to perform a close monitoring of intra-abdominal pressure in children with severe HUS and colitis. Surgical exploration is required in critical cases.

P262 - A new proteomic approach to the study of Peritoneal effluents in pediatric patients

MAURIZIO BRUSCHI[1], GIOVANNI CANDIANO[2], LAURA SANTUCCI[1], SALVATORE LUZIO[1], ROSSELLA CANNAVO[1], GIAN MARCO GHIGGERI[2], ENRICO VERRINA[2]
[1]*RENAL CHILD'S FOUNDATION*
[2]*GASLINI CHILDREN'S HOSPITAL*

Introduction: Peritoneal dialysis effluent (PDE) represents an attractive biochemical window into the peritoneum. The predominant proteins in the PDE are Albumin, serotransferrin, a1-antitrypsin, a1-microglobulin and immunoglobulins. The abundance of these proteins may limit the ability to identify other potential biomarkers of peritoneal function or damage.
Material and methods: In this study, combinatorial peptide ligand library (CPLL) was used to enrich low abundance proteins and simultaneously reduce proteins which are highly represented. The CPLL elutions of PDE (PM-PDE) obtained from paediatric patients were analysed by two-dimensional electrophoresis. We studied 19 patients with a median age of 3.9 years (range 0.2-16.6), and body surface area of 0.59 m2 (0.18-1.53). Patients' primary renal disease was renal dysplasia in 6 cases, nephronophthisis in 5 cases, hemolytic uremic syndrome, focal segmental glomerulosclerosis, membranoproliferative glomerulonephritis, renal cortical necrosis, congenital nephrotic syndrome, autosomal recessive polycystic kidney disease, diffuse mesangial sclerosis and polycystic kidneys in 1 case each. At the moment of the study, patients had been on automated peritoneal dialysis (APD) with glucose-based solutions for a median of 12.5 months (range 1–38 months), and had not suffered from peritonitis in the previous month.
Results: Image gel analysis revealed more than 1700 spots in the PM-PDE and about 1000 spots in the PDE. Therefore, combined proteomic approach highlighted a mean of 700 new proteins in each gel. Some differences in PM-PDE proteome profile were observed in relation with the duration of APD treatment. In particular, in patients on APD for more than 18 months, we observed an increase of intelectin-1 a protein associated with chronic inflammation, and a decrease of gelsolin a protein involved in extracellular matrix modulation.
Conclusions: The further step of our study will consist in the identification of other proteins whose concentration may change with time of APD in order to clarify the biological meaning of the observed differences.

P263 - ACUTE KIDNEY INJURY (AKI) IN CHILDREN WITH EXOGENOUS POISONING

MARIA CHEMODANOVA, NADEZDA SAVENKOVA
SAINT-PETERSBURG STATE PEDIATRIC MEDICAL ACADEMY

Introduction: The problem of exogenous poisoning in children is important because of frequent development of AKI. The aim of our study is identify the features of the course and outcome of AKI in children with exogenous poisoning.
Material and methods: Seventy children (36 girls, 34 boys) aged between 1–18 years with exogenous poisoning, were included in our research. Anamnesis, clinical symptoms, glomerular filtration rate (GFR) were analyzed. The GFR was calculated by Schwartz formula, and patients were classified according to p-RIFLE classification of AKI (Akcan-Arikan A. et al., 2007).
Results: From 70 children with exogenous poisoning 68 (97 %) children had acute interstitial nephritis, 2 patients (3 %) – nephrotic syndrome. AKI was diagnosed in 37 patients (53 %) in case of poisoning nonsteroidal anti-inflammatory drugs (12), a mixture of drugs (7), vitamin A (1), gentamicin (1), enalapril (1), iron (1), energy drinks (1), alcohol (2), gasoline (2), psychotropic substances (1), anticonvulsants (carbamazepine) (1), cadmium (1) mushrooms (1), narcotic drugs – amphetamines, heroin, methadone (5). From 37 patients with AKI 16 (43 %) had class R (risk), 7 (19 %) – class I (injury), 13 (35 %) – class F (failure), 1

patient (3 %) – Class L (loss of kidney function). Renal replacement therapy with hemodialysis was required for 2 patients with AKI (alcohol, gasoline poisoning) (Class F and L). In 2 cases the poisoning was accompanied with the development of polyogranic failure (gasoline and mushrooms poisoning). Thirty six patients with AKI recovered renal function as a result of therapy, renal replacement therapy with hemodialysis continued in one patient with Class L.

Conclusions: In most children with exogenous poisoning diagnosed initial stage of AKI (class R). The therapeutic strategy of the acute kidney injury based on the class of AKI. The therapy started in time improved the prognosis of AKI.

P264 - PERIOPERATIVE DYNAMICS OF RENAL BIOMARKERS IN CHILDREN UNDERGOING OPEN HEART SURGERY.

JEKABS KRASTINS, ZANE STRAUME, JANIS AUZINS
UNIVERSITY CHILDRENS HOSPITAL

Introduction: Cardiac surgery with cardiopulmonary bypass (CPB) is commonly perceived as a risk factor for decline in renal function, especially in infants and children having immature kidney. Hypothermia, hypoxia, hypotension, non-pulsatile blood flow during CPB, use of ACE inhibitors, inotropic and (or) vasoactive substances affects kidney and contributes to the development acute kidney injury (AKI). Objective of our study was to evaluate dynamics of renal biomarkers – serum creatinine (SCr) and glomerular filtration rate (GFR) in children undergoing surgical correction of congenital heart disease (CHD).

Material and methods: We conducted prospective, non-randomized observational study at the tertiary care University Children's Hospital Pediatric ICU. The study included 30 patients, 12 boys and 18 girls with CHD. Their median body weight was 6,8 kg, (IQR 5,2<8,2 kg) and median age 7 months (IQR 5<10 months). SCr was determined by Jaffé's method (Cobas 6000 analyzer, Roche) and preoperative and postoperative creatinine clearance (ClCr) was estimated using Schwarz formula. During surgical repair and till the end of the first 24 hours urine was collected to measure of ClCr, using the difference in urine (UCr) and SCr concentrations. Urine output, body temperature, duration of aortic cross clamping and cardiopulmonary bypass was recorded.

Results: Median duration of aortic cross-clamping was 95 min., (IQR 70,5<133 min.), median CPB time was 147 min. (IQR 116,75<205 min.). Median lowest body temperature (°C) during CPB was 29,75 °C (IQR 27,48<30,83), median urine output during surgical correction was 2,4 ml/kg/h (IQR 1,29<3,15 ml/kg/h). Intraoperative SCr rised up to 35 mmol/l (IQR 27,5<50,5) vs preopertive SCr 29 mmol/l (IQR 24<32,9), p<0,0001. GFR declined from preoperative 98,4 ml/min./1,73 m2 (IQR 89,6<123,04) to intraoperative 39,8 ml/min./1,73 m2, (IQR 24,9<65,5), P<0,0001.

Conclusions: Surgical repair of CHD in children using CPB has severe, but transient effect on expression of renal biomarkers. Before discharge from the hospital SCr and GFR returned to normal values.

P265 - Renal biopsy findings in a patient with loss-of-function of ITGA3

AOIFE WATERS[1], LESLEY REES[1], GIUSEPPINA SPARTA[2], VIRGINIA VEGA-WARNER[3], CRISTINA HAS[4], FRIEDHELM HILDEBRANDT[3], GUIDO LAUBE[2], NEIL SEBIRE[1], DETLEF BOCKENHAUER[1]
[1]*UCL INSTITUTE OF CHILD HEALTH AND GREAT ORMOND STREET HOSPITAL, UK*
[2]*CHILDREN'S HOSPITAL ZUERICH, SWITZERLAND*
[3]*DEPARTMENT OF PAEDIATRICS OF THE UNIVERSITY OF MICHIGAN, ANN ARBOR, USA*
[4]*DEPARTMENT OF DERMATOLOGY OF THE UNIVERSITY FREIBURG MEDICAL CENTER, GERMANY*

Introduction: Rare monogenic diseases can provide molecular insight into critical physiological processes as highlighted by recent reports of disrupted glomerular permselectivity in patients with mutations in integrinα3 (ITGA3). Highly expressed in developing podocytes, integrins are heterodimeric transmembrane receptors (composed of an α and a β subunit) that regulate podocyte function by linking the foot process actin cytoskeleton at the basolateral membrane to the extracellular matrix of the GBM. We report the histological characteristics of ITGA3-loss of function within the human glomerular basement membrane.

Material and methods: Review of a renal biopsy from a 5 month old patient with a homozygous missense mutation in ITGA3 (c.1883 G>C, p.Arg628Pro) and additional staining for ITGA3 and collagen aIV.

Results: Light microscopic findings revealed focal and segmental glomerulosclerosis. Immunohistochemistry revealed loss of ITGA3 and collagen aIV staining along the glomerular basement membrane. Ultrastructural features of a disorganised glomerular basement membrane (GBM) associated with effaced podocyte foot processes were evident on transmission electron microscopy reminiscent of a "basket-weave" pattern, otherwise seen in Alport or Pierson syndrome.

Conclusions: ITGA3 mediates crosstalk between podocyte and basement membrane. This interaction is crucial not only for podocyte function, but also for proper organisation of the basement membrane.

P266 - FOUR ATYPICAL HEMOLYTIC UREMIC SYNDROME CASES

CENGIZ ZEYBEK[1], ZEYNEP BİRSİN ÖZÇAKAR[2], BURCU BULUM ÖZTÜRK[2], ASLI KAVAZ[2], MESIHA EKIM[2], FATOŞ YALÇINKAYA[2]
[1]*GULHANE MILITARY MEDICAL ACADEMY, PEDIATRIC NEPHROLOGY, ANKARA TURKEY*
[2]*ANKARA UNIVERSITY SCHOOL OF MEDICINE,PEDIATRIC NEPHROLOGY,ANKARA TURKEY*

Introduction: Approximately 10 % of the hemolytic uremic syndrome (HUS) cases are classified as atypical and are thought to be associated with uncontrolled activation of the complement system.
Material and methods: Here we planned to present clinical data of our patients with atypical HUS.
Results: Our first patient is a 6 years old girl. Her complaints started at 6 months of age with anemia. HUS findings developed, factor H levels and C3 were found to be low. Chronic peritoneal dialysis was started at 8 months of age. At 6 years of age, cadaveric renal transplantation was performed with prophylactic eculizimab therapy. She is still continuing to take eculizimab without any relapse. The second patient is a 7 years old boy. HUS was diagnosed at 4 years of age. Family history revealed atypical HUS in two close relatives. Mutations in both factor H and factor I were detected. Acute peritoneal dialysis was performed for 3 months and then all of the laboratory abnormalities returned to normal and no relapse was seen. The third patient is a 6 years old girl. HUS findings started at 4 years of age. C3 level was low and anti factor H antibodies were detected. She was treated with fresh frozen plazma therapy for 3 months. Then all her clinical and laboratory findings returned to normal. The patient has no complaints in the last two years. The fourth patient is a 7 years old boy. He was referred to our hospital with atypical HUS and ESRD findings at 5 years old. Anti factor H antibodies were detected. The patient was on peritoneal dialysis for 3 years.
Conclusions: Atypical HUS is a rare renal disorder that occurs due to a variety of genetic abnormalities. It seems that prognosis and severity of the attacks vary according to the underlying genetic defect.

P267 - IMMUNOADSORPTION FOR POST-DIARRHEOA HUS WITH SEVERE NEUROLOGICAL INVOLVEMENT

PIETREMENT CHRISTINE[1], BEDNAREK NATHALIE[1], FILA MARC[2], BAUDOUIN VERONIQUE[2], MACHER MARIE-ALICE[2], DESCHENES GEORGES[2]
[1]*CHU REIMS*
[2]*HOPITAL ROBERT DEBRE APHP*

Introduction: While Eculizumab is now the first line of treatment in atypical HUS, treatment of life threatening form of Shiga-toxin-producing Escherichia coli (STEC) HUS is not well defined, with controversial data on efficiency of plasma exchange (PE) and Eculizumab treatment. Recently, IgG depletion through immunoadsorption (IgG IA) was successfully used for adult patients with delayed neurological presentation.
Material and methods: A 26 month-old girl presented a severe STEC-HUS requiring dialysis with hepatic, pancreatic and cardiac involvement. Eculizumab was administrated at day 1 of admission because of neurological signs (coma, extrapyramidal syndrome, Glasgow score 8/15) and bilateral thalami infarction on MRI. PE followed by a second Eculizumab infusion were added at day 3, and a third Eculizumab infusion was performed on day 8 because of the absence of improvement. Despite this treatment, her neurological status worsened with occipital recurrent seizures and a need of a mechanical ventilation support and apparition of lenticular with right occipital cortical lesions on MRI. In this life threatening situation we decided to perform IgG IA as a rescue therapy (6 sessions between day 9 to 13).
Results: Dialysis was stopped on day 13 and there was a moderate clinical improvement (seizures resolved, tube removal on day 14) whereas platelet count increased rapidly. The child was discharged on day 60 with severe neurological signs: absence of eyes tracking, quadriplegia, major cortical and subcortical atrophy and basal ganglia involvement on MRI. Creatinine clearance was 45 mL/min with proteinuria 2 g/L. But, at day 120, the patient had an excellent neurological recovery with independent walking and language adapted communication. Screening for complement function abnormalities (CFH, CFI, MCP, C3, C4) and testing for anti CFH antibody were negative.
Conclusions: Despite previous encouraging results Eculizumab and IgG IA are not efficient in all severe neurological forms of post-diarrhea HUS. Protocols are needed to study the relevance of treatments' association and the timing of their utilization in post-diarrhea HUS with neurological involvement in children.

P268 - URINARY NGAL IN SEPTIC PRETERM BABIES: A PRELIMINARY STUDY

GURKAN GENC[1], BAHATTIN AVCI[3], CANAN AYGUN[2], OZAN OZKAYA[1], SUKRU KUCUKODUK[2]
[1]*ONDOKUZ MAYIS UNIVERSITY FACULTY OF MEDICINE, PEDIATRIC NEPHROLOGY DEPARTMENT*
[2]*ONDOKUZ MAYIS UNIVERSITY FACULTY OF MEDICINE, NEONATOLOGY DEPARTMENT*
[3]*ONDOKUZ MAYIS UNIVERSITY FACULTY OF MEDICINE, BIOCHEMISTRY DEPARTMENT*

Introduction: This study was conducted to evaluate the predictive value of uNGAL for AKI among septic premature infants.
Material and methods: Twenty six preterm, very low birth weight (VLBW) babies were included in the study. Patients were separated into three groups as: Group I; healthy prematures, Group II; prematures with sepsis without AKI, Group III; prematures with sepsis and AKI. Demographic, clinical and laboratory data of the babies were recorded. UNGAL and creatinine values were obtained on day 1, 3 and 7 of life.
Results: UNGAL levels differed statistically among three groups on 1st and 3rd day of life. In Group I, these levels were lower than both Group II and III (9.4±5.8 ng/ml and 13±9.7 ng/ml respectively). In Group III these days' NGAL levels were statistically higher than Group II ($p=0.001$, 0.016 respectively). There was no statistical difference among three groups on day 7.
Conclusions: First day uNGAL levels were higher in VLBW preterms that later developed sepsis; whether the baby had AKI or not; but uNGAL levels were higher in septic babies with AKI compared to the ones without AKI.

P269 - Age-specific reference ranges for urinary neutrophil gelatinase-associated lipocalin in children and adolescents.

AGNIESZKA RYBI - SZUMINSKA[1], ANNA WASILEWSKA[1], MIECZYSLAW LITWIN[2], ZBIGNIEW KULAGA[2], KATARZYNA JANICKA[1], MICHAŁ SZUMIńSKI[1]
[1]*UNIVERSITY OF BIALYSTOK*
[2]*THE CHILDREN'S MEMORIAL HEALTH INSTITUTE, WARSAW*

Introduction: Introduction: Urinary neutrophil gelatinase-associated lipocalin (uNGAL) emerges as a useful marker of renal function impairment. However, clinicians must be careful in interpretation of the test results, because of lack of reference values in pediatric population. The aim of this study was to establish pediatric reference values for uNGAL/creatinine ratio.
Material and methods: Material and methods: The study was performed on a group of 172 healthy children and adolescents (M - 88, F - 84), aged 0.2 to 17.9 years. Urinary NGAL was measured using commercially available ELISA kit.
Results: Results: Urinary NGAL/cr. was higher in younger children (<6 years of age). Statistically significant negative correlation between uNGAL/creatinine and age of all subjects was found ($r=-0.29$, $p<0.05$). UNGAL was higher in girls 5.42 (median: 2.70) ng/ml than in boys 3.72 (median: 1.64) ng/ml, $p<0,05$. This difference was also significant when comparing logtransformed mean of NGAL. After adjusting uNGAL for urinary creatinine, statistically significant association between boys and girls was lost. In our analysis we showed age-specific uNGAL/cr. reference ranges including median, interquartile range and 95 % reference intervals (2.5-97.5 percentile).
Conclusions: Conclusion: In the present study, reference values for urinary NGAL/cr. ratio have been established based for subjects between 0.2 to 17.9 years of age. We conclude that these reference values are reliable and form a basis for quantitative interpretation of urinary NGAL/cr. in pediatric patients with kidney diseases. Further studies using numerous data should be conducted in pediatric population to add reference values for urinary NGAL and uNGAL/cr. ratio for partitioning by age and gender simultaneously.

P270 - Hemolytic Uremic Syndrome and Cardiac Involvement : Three Case Reports

NURAN CETIN[1], BILAL YILDIZ[1], NURDAN KURAL[1], ALI YILDIRIM[2], GOKMEN OZDEMIR[2], TEYFIK DEMIR[2]
[1]*ESKISEHIR OSMANGAZI UNIVERSITY FACULTY OF MEDICINE DEPARTMENT OF PEDIATRIC NEPHROLOGY*
[2]*ESKISEHIR OSMANGAZI UNIVERSITY FACULTY OF MEDICINE DEPARTMENT OF PEDIATRIC CARDIOLOGY*

Introduction: Hemolytic uremic syndrome (HUS) is characterized by the acute renal failure, microangiopathic hemolytic anemia, and thrombocytopenia. Cardio-vascular involvement as an extra-renal manifestation of HUS is rarely seen but potentially fatal complication in children.
Material and methods: We report 3 cases of severe cardiac failure in children in the acute phase of HUS.
Results: Atypical HUS has been diagnosed in 2 patients and one patient have had diarrhea (D+) HUS. One of the patients with atypical HUS was successfully treated with plasmapharesis and hemodialysis. The other patient with atypical HUS was treated with fresh frozen plasma (FFP) and peritoneal dialysis. Complement C3 levels were low in D+HUS patient that there was no improvement of renal functions despite plasmapharesis and hemodialysis therapy therefore diagnosis of ESRD was done in this patient. In follow-up period, the signs of heart failure and respiratory distress including poor peripheral perfusion, S3 gallop and pulmonary edema were found in our patients despite no problems of fluid retention, electrolyte, hypertension etc. Echocardiography revealed pericardial effusion without signs of tamponade and decreased left ventricular function in all patients. Cardiomyopathy was also showed in patients with D+HUS [troponin-T level: 0,151 ng/ml (range:0.013-0.025)] and in patient with atypical HUS who successfully treated with plasmapharesis [troponin-I level: 0,25 ng/ml

(range:0–0.1)]. Troponin levels were also high in patients with atypical HUS who treated with FFP and peritoneal dialysis [troponin-T level: 0,108 ng/ml (range:0.013-0.025)]. The patients were treated with inotropic agents (dopamine/dobutamine) and early ultrafiltration with hemodialysis and peritoneal dialysis allowed easy control of the circulating mass (pre-load) in our patients.

Conclusions: In conclusion, our patients showed that given the potential for morbidity/mortality in patients with HUS who developed myocardial involvement, routine evaluation of myocardial function and troponin levels assay may be indicated in patients with HUS.

P271 - Follow-up of clinical remission in atypical hemolytic uremic syndrome with anti-complement factor H autoantibodies after cyclophosphamide pulse therapy.

SANA GWENAELLE[1], BOYER OLIVIA[1], CHARBIT MARINA[1], ROUSSET-ROUVIERE CAROLINE[2], BERARD ETIENNE[3], SALOMON REMI[1], DRAGON-DUREY MARIE-AGNES[4], FREMEAUX-BACCHI VERONIQUE[4], NIAUDET PATRICK[1]

[1]*NEPHROLOGIE PEDIATRIQUE, HOPITAL NECKER – ENFANTS MALADES, APHP, MARHEA, INSERM U983, IMAGINE, UNIVERSITE PARIS DESCARTES, PARIS, FRANCE*

[2]*UNITE DE NEPHROLOGIE PEDIATRIQUE, HOPITAL LA TIMONE, AP-HM, UNIVERSITE DE LA MEDITERRANEE, MARSEILLE, FRANCE*

[3]*NEPHROLOGIE PEDIATRIQUE, HOPITAUX PEDIATRIQUES DE NICE CHU-LENVAL, UNIVERSITE DE NICE-SOPHIA-ANTIPOLIS, NICE, FRANCE*

[4]*LABORATOIRE D'IMMUNOLOGIE, HOPITAL EUROPEEN GEORGES-POMPIDOU, APHP, INSERM U872, UNIVERSITE PARIS DESCARTES, PARIS, FRANCE*

Introduction: Anti-complement factor H (CFH) associated atypical hemolytic uremic syndrome (aHUS) is a rare form of thrombotic microangiopathy associated with a poor prognosis and a high relapsing course despite plasmatherapy. The addition of immunosuppressive drugs may prevent the relapses.

Material and methods: We previously reported the remission of anti-CFH associated aHUS after plasma exchanges (PEs) and cyclophosphamide pulses in 3 children with a median follow-up of 15 months. We present herein the long-term follow-up of these children with the evolution of the anti-CFH autoantibody titers and the kidney function 4 to 6 years after the onset.

Results: The 3 children initially presented with hematuria, nephrotic syndrome, hypertension, hemolytic anemia, thrombocytopenia and acute kidney injury. At the disease onset, anti-CFH antibody titers were increased (15,000 to >32,000 arbitrary units [AU]). Patient 1 relapsed twice after PEs and then PEs+Rituximab and received prednisone+cyclophosphamide pulses. The 2 following patients were treated with PEs+prednisone+cyclophosphamide pulses as a first line therapy. In our 3 patients, PEs+prednisone+cyclophosphamide pulses led to a rapid and sustained remission after 6 and 4 years. The kidney function remained normal with an estimated GFR between 95 and 108 ml/min/1.73 m2. In all patients, anti-CFH antibodies decreased but remained detectable during remission with a maximal anti-CFH antibody titer at 3000 AU observed in patient 1 without any clinical or biological signs of relapse. Two patients presented persistent hypertension requiring medical treatment. None of our patients developed any side effect from cyclophosphamide during follow-up. A fourth patient recently received PEs+prednisone+cyclophosphamide pulses at the onset disease, his follow-up is ongoing.

Conclusions: We confirm the long-term efficiency and safety of cyclophosphamide pulses combined with PEs and prednisone in anti-CFH antibody associated aHUS leading to a prolonged decrease in anti-CFH antibodies titers and prevention of relapses.

P272 - Investigation of Oxidative Stress Status and Gene Polymorphisms of MnSOD and PON1 in children with Henoch-Schonlein Purpura

FARUK OKTEM[1], ELVAN KUMKAYIR[2], AYÇA ESRA KUYBULU[2], RECEP SUTCU[3], MUSTAFA AKCAM[1]

[1]*BEZMİ ALEM VAKIF UNIVERSITY FACULTY OF MEDICINE*

[2]*SÜLEYMAN DEMIREL UNIVERSITY FACULTY OF MEDICINE*

[3]*KATIP CELEBI UNİVERSİTY FACULTY OF MEDICINE*

Introduction: In this study, we aimed to state the role of oxidative stress in the pathogenesis of Henoch Schönlein Purpura (HSP), also to investigate the relation between gene polymorphisms of the antioxidant enzymes paraxonase (PON1) and Manganese superoxide dismutase (MnSOD) with HSP.

Material and methods: Seventy patients with HSP (27 male, 43 female) and 64 healthy children as control group were enrolled in this study. Oxidative stress and biochemical markers in active and remission periods of disease of sixteen randomly selected HSP patients were evaluated and compared with the results of 14 randomly selected healthy children from control group. PON1 Q/R192, L/M55 and MnSOD A16V gene polymorphisms of patients and controls were also evaluated.

Results: Urine N-acetyl-β-D-glucoseaminidase (NAG) levels were higher in patients with active period of the disease than control group. Tubular phosphorus reabsorption (TPR)

ratio in patients within active period of the disease, was lower than patients within remission period. When considering oxidative stress markers; malondialdehyde (MDA) levels in active period of the disease is high than remission period, PON activity and total antioxidation capacity (TAC) decreased when compared with remission group($p<0.05$). When we assessed distribution of PON1 Q/R192 genotypes, no difference was present between patients and control. In allele distribution, Q allele frequency was higher in patients ($p<0,05$). In view of PON1 L/M55 genotype distribution, MM genotype frequency was higher in HSP group than controls($p<0,05$). In allele distribution of patient group, M allele frequency was higher ($p<0.05$). In view of MnSOD A16V genotype distribution, AA genotype frequency higher in HSP group but this difference was not statistically significant($p>0,05$).

Conclusions: Our findings indicate that oxidative stress and lipid peroxidation is triggered. Renal tubular involvement is frequent even in asymptomatic cases. PON1 Q/R192 and PON1 L/M55 polimorphisms might be risk factors for development of HSP whereas the relation between MnSOD A16V polimorphisms and HSP is not very clear.

P273 - Assessment of Acute Kidney Injury (AKI) in children after cardiac surgery in intensive care units.

MURAT TANYILDIZ[1], MESIHA EKIM[1], TANIL KENDIRLI[2], ERCAN TUTAR[3], ZEYNEP EYILETEN[4], ZEYNEP BIRSIN OZCAKAR[1], ASLI KAVAZ[1], BURCU BULUM OZTURK[1], FATOS YALCINKAYA[1], DENIZ BOZDOGAN[4], CEM KARADENIZ[3], FIKRI DEMIR[3], ERDAL INCE[2], ADNAN UYSALEL[4], SEMRA ATALAY[3]
[1]*ANKARA UNIVERSITY FACULTY OF MEDICINE, PEDIATRIC NEPHROLOGY DEPARTMENT*
[2]*ANKARA UNIVERSITY FACULTY OF MEDICINE, PEDIATRIC INTENSIVE CARE UNIT DEPARTMENT*
[3]*ANKARA UNIVERSITY FACULTY OF MEDICINE, PEDIATRIC CARDIOLOGY DEPARTMENT*
[4]*ANKARA UNIVERSITY FACULTY OF MEDICINE, CARDIOVASCULAR SURGERY DEPARTMENT*

Introduction: AKI is associated with an increased risk of mortality and morbidity in hospitalized patients especially in intensive care units. Between 5 %-33 % of pediatric patients undergoing cardiac surgery may have postoperative AKI, with an associated mortality of 20 %-79 %. The aim of this study is to determine the incidence, severity, risk factors of AKI in children undergoing cardiac surgery for congenital heart defect by using pRIFLE criteria.

Material and methods: A retrospective analysis of patients undergoing congenital heart surgery, aged between 1 month-18 years, that were operated between January 2008-October 2011 and were observed in cardiovascular and pediatric intensive care units(PICU) was performed.

Results: One hundred and thirty-seven patients (mean age 36.6±43.3 months; 73 males) were enrolled. 61.3 % of the patients developed AKI by pRIFLE criteria (25.5 % Risk, 20.4 % "Injury", 15.3 % "Failure"). The mean age of patients who had AKI was 22,47±32,35 months. Younger children whose age less than 11 months were more likely to develop AKI ($p<0.005$). Longer cardiyopulmonary bypass-time, longer aortic crossclamp time, longer period of mechanical ventilation time, postoperative arythmia and ventilator associated pneumonia were associated with an increased risk of AKI ($p<0.05$). Longer cardiopulmonary bypass-time and high postoperative hypotension score were independently associated with AKI. The mean length of PICU stay was longer, need for mechanical ventilation, PRISM-III and PELOD score, incidence of multi-organ failure, and mortality rates (13.1 %) were higher in patients with AKI compared to those without AKI ($p<0.005$). Dialysis was performed in 14.2 % of patients with AKI and mortality rate (66 %) was higher in patients that needed dialysis.

Conclusions: AKI is quite a common problem in PICU after congenital cardiac surgery and constituted an increased risk for morbidity and mortality. Longer cardiopulmonary bypass-time and higher postoperative hypotension score were independently associated with AKI therefore close monitoring of renal function in these patients is important.

P274 - Acute Kidney Injury in Cyanotic Heart Disease patients admitted to PICU – A retrospective case control study

SHEETAL BHOJANI, CHRIS KIDSON, IAN RAMAGE
ROYAL HOSPITAL FOR SICK CHILDREN, GLASGOW

Introduction: Acute kidney injury (AKI) is a potentially life threatening complication of intensive care treatment especially after cardiac surgery. AKI causes renal dysfunction affecting electrolytes and extracellular water handling, and impacts upon the provision of medical therapies. The Acute Kidney Injury Network defined AKI as an acute absolute increase in serum creatinine (SrCr) of≥ 26.4 mmol/L or a ≥50 % increase from baseline. We studied AKI in cyanotic heart disease (CHD) patients in our tertiary referral paediatric intensive care unit (PICU).

Material and methods: We retrospectively identified CHD patients admitted to PICU in 2010. Patients who met the diagnostic criteria for AKI (cases) were compared with those without AKI (controls). The demographic and clinical data was collected from the clinical information system.

Results: In 2010, 97 CHD patients were admitted to PICU of which 44 (45 %) developed AKI. 4 cases (9 %) required renal replacement therapy. In 32 (73 %) cases, SrCr returned to baseline before discharge. None of the cases had routine

renal follow up post-discharge. Comparing the cases to the controls, the male female ratio and the underlying cardiac disease distribution was comparable. The cases were younger (p 0.007), with a longer PICU stay (<0.001), bypass (p 0.002) and X clamp time (p 0.017). The use of nephrotoxic drugs was more common in the cases (0.048). The 2 groups were comparable in their use of inotropes, diuretics and antibiotics.

Conclusions: The development of AKI is common, especially in critically ill patients who also receive nephrotoxic drugs. Younger age, prolonged PICU stay, long bypass and X clamp time are known risk factors for AKI. The concomitant use of nephrotoxic drugs may be unavoidable, however with early identification of AKI, modification of therapy may minimise the duration of AKI. The long term renal outcome of AKI in the PICU population is unclear and warrants further investigation.

P275 - DIARRHEA ASSOCIATED HEMOLYTIC UREMIC SYNDROME CASES INCREASED IN TURKEY IN 2011: SINGLE CENTER EXPERIENCE

ALEV YILMAZ, ZEYNEP YURUK YILDIRIM, BAGDAGUL YAVAS AKSU, ILMAY BILGE, SEVINC EMRE

ISTANBUL UNIVERSITY ISTANBUL MEDICAL FACULTY PEDIATRIC NEPHROLOGY DEPARTMENT

Introduction: Although Hemolytic Uremic Syndrome (HUS) is not very frequent in Turkey, during the outbreak of STEC HUS epidemic in Europe in 2011, we observed diarrhea associated HUS cases in İstanbul. The aim of this study is to assess the clinical features and prognosis of the patients treated and followed during this period.

Material and methods: A total of 9 cases were identified with diarrhea associated HUS in 2011.

Results: The mean age was 5.8±4.2 years (3 months-12 years). Mean hemoglobin level was 8±1.6 gr/dl, mean platelet count was 59800±21200/mm3 and mean creatinine clearance was 15.4±10.4 ml/min/1.73 m2 at presentation. Six of the patients were completely anuric. Mean duration of hospitalization was 17.66±13.77 days (8–52). Seven patient received renal replacement therapy. All of our patients had complete recovery. One patient had an atypical course of the disease with cerebral and pulmonary involvement and decreased complement C3 level despite diarrhea prior to HUS. Verotoxin was negative. Plasma exchange was performed 4 times along with hemodialysis and creatinine clearance increased from 12.2 ml/min/1.73 m2 to 32.4 ml/min/1.73 m2. Eculizumab was administered for 3 consecutive weeks and every two weeks thereafter. First two doses of Eculizumab were 600 mg per dose and 900 mg from third dose on. Serum creatinine level began to decrease rapidly after the second dose of Eculizumab and creatinine clearance reached 92 ml/min/1.73 m2 within a month. Her therapy still continues.

Conclusions: The HUS outbreak in Germany affected numerous adult patients and caused neurological symptoms. We encountered diarrhea associated HUS cases in children at the same time. The mean age of our patients was higher than the other series reporting diarrhea associated HUS cases in children. All our patients had complete recovery following the same course of the disease but one of them had neurological and pulmonary involvement treated with Eculizumab.

P276 - CLINICAL ASPECTS AND OUTCOME OF HEMOLYTIC-UREMIC SYNDROME IN CHILDREN IN NORWAY, 1999–2008

GAUTE REIER JENSSEN[1], EIRIK HOVLAND[1], HANS-JACOB BANGSTAD[2], ANNA KRISTINA BJERRE[2], LINE VOLD[1], KARIN NYGåRD[1]

[1]*NORWEGIAN INSTITUTE OF PUBLIC HEALTH*

[2]*OSLO UNIVERSITY HOSPITAL*

Introduction: Hemolytic-uremic syndrome (HUS) is characterized by hemolytic anemia, thrombocytopenia and acute kidney injury (AKI). It is one of the most common causes of AKI in children. Our aim was to describe the clinical aspects and outcome of HUS in patients <16 years of age in Norway, 1999–2008.

Material and methods: This was a retrospective, descriptive study, based on data collected from medical records in the Norwegian pediatric departments. A case was defined by the characteristic clinical picture, and divided into diarrhea-associated (D+) and non-diarrhea-associated (D-) HUS.

Results: 48 cases of HUS were identified; 39 (81 %) D+ HUS and nine (19 %) D-HUS cases. Data and symptoms from the D+HUS and D-HUS group respectively: 80 % versus 78 % of patients were <5 years of age; median time from date of first symptoms to date of primary admittance was six days (range, 0–38) versus five days (range, 2–14); median duration of primary hospital stay was 15 days (range, 2–124) versus 16 days (range, 3–150). Anuria or oliguria occurred in 77 % versus 56 % of patients; neurological complications were seen in 26 % versus 22 %. Dialysis and/or plasmapheresis was needed in 59 % versus 33 % of cases, with a median 8 (range, 2–81) and 5 days (range, 5–13) of treatment, respectively. One year after primary admittance, 22 % versus 44 % of patients still had proteinuria and 14 % versus 44 % had moderate hypertension. One patient needed a kidney transplant, two patients died (case fatality rate: 4 %). All these three were D+HUS.

Conclusions: Patients with HUS in Norway, either diarrhea-associated or atypical, had lengthy hospital stays, requiring expensive supportive treatment. Outcome and case fatality rate for D+HUS patients were comparable to similar studies abroad, while atypical HUS patients had a high proportion of lasting hypertension and proteinuria. Fewer patients, however, developed acute neurological complications.

P277 - CRESCENTIC GLOMERULONEPHRITIS IN CHILDREN: A SINGLE CENTRE EXPERIENCE

SARE GÜLFEM AKYÜZ, AYSUN ÇALTIK, ÖZLEM AYDOĞ, MEHMET BÜLBÜL, GÜLAY DEMİRCİN, EVRIM ÇAKICI, AYŞE ÖNER
DR SAMI ULUS CHILDREN AND MATERNITY HOSPITAL

Introduction: To evaluate the prognostic factors and the long-term outcome of crescentic glomerulonephritis (CGN) in childhood.

Material and methods: Between January 2000 and December 2010, 45 children (26 girls, 19 boys) with biopsy-proven CGN (> 50 % crescents) were investigated in this study retrospectively. The mean age of children was 10.8±2.75 years.The mean duration of follow up was 69.64±36.26 (3 months to 116 months).Clinical fetaures, laboratory parameters and histopathologcal findings of the patients were analysed. Based on renal histopathology and clinical presentation, patients were treated with oral prednisone, intravenous pulses of methyl prednisolone and oral or intravenous cyclophosphamide.

Results: The etiologies of 45 patients with CGN were HSP nephritis(n:24), MPGN (n:4), postinfectious GN (n:3), SLE nephritis (n:2), pauci-immun CGN (n:3)and idiopathic CGN (n:9).The final clinical status of the patients was complete remission (n:21); partial remission (n:5) and chronical renal failure (CRF) (n:19). Adverse outcome was significantly associated with long duration between onset of symptoms and initiation of treatment (p:0.038), and teh presence of oliguria(p: 0.006), decreased GFR (< 30 ml/min/1.72 m²) and need of dialysis (p: 0.003) at admission. Ther was no significant relation between hypertension and/or heavy proteinuria and outcome. Pathologic features associated with poor prognosis were the ratio of crescents (>75 %) (p:0.03) and particularly the ratio of fibrous crescents (p:0.015). Among etiological factors, HSP nephritis had the most favorable outcome.

Conclusions: We conclude that the prognosis of CGN in children is primarily dependent on the histopathological lesions and severity of the clinical renal disease at admission. Since duration of the symptoms and initiation of treatment is crucial prompt diagnosis and management is very important.

P278 - Septex® and OXiris® - new systems of blood purification in SIRS treatment in children

ANNA MUSIELAK[1], MAGDALENA SILSKA[1], KATARZYNA LIPKOWSKA[1], JOLANTA SOŁTYSIAK[1], ALFRED WARZYWODA[1], ALICJA BARTKOWSKA-ŚNIATKOWSKA[2], DANUTA OSTALSKA-NOWICKA[1], JACEK ZACHWIEJA[1]
[1]*DEPARTMENT OF PEDIATRIC NEPHROLOGY, POZNAN UNIVERSITY OF MEDICAL SCIENCES*
[2]*DEPARTMENT OF PEDIATRIC ANAESTHESIOLOGY AND INTENSIVE THERAPY, POZNAN UNIVERISTY OF MEDICAL SCIENCES*

Introduction: Systemic Inflammatory Response Syndrome (SIRS) is severe condition with non-specific symptoms such as abnormal body temperature, increased respiratory and heart rate. Among the most common causes of SIRS ischemia, trauma and infection are mentioned. Development of systemic inflammation may lead to multiple organ failure and ultimately to death. The clinical course of SIRS is determined by overexpression of inflammatory cytokines. Among the methods of supporting treatment, CRRT with modified membranes is pointed out as the most modern, capable of selective absorption of endotoxins, proinflammatory cytokines and anaphilatoxins. An example of this treatment option is the oXiris® technology. The aim of our study was to analyze the effectiveness and safety of new techniques using oXiris®system in children with SIRS.

Material and methods: Study group consisted of three children aged 6 to 17 years, fulfilling the criteria for SIRS and with biochemical markers of inflammation (CRP, PCTK), hospitalized in 2011. CRRT treatment was based on the use of vascular catheters, under the control of morphology and coagulation of blood, with reduced heparinization. Patients state was monitored through the clinical assessment and control of laboratory markers of inflammation (cell count, CRP, PCTK) at the start of the procedure and after 24, 48 and 72 h.

Results: In the group of three patients with SIRS after 24 hours from the beginning of continuous haemodiafiltration with oXiris filter treatment clinical state stabilization and statistically significant decrease in biochemical markers of inflammation in the blood serum was observed. Improvement continued in subsequent days of treatment. No significant potential complications of treatment were seen.

Conclusions: The technique of continuous blood purification using the new oXiris ® system can provide an effective and safe therapeutic alternative in patients with SIRS, allowing for relatively rapid and selective elimination of pro-inflammatory cytokines from the body while maintaining normal protein levels and constant composition of body fluids.

P279 - Proteomic analysis of renal ishaemia/reperfusion injury: identification of potential new targets

ERNA SZIKSZ[1], LEONóRA HIMER[1], KATALIN ADRIENNA KéKESI[2], GáBOR JUHáSZ[2], ATTILA SIMOR[2], PéTER GULYáSSY[2], ZSUZSANNA DARULA[3], BEáTA SZEBENI[1], TIVADAR TULASSAY[1], ÁDáM VANNAY[1]

[1]*RESEARCH GROUP FOR PEDIATRICS AND NEPHROLOGY, SEMMELWEIS UNIVERSITY AND HUNGARIAN ACADEMY OF SCIENCES AND SEMMELWEIS UNIVERSITY, 1ST DEPARTMENT OF PEDIATRICS, BUDAPEST, HUNGARY*

[2]*LABORATORY OF PROTEOMICS, EÖTVÖS LORáND UNIVERSITY, BUDAPEST, HUNGARY*

[3]*HAS BIOLOGICAL RESEARCH CENTER, INSTITUTE OF BIOCHEMISTRY, SZEGED, HUNGARY*

Introduction: Ishaemia/reperfusion (I/R) injury is a leading cause of acute kidney failure (ARF), which is observed most frequently in patients after major surgery, burns, severe hypovolemia, and renal transplantation. Mortality rate and treatment of ARF means a serious problem in the intensive health care. Ischaemic preconditioning (IP) may induce tissue adaptation to stress and protect it from a subsequent severe I/R insult. Because the complex molecular pathomechanism of renal I/R injury is not fully understood, our present aim is to analyse I/R and IP induced protein changes in the kidney to find potential key molecules and therapeutic targets.

Material and methods: Proteins from the kidneys of ishaemized, preconditioned/ishaemized and control rats were isolated and analyzed using two dimensional gel electrophoresis and mass spectrometry. Functional protein analysis was performed by Pathway Studio software. Our selected target molecules will be further analyzed by real-time RT-PCR, western blot and immunofluorescent staining in the future.

Results: 108 proteins were altered after insult. They were ranked into functional groups: components of cytoskeleton, elements of different metabolism, proteolysis, DNA/RNA processing, signaling and miscellaneous. All proteins were manually validated and searched in the literature. Some proteins of interest were choosen for further experiments, such as DJ1/PARK7, which may exert cytoprotective effects.

Conclusions: Here we investigate the alteration in the complex interaction of different proteins of the kidney during ARF. Our results may contribute to the identification of new biomarkers of I/R injury leading to kidney damage. Determination of the protective IP induced proteomic changes will help us to find new targets for therapeutic intervention.

P280 - Hemolytic Uremic Syndrome Due To Complement Factor H Antibody Succesfully Treated With Eculizumab (Case Report)

ZEYNEP YURUK YILDIRIM, ALEV YILMAZ, SEVINC EMRE, ILMAY BILGE, BAGDAGUL YAVAS AKSU, AYDAN SIRIN

ISTANBUL UNIVERSITY ISTANBUL MEDICAL FACULTY PEDIATRIC NEPHROLOGY DEPARTMENT

Introduction: Atypical hemolytic uremic syndrome (aHUS) is a rare, chronic disease with frequent progression to end-stage renal disease. Factor H (CFH) autoantibodies have been reported in 6-10 % of patients with aHUS.

Material and methods: A case of aHUS due to CFH antibody who succesfully treated with Eculizumab was presented in this report.

Results: Eight year-old boy was admitted to our hospital with aHUS in September 2010. Creatinine clearence was 12 ml/min/1.73 m2. Plasma Exchange (PE) was performed for 5 sessions. After initiating PE, his renal function and platelet counts returned to normal. However, HUS recurred 20 days after discontinuation of PE. CFH antibody was determined as 322 AU/ml by ELISA (normal value: <100). The PE therapy was performed for 5 consecutive days, and was continued for 5 sessions per week for 2 weeks, 3 sessions per week for another 2 weeks and one session per week thereafter during one year. His renal function returned to normal at the end of the second week of the therapy and remained stable with this treatment but CFH antibody titers were still high. Rituximab therapy was initiated in April 2011 and PE was discontinued after the second rituximab dose. HUS recurred 45 days after cessation of PE and CFH antibody titer was high (201 AU/ml). Rituximab treatment was stopped and PE was reinitiated. After his creatinine clearence returned to normal with PE, therapy was continued with Double Filtration Plasmapheresis (DFPP) from October 2011 on because he developed allergic reaction to plasma components during PE. Eculizumab was administered for 3 consecutive weeks and every two weeks thereafter. First two doses of Eculizumab were 600 mg per dose and 900 mg from third dose on. CFH antibody titer decreased to 103 AU/ml after Eculizumab therapy was initiated and DFPP was discontinued. Alternate-week Eculizumab infusions are being continued and his renal function remained normal without PE.

Conclusions: Eculizumab may be the first-line therapy in the patients with aHUS due to CFH antibody.

P281 - ACUTE RENAL FAILURE DUE TO CARNITINE PALMITOYL TRANSFERASE DEFICIENCY IN CHILDREN

KIBRIYA FIDAN, YASAR KANDUR, MELTEM AKCABOY, EMEL ISIYEL, SEVCAN A. BAKKALOGLU, ENVER HASANOGLU, OGUZ SOYLEMEZOGLU

DEPARTMENT OF PEDIATRIC NEPHROLOGY, GAZI UNIVERSITY,ANKARA,TURKEY

Introduction: CPT II deficiency is an autosomal recessive long-chain fatty acid oxidation disorder which may cause rhabdomyolysis resulting in acute tubular necrosis. In this report, we will present two cases of severe rhabdomyolysis with acute renal failure due to carnitine palmitoyl transferase deficiency.
Material and methods: CASE 1 A 15-year-old male presented with respiratory distress, inability to walk, dark urine following tiredness and widespread muscle pain after exercise. On physical examination, the blood pressure (BP) was 160/90 mmHg. Muscle strength in all extremities was 2/5. There was myoglobinuria: 370.5 ng/ml (N: 0–200 ng/ml). Blood chemistry showed creatinine 4,8 mg/dl,creatinine kinase (CK) 2458 u/L, AST 898 u/L, ALT 181 u/L. An analysis for carbamoylphosphate transferase (CPT) II in leukocytes showed 0.03 nmol/min protein (N. 0.2-1) and the patient was diagnosed as CPT II deficiency. He was treated with urine alcalinization, carnitine and intravenous fluids and medium-chain fatty acids-rich diet. CASE 2 A 12-year-old male presented with dark urine, widespread muscle pain, edema of the eye lids and oliguria. On physical examination, BP was 130/94 mm/Hg. There was facial, pretibial edema and muscle strength in all extremities was 3/5. Laboratory examination showed ALT 1094 u/L, creatinine 5.26 mg/dl, CK 42670 u/L. In urinalysis there was moderate proteinuria with no erythrocytes. An analysis for CPT II showed extremely low values of the patient, his mother and father (0.02, 0.12 and 0.05 nmol/min protein, respectively) so the patient was diagnosed as CPT 2 deficiency. After five sessions of hemodialysis, creatinine was 0.94 mg/dl, CK 107u/L and urinary output 2.5 ml/kg/hr.
Results: -
Conclusions: CPT II deficiency should be included in the differential diagnosis of myoblobinuric acute renal failure when it is associated with accompanying muscle weakness.

P282 - Risk factors and prevalence of anemia in children with renal transplant recipients

IPEK KAPLAN BULUT, NIDA DINCEL, BETUL SOZERI, SEVGI MIR
EGE UNIVERSITY MEDICAL FACULTY, DEPARTMENT OF PEDIATRIC NEPHROLOGY

Introduction: Despite the presence of anemia is known to be a problem after renal transplantation, there are not enough data on the prevalence. Especially, after transplantation, information with anemia is insufficient data reported associated with early and long term period in children. This study evaluated the prevalence and risk factors for anemia in children with renal transplantation on the early and long term period post transplantation.
Material and methods: This study was performed in children who underwent renal transplant on Ege University. Retransplant children, patients with multiple organ transplantation (liver-kidney transplants), patients who died, and patients with less than one year from the transplantation were excluded from the study. Hematocrit (HCT) level greater than 2 SD below for age was defined anemia. Patients were divided two groups according to after transplant time.
Results: The total 105 patients were included in this study. The prevalence of anemia was found 69.5 % at the time of transplantation in pediatric recipients. This ratio was detected 39 % in the first month after transplantation. In early post-transplant period, anemia was found 18 %. The prevalence of anemia was detected 27.5 % at late posttransplant period on 60 months. In addition, 44.5 % patients had anemic at the 120 months. Anemia was detected at least once in 67.6 % patients among renal transplant recipients at all posttransplant follow-up period. Angiotensin converting enzyme inhibitor use was not associated with anemia. Donor type and donor age are not significantly associated with late PTA. Post transplant anemia (PTA) was significantly associated with history of rejection and eGFR.
Conclusions: Early and late PTA in pediatric renal transplant recipients is a common complication, which is underrecognized. Low GFR, postransplant time and rejection are risk factor for anemia in pediatric renal transplant recipients. Prevalence of PTA has been increased associated with posttransplant time.

P283 - Granulomatous interstitial nephritis associated with influenza A:H1N1 infection – case report

GORDANA MILOšEVSKI-LOMIć[1], MIRJANA KOSTIć[1], PREDRAG RODIć[1], DIVNA KRUščIć[1], DUšAN PARIPOVIć[1], BRANKICA SPASOJEVIć-DIMITRIJEVA[1], JASMINA LIPKOVSKI-MARKOVIć[2], AMIRA PECO-ANTIć[1]
[1]*1. UNIVERSITY CHILDREN'S HOSPITAL, NEPHROLOGY DEPARTMENT, BELGRADE, SERBIA*
[2]*2. INSTITUTE OF PATHOLOGY, SCHOOL OF MEDICINE, UNIVERSITY OF BELGRADE, BELGRADE, SERBIA*

Introduction: Involvement of the tubulointerstitial compartment in renal diseases can be either primary or secondary due to glomerular, vascular or structural disease. The causes of primary acute tubulointerstitial nephritis can be grouped into four broad categories: medications, infections, immunologic diseases, or idiopathic processes.

Material and methods: Case report: We present the case of a 17 year old female who developed rapidly progressive renal failure (RPRF) and granulomatous interstitial nephritis (GIN) as a presenting manifestation of influenza A:H1N1 infection.
Results: The illness was presented after two weeks history of respiratory tract infection, skin rash and hypermenorrhoea. Physical examination on admission revealed fever, bilateral pedal oedema, macular skin rash, and pneumonia. Laboratory investigations showed normocytic anemia, azotemia, hematuria and proteinuria. Renal ultrasound was normal. Antinuclear antibodies, antineutrophil cytoplasmic antibodies, lupus anticoagulant, antiphospholipid antibodies were negative with normal complement. Urin cultures for Mycobacterium tuberculosis were negative. Diagnosis of influenza A:H1N1 infection was made by positive serology. A kidney biopsy showed interstitial nephritis with peritubular granulomas. Glomeruli were normal. Staining for immunoglobulins A, M, G and E was negative. The girl was treated with oseltamivir phosphate (Tamiflu) for five days as well as with tapered prednisone after a starting dose of 2 mg/kg. The treatment resulted in a complete remission that lasted up to one year of follow up.
Conclusions: GIN is present in only 0.5-0.9 % of native renal biopsies. Most influenza infections are limited to upper respiratory tract, unfortunately, a number of patient groups are at risk of complications affecting multiple organ systems. In summary, we presented a severe but reversible case of GIN and RPGN associated with influenza A:H1N1 infection. Although a causal effect cannot be confirmed, this case suggests that influenza A:H1N1 should be considered in the differential diagnosis of GIN manifested with a RPGN in children.

P284 - Acute kidney injury in pediatric patients hospitalized in two Serbian tertiary care centers during one year

NATASA STAJIC[1], RADOVAN BOGDANOVIC[1], BRANKICA SPASOJEVIC-DIMITRIJEVA[2], IVANA IVANISEVIC[2], NEVENA VUNJAK-MAKSIMOVIC[2], MILA STAJEVIC[1], BILJANA MEDJO[2], JASNA KALANJ[2], SNEZANA RSOVAC[2], IGOR KRUNIC[1], AMIRA PECO-ANTIC[2]
[1]*INSTITUTE FOR MOTHER AND CHILD HEALTH CARE "DR VUKAN CUPIC", BELGRADE*
[2]*UNIVERSITY CHILDREN'S HOSPITAL, BELGRADE*

Introduction: The incidence of acute kidney injury (AKI) rises or at least AKI is increasingly better recognized problem in tertiary care pediatric centers. The aim of our study is to analyze an epidemiology, etiology and mortality rate of AKI in two large pediatric centers in charge of about two thirds of Serbian pediatric population.
Material and methods: A retrospective analysis of clinic laboratory data of patients in whom AKI had developed from January the 1st till December the 31st 2011. Patients were treated in pediatric and cardio surgery intensive care units or nephrology wards.
Results: AKI occurred in 88 patients, whose age ranges from 1 day to 19 years (median 17 ±7.7) months. There were 49 males (55, 7 %) and 39 females (44, 3 %). Fifty three patients (60, 2 %) were treated in pediatric and cardio surgery intensive care units and 35 (39, 8 %) in nephrology wards. Ischemia caused AKI in 47 patients (53 %), intrinsic kidney disease in 29 (33 %) and sepsis with multiple organ dysfunction syndrome (MODS) in 12 patients (14 %). Renal replacement therapy was performed in 18 patients (20 %), peritoneal dialysis in 11 and continuous veno-venous hemodiafiltration in 7. Sixty seven patients (76 %) survived. The most frequent cause of AKI with lethal outcome was sepsis with MODS (11 patients - 52 %). There was no mortality in patients with the intrinsic kidney disease as a cause of AKI.
Conclusions: More than half of patients with AKI were treated in intensive care units. Two thirds had other than intrinsic renal disease as a cause of AKI. Ischemia was the leading cause of renal injury. Considering the fact that sepsis with MODS was the cause of AKI in more than a half of the patients who did not survived, we could conclude that our results are comparable with the results of other similar pediatric health care centers.

P285 - DISORDERS OF HEMOSTASIS IN CHILDREN WITH ACUTE KIDNEY INJURY

SZCZEPANSKA MARIA[1], KARPE JACEK[2], ADAMCZYK PIOTR[1], DYRGA URSZULA[3], NOWAK DAWID[3], SZIRER GRAżYNA[2]
[1]*DEPARTMENT AND CLINIC OF CHILDREN'S NEPHROLOGY IN ZABRZE*
[2]*DEPARTMENT AND CLINIC OF PEDIATRIC INTENSIVE CARE IN ZABRZE, MEDICAL UNIVERSITY OF SILESIA IN KATOWICE*
[3]*STUDENT'S SCIENTIFIC SOCIETY*

Introduction: In children with acute kidney injury (AKI) thrombocytopenia, plasma coagulation and fibrinolysis disorders are often present. They result in growing tendency for bleeding and thromboembolic complications. During the treatment with dialysis the impairment of hemostasis increases. The study aimed at estimation of the prevalence of coagulation disorders in children with AKI undergoing renal replacement therapy and treated conservatively.
Material and methods: Medical records of 20 children (8 girls and 12 boys) hospitalized in the years 2007–2011 in the Departments and Clinics of Children's Nephrology (n =13) and Pediatric Intensive Care (n =7), in Zabrze. In

9 children hemodialysis, in 8 peritoneal dialysis were applied. Three children didn't require dialysis. The mean age was 7.1±4.6 years, mean creatinine concentration at admission 282.5±167.5 μmol/l, mean fibrinogen 300.9± 135.1 mg/dl, prothrombin time 15.1±3.6 s, APTT 34.4± 16.6 s, D-dimer 7.5±8.1 μg/l and platelet count 93.1*109/l ±68.8*109 /l. All the children received low-molecular-weight heparin.

Results: Of the study group 18 children (90 %) were cured, 2 children (10 %) died. Serious thromboembolic events and hemorrhagic complications were not observed. All patients had an improvement of laboratory parameters values: D-dimer 1.39± 1.39 mg/l, platelets 285.7*109/l ±161.4*109/l (at discharge). Prothrombin time 13.82±1.8 sec, APTT 28.68±3.3 sec and fibrinogen 300.8±106.7 mg/dl values remained within the normal range throughout the hospitalization. Currently, none of the children require continuation of anticoagulation.

Conclusions: Coagulation and fibrinolysis disorders in children treated for AKI increase the risk of bleeding and thromboembolic complications, which significantly worsen the prognosis. The use of low-molecular-weight heparin allows for the adequate prophylaxis and treatment of these complications.

P286 - CARDIOVASCULAR DISEASE AFTER PEDIATRIC RENAL TRANSPLANTATION

EVA KIS, ORSOLYA CSEPREKAL, ANDREA KERTI, ARIANNA A DEGI, PETER SALLAY, ATTILA J SZABO, TIVADAR TULASSAY, GYORGY S REUSZ
SEMMELWEIS UNIVERSITY, 1ST DEPT OF PEDIATRICS, BUDAPEST, HUNGARY

Introduction: Chronic kidney disease is associated with an increased arterial stiffness (Ast) and left ventricular mass (LVM). Increased ASt results in an elevated pulse wave velocity (PWV). Few data are available on the evolution of PWV and LVM following renal transplantation (RTx) in children

Material and methods: Children (aged 13,4(0,88) years / mean(SD)/) with end stage renal disease followed by successful RTx were identified. 26 patients underwent PWV measurement 2,81(0,03) years after RTx, with repeat PWV measurement and echocardiography 3,5(1,08) years after RTx. The LVM index (LVMi) was calculated as follows: 0.8×(1.04 [(LV diameter at end diastole+posterior wall thickness at end diastole+interventricular septum at end diastole)3 - (LV diameter at end diastole)3])+0.6 g/body surface1,5 . PWV was measured by applanation tonometry. Age and height matched PWV normal values were used, SD score was calculated. Candidate clinical variables for an association with LVMi and PWV were assessed, including age, rutine laboratory findings, medications (serum levels, cumulative doses) and co-morbidities.

Results: PWV age SDS (1,18(1,22)) and PWV height SDS (1,47(1,21)) of RTx were increased compared to healthy pediatric population. Follow-up measurement of PWV revealed increased PWV age SDS (1,18 vs 0,19) 3.5 years after RTx. Follow-up measurement of PWV age SDS correlated with LVMi (r: 0,61, p:0,01). There was a bimodal correlation between LVMi and cumulative calcitriol dose before RTx. In this RTx study population there was no correlation between PWV parameters and blood pressure, creatinine, Ca-P parameters and lipid levels.

Conclusions: Controls matched both for age and height should be used to assess PWV in RTx children with growth failure. Ast determined by PWV increased after RTx, and correlated with left ventricular hypertrophy (LVMi). Cumulative dose of calcitriol is among the major determinants of left ventricular hypertrophy after RTx. The study was supported by the grants OTKA83431; 100909; LP2011-008/ 2011 TÁMOP-4.2.2/B-10/1-2010-0013 and TÁMOP-4.2.1/ B-09/1/KMR-2010-0001

P287 - CRP, PROCALCITONIN and IL-18 LEVELS IN REFLUX NEPHROPATHY

SEVGI YAVUZ, ALI ANARAT, AYSUN KARABAY BAYAZIT
CUKUROVA UNIVERSITY

Introduction: Vesicoureteral reflux (VUR) is still a major cause of chronic kidney disease (CKD) in developing countries. Approximately 30–60 percent %of patients with VUR have reflux nephropathy (RN) and nearly 5–12 percent of them progress to CKD. However which patient progress to RN and which of them progress to CKD is not known. The aim of this prospective study is to evaluate the role of proteinuria and inflammation on development of RN in children with VUR and to determine the prognostic factors in these patients.

Material and methods: Ninethy-three (35 boys and 58 girls) children aged 3,5 to 17,5 years with primary VUR were enrolled into the study. Microalbuminuria (MA: urinary microalbumin≥30 mg/g creatinine) was postulated as the cardinal determinant of reflux nephropathy and patients were divided into two groups according to the presence of microalbuminuria. Inflammatory parameters (White blood cell counts (WBC), erithtrocyte sedimentation rate (ESR), C-reactive protein (CRP), Procalcitonin (PCT)), serum and urinary Interleukin-18 (IL-18) levels were assessed on urinary tract infection free period. To standardize the samples, urinary IL-18 levels were rated with urinary creatinine (pg/mg).

Results: WBC, ESR, CRP and PCT were similar in MA(+) and MA(−) groups (p>0,05). Mean serum IL-18 levels were in MA (−) and MA (+) groups were 66 pg/ml and 44,7 pg/ml respectively. Mean urinary IL-18/creatinine levels were

544,8 pg/mg and 913,8 pg/mg in MA (−) and MA (+) groups respectively. These measurements were higher than normal levels reported in literature. However no statistically significant difference found between two groups (p>0,05).
Conclusions: WBC, ESR, CRP, PCT and IL-18 might not have a good prognostic value in predicting RN.

P288 - Fibroblast growth factor 23 and klotho in children with chronic kidney disease

MANDY WAN[1], COLETTE SMITH[2], VANITA SHAH[3], AMBROSE GULLET[1], DAVID WELLS[1], LESLEY REES[1], RUKSHANA SHROFF[1]
[1]*GREAT ORMOND STREET HOSPITAL FOR CHILDREN NHS FOUNDATION TRUST*
[2]*UNIVERSITY COLLEGE LONDON*
[3]*INSTITUTE OF CHILD HEALTH*

Introduction: Fibroblast growth factor 23 (FGF23), a bone derived phosphaturic hormone, is elevated in children with chronic kidney disease (CKD). FGF23 increases renal phosphate (P) excretion and inhibits 1,25-dihydroxyvitmain D [1,25(OH)2D] production. There are scarce data on the circulating levels of its essential co-receptor klotho, and longitudinal changes in FGF23 levels are also unknown.
Material and methods: We examined FGF23 and klotho levels in 154 children with CKD stages 1–5, dialysis and transplant. Serial measures of FGF23 levels over one year were performed and its association with biochemical markers of CKD-mineral and bone disorder examined.
Results: In children with CKD1-5 and dialysis, plasma levels of FGF23 correlated inversely with estimated glomerular filtration rate (eGFR) ($P<0.001$, $r=-0.73$) whereas a decrease in klotho was observed with lower eGFR ($P=0.01$, $r=0.30$), suggesting a resistance to circulating FGF23 with advancing renal failure. There was no correlation between FGF23 and serum P or parathyroid hormone (PTH) in our cohort wherein 89 and 66 % respectively had normal levels. FGF23 increased by 6 folds over a one year period in children with eGFR 15–29 mL/min/1.73 m2, with an overall 5 % annualized increase in the CKD cohort. There was a positive correlation between FGF23 and albumin-adjusted serum calcium (Ca) levels ($P<0.001$, $r=0.57$), and a negative correlation with both 25-hydroxyvitmain D [25(OH)D] and 1,25(OH)2D ($p=0.05$, $r=-0.20$ and $p=0.05$, $r=-0.20$ respectively). The FGF23/klotho ratio correlated positively with PTH ($p=0.04$, $r=0.25$). In transplanted patients FGF23 correlated with eGFR and 25(OH)D only.
Conclusions: This study shows increasing FGF23 and reduced klotho levels with progressive renal decline even in a population of children with well controlled P levels. Novel associations between FGF23 and 25(OH)D challenge the popular 'trade-off' hypothesis and suggest that 25(OH)D supplementation may be beneficial. The effect of Ca-based P-binders on FGF23 levels should be examined in future studies.

P289 - Short Stature/Delayed Puberty in an adolescent: An unusual presentation of posterior urethral valves

MAMATHA MALLYA, MONA ASLAM, VIJITH PUTHI
PETERBOROUGH CITY HOSPITAL

Introduction: Posterior urethral valves are usually detected on antenatal ultrasound scans and late presentation is rare. Common symptoms of delayed presentation include diurnal enuresis (60 %), urinary tract infections (40 %) and voiding pain (10 %). Less common symptoms include poor stream, gross haematuria and proteinuria. We report an unusual case of posterior urethral valves in an adolescent boy presenting as short stature and delayed puberty.
Material and methods: A 15 year old boy was referred to the Endocrine clinic with short stature. His growth had been static over the last 3 years. He was well apart from a history of bedwetting at night once or twice a week. He denied any voiding problems or urinary tract infections. On examination, he had a palpable mass in his abdomen extending upto his umbilicus. His weight and height were below the 0.4th centile and had prepubescent testes.
Results: CT scan showed bilateral large kidneys with a dilated renal tract and trabeculated bladder in keeping with a diagnosis of posterior urethral valves. Blood results were consistent with chronic renal impairment (creatinine - 115 μmol/L). He underwent valve resection with complete resolution of his symptoms within a few months. Post operatively he had a pubertal growth spurt and increase in testicular volume to 10 mls. Follow up ultrasound scan showed a large bladder with poor emptying and pelvicalyceal dilatation. His renal impairment is being managed conservatively and now reports a slower urinary stream.
Conclusions: This case highlights the varied clinical manifestation of late presenting valves and the importance of considering nephro-urological causes of delayed growth. In our patient, the growth velocity was marked post surgery with onset of puberty within a year. His renal function remains unchanged and has stage 3 Chronic kidney disease (estimated GFR-53). Long term outcomes are variable and delayed presentation can be associated with poor renal outcome.

P290 - CYSTINOSIS COMPLICATED WITH NEPHROTIC RANGE PROTEINURIA IN TWO CASES

DUYGU OVUNC HACIHAMDIOGLU, CENGIZ ZEYBEK, HALIL IBRAHIM AYDIN, SULEYMAN KALMAN, ERKAN DEMIRKAYA, FAYSAL GOK

GULHANE MILITARY MEDICAL ACADEMY MEDICINE SCHOOL DEPARTMENT OF PEDIATRIC, DIVISION OF PEDIATRIC NEPHROLOGY

Introduction: Infantile cystinosis (MIM #219800) is the most frequent and most severe form of the disease. Proteinuria can rarely reach grams per day, and consists of LMW proteins, albumin, and high molecular weight proteins. We described the clinical history of two female infantile cystinosis 6 and 7 year-old, which had nephrotic range proteinuria during the disease course.
Material and methods: Both patients presented with failure to thrive, episodes of high fever, polyuria and polydipsia in infancy. Cysteamine was started at 6 and 8 month-old. The diagnosis was confirmed by slit-lamp examination of the cornea showing cystine crystal deposits at 14 and 12 month-old. Two cases have both glomerular and tubular proteinuria at 5 and 6 year-old. The first patient was 5 year-old, while decreased serum albumin, developed nephrotic range proteinuria and hyperlipidemia with edema. Leucocyte cystine level was 1,43 nmol / mg protein, but mutation in the CTNS gene was not performed. The second patient also has nephrotic range proteinuria. Genetic screening test showed that patient has homozygous for c.90delC mutation in the CTNS gene. The latest leucocyte cystine level was 1,35 nmol / mg protein.
Results: Two female infantile cystinosis have nephrotic range proteinuria. The first patient progressed toward end stage renal failure at 5 9/12 year and peritoneal dialysis was started. The second patient is 7 years old girl and in stage 4 chronic renal failures.
Conclusions: Nephrotic range proteinuria association with cystinosis may relate to result of mutation or co-incidental variations. The high rate proteinuria probably associated with high progression rate, even if cysteamine treatment early started. The amount of urine protein may be predicted for prognosis as a marker of tubular and glomerular damage, in cystinosis.

P291 - Can decreased relative renal function be detected by glomerular filtration rate and/or ultrasonography?

JAKUB ZIEG[1], PAVEL GEIER[2], SCOTT WALKER[2], MARTA PYTLAK[2], JANUSZ FEBER[2]
[1]*DEPARTMENTS OF PAEDIATRICS, SECOND MEDICAL SCHOOL, CHARLES UNIVERSITY, MOTOL UNIVERSITY HOSPITAL, PRAGUE, CZECH REPUBLIC*
[2]*CHILDREN'S HOSPITAL OF EASTERN ONTARIO, OTTAWA, CANADA*

Introduction: Decreased relative renal function (RRF) is an important marker of parenchymal renal damage and can be assessed by isotope scintigraphy (DMSA), which is however associated with radiation load. The aim of the study was to assess whether loss of RRF can be predicted by estimated glomerular filtration rate (GFR) and/or kidney length on ultrasonography (US).
Material and methods: We performed a retrospective review of 123 patients (65 boys, median age 4.98 years) who had DMSA done for structural kidney anomalies, recurrent urinary tract infections and arterial hypertension. GFR was assessed by the revised Schwartz and CKiD GFR formulas. Loss of RRF was calculated as 50 minus the actual RRF of the worse functioning kidney. Kidney length on US was expressed in SDS.
Results: Median Schwartz and CKID GFR were not significantly different. A significant borderline correlation was found between the Schwartz GFR and the loss of RRF ($p=0.04$), but the slope of Schwartz GFR did not differ from the slope of serum creatinine. In contrast, the regression line of CKID GFR was highly significant ($y=102.8-0.27x$, $p=0.02$) and the slopes between the CKID GFR and CysC were significantly different ($p=0.01$). This suggests that the CKID GFR is sensitive enough to detect changes in the RRF, but cannot discriminate normal versus decreased RRF <35 %. Kidney lengths of<-1 SDS on US were significantly associated with the RRF of less than 35 % ($p=0.0001$).
Conclusions: In conclusion, CKID GFR can detect changes in RRF but is not powerful enough to detect patients with a poorly functioning kidney (RRF<35 %). In contrast, the kidney length is a powerful predictor of the decreased RRF. The combination of CKID GFR and US may obviate the need for performing the DMSA in selected patients.

P292 - R990G polymorphism of the calcium-sensing receptor and serum parathyroid hormone level in children with stage 2–5 chronic kidney disease

MARIA MOLCHANOVA[1], EUGENE TIKHOMIROV[2], EDITA PETROSYAN[1]
[1]*RUSSIAN NATIONAL RESEARCH MEDICAL UNIVERSITY NAMED AFTER N.I. PIROGOV*
[2]*NATIONAL RESEARCH VIROLOGY INSTITUTE*

Introduction: In present study we investigated occurrence frequency and association with serum parathyroid hormone (PTH) level of three polymorphisms: A986S, R990G and Q1011E in a group of children with stage 2–5 chronic kidney disease (CKD).
Material and methods: We examined 80 children with stage 2–5 CKD (44 boys, 36 girls). Mean age was 11.5± 4.2 (1.6-17.3) years. As a control group we took a sampling of 40 people not suffering from CKD (14 men, 26 women), mean age was 32.9±11.5 (22–45) years. We genotyped calcium sensing receptor (CaSR) gene variants A986S,

R990G и Q1011E by sequence. Two sub-groups of patient children were formed depending on PTH serum level: 70 children with secondary hyperparathyroidism (PTH>62 pg/ml), 10 children with hypoparathyroidism (PTH<62 pg/ml).
Results: The analysis revealed no significant difference in frequency occurrence of allele and genotype distribution between the whole patients group, the control group and the subgroup of patients with hyperparathyroidism. The study showed most frequent occurrence of allele G and genotype RG990 in the sub-group with hypoparathyroidism than in the other groups. Allele G frequency was 25 % in the sub-group with hypoparathyroidism, 6.2 % in controls ($\chi2=6.25$, $p=0.01$) and 9.3 % in the sub-group with hyperparathyroidism ($\chi2=4.33$, $p=0.04$). Genotype RG frequency amounted to 50 % in the sub-group with hypoparathyroidism, 12.5 % in controls ($\chi2=7.03$, $p=0.008$) and 18.6 % in the subgroup with hyperparathyroidism ($\chi2=4.96$, $p=0.03$).
Conclusions: The present data suggested that there is a correlation between CaSR gene polymorphism and calcium-phosphorus disorders in patients with CKD. Patients carrying allele G in R990G polymorphism demonstrated lower serum PTH level and tendency to hypoparathyroidism.

P293 - Effects of paricalcitol versus calcitriol in an experimental model of young rat with hyperparathyroidism secondary to chronic renal failure.

NATALIA MEJIA[1], HELENA GIL-PENA[2], VANESSA LOREDO[1], ROCIO FUENTE[1], FLOR ANGEL ORDOñEZ[2], FERNANDO SANTOS[2]
[1]*UNIVERSITY OF OVIEDO*
[2]*HOSPITAL UNIVERSITARIO CENTRAL DE ASTURIAS*

Introduction: New Vitamin D receptor activators (VDRA´s) are used to treat and prevent secondary hyperparathyroidism in chronic kidney disease (CKD). Paricalcitol is effective in PTH suppression with lower hypercalcemic and hyperphosphoremic effect than calcitriol, which is a determinant factor in vascular calcification risk. VDRA´s selectivity carries other beneficial properties like anti-inflammatory activity, inhibition of the renin angiotensin system and reduction of progression of CKD. Our aim was to compare the effect of paricalcitol and calcitriol on mineral metabolism and renal function in an experimental model of young rat.
Material and methods: Weaning female Sprague Dawley rats, were kept 32 days with high phosphorus diet (0.9 %). Nx (n=8): nephrectomy 5/6; NxP (n=7): nephrectomy 5/6+1 μg oral paricalcitol/48 h, 7 doses; NxC (n=8): subtotal nephrectomy 5/6+0,25 μg oral calcitriol/48 h, 7 doses. Renal function, Ca/P metabolism and renal histology were evaluated.
Results: Both paricalcitol and calcitriol reduced PTH levels (mg/dl) with no differences between groups (Nx: 7854.2± 2378.8 vs NxP: 4871.3±3078.0 vs NxC: 3373.0±2094.7). BUN (mg/dl) was lower in paricalcitol group (Nx: 53.6± 10.91 vs. NxP: 42.3±10.92) while calcitriol treated group showed improved renal clearance (ml/min/100 g) (Nx: 18.98±4.51 vs NxC: 27.46±7.93) and decreased serum creatinine (Nx: 1.1±0.26 vs. NxC: 0.8±0.23). There were no differences in proteinuria. CaxP was similar in all groups, but CaU/CrU and CaU/100 g was higher in paricalcitol group (CaU/CrU: Nx: 0.13±0.052; NxP: 0.23±0.069 and NxC: 0.19±0.126) (CaU/100 g weight: Nx: 2.07±0.62, NxP: 3.84±1.08 and NxC:3.14±2.18). An increase in tubular, arterial and interstitial calcification was detected by semiquantitative score (z-score 0–3) in NxP group compared with control group and those with calcitriol (Nx: 1.37, NxP: 1.86, NxC: 0.28).
Conclusions: Our study shows that in a group of young rats paricalcitol failed to improve CKD progression and, although it is less hypercalcemic, has a greater hypercalciuric effect than calcitriol, resulting in tubular, arterial and interstitial renal calcification.

P294 - Systemic multi-organ complications in patients with atypical hemolytic uremic syndrome (aHUS): retrospective observations of a medical practice setting

CRAIG LANGMAN[1], GIACOMO SIMONETTI[2], VéRONIQUE BAUDOUIN[3]
[1]*FEINBERG SCHOOL OF MEDICINE, NORTHWESTERN UNIVERSITY AND CHILDREN'S MEMORIAL HOSPITAL, CHICAGO, USA*
[2]*UNIVERSITY CHILDREN'S HOSPITAL, INSELSPITAL AND UNIVERSITY OF BERN, BERN, SWITZERLAND*
[3]*HôPITAL ROBERT DEBRé – APHP, PARIS, FRANCE*

Introduction: aHUS is a life-threatening and systemic genetic disease in which chronic, uncontrolled complement activation leads to platelet activation, endothelial damage, and systemic thrombotic microangiopathy (TMA). Historically, the prognosis for aHUS patients is very poor and despite plasma exchange/infusion, 33 %-40 % of aHUS patients progress to end-stage renal disease or die with the first clinical aHUS manifestation, and 65 % of patients require dialysis, have permanent kidney damage, or die within 1 year of diagnosis. The high rates of cardiovascular (43 %) and neurologic (48 %) complications reported in the medical literature highlight only some of the many extra-renal complications that can result from ongoing TMA in aHUS patients.
Material and methods: A retrospective analysis of medical records for 30 aHUS patients (19 pediatric, 11 adult) receiving eculizumab outside of clinical trials between 2007 and 2009 was conducted. Data corresponding to the time period before first eculizumab dose are presented.

Results: Medical history data for all 30 aHUS patients (100 %) showed evidence of kidney impairment prior to eculizumab treatment. Nineteen of these patients (63 %) experienced ≥1 extra-renal complication, including 14 patients (47 %) with cardiovascular complications (eg, thrombi in various locations, cardiac arrest, cardiomyopathy); 11 (37 %) with gastrointestinal complications (eg, diarrhea, vomiting, pancreatitis, splenic vein occlusion); and 6 (20 %) with neurologic complications (seizures, acute disseminated encephalomyelitis, stroke, transient ischemic attacks, facial paralysis, headache).
Conclusions: aHUS is a devastating and progressive disease in which TMA can result in sudden and potentially fatal systemic morbidities. Our contemporary study data are consistent with historical reports of multi-organ complications due to systemic TMAs and suggest that evidence of TMA or systemic organ involvement of the heart, gastrointestinal tract, and brain, as well as peripheral thrombi, should prompt high suspicion of aHUS as a clinical diagnosis, even in the absence of overt kidney failure.

P295 - THE EFFECT OF HIGH FGF 23 LEVELS ON CARDIAC MORBIDITY AND RENAL OSTEODYSTROPHY IN CHRONIC KIDNEY DISEASE

CAGLA SERPIL DOGAN[2], AYSE SIMSEK[1], ELIF COMAK[2], ARIFE USLU GOKCEOGLU[2], SEBAHAT OZDEM[3], MUSTAFA KOYUN[2], SEMA AKMAN[2]
[1]*AKDENIZ UNIVERSITY MEDICAL FACULTY DEPARTMENT OF PEDIATRIC CARDIOLOGY*
[2]*AKDENIZ UNIVERSITY MEDICAL FACULTY DEPARTMENT OF PEDIATRIC NEPHROLOGY*
[3]*AKDENIZ UNIVERSITY MEDICAL FACULTY DEPARTMENT OF BIOCHEMISTRY*

Introduction: Fibroblast growt factor 23(FGF 23) is a phosphorus-regulating hormone, increasing in chronic kidney disease (CKD). Although its association with cardiovascular complications and bone mineral metobolism in adult CKD patients has been demonstrated, there is little information in pediatric patients. The aim of this study was to investigate the effect of the level of FGF 23 on bone mineral metabolism and cardiovascular morbidity in pediatric CKD patients.
Material and methods: In this cross-sectional study, 58 children with chronic kidney insufficiency (stage 2–4) and 17 control subjects with normal kidney function underwent echocardiograms, left ventricular mass index (LVMI), myocardial performance index (MPI) and ratio of early diastolic transmitral flow velocity/ early diastolic mitral annular velocity (e/e') were evaluated in all patients. Serum creatinine, calcium, phosphorus, alkaline phosphatase (ALP), parathyroid hormone (PTH), 25 hydroxyvitamin D [25(OH)D] and 1,25-dihydroxyvitamin D [1,25(OH)2D] levels, FGF-23 and Klotho concentrations were analyzed.
Results: Serum FGF23 levels were elevated when compared with control subjects (median 476 .3 pg/ml; interquartile range 10.8- 15681 pg/ml vs median 28 pg/ml; interquartile range 5.4- 604 pg/ml, $p<0.001$). Mean serum Klotho levels were 5.4±5.0 ng/ml (median; 3.6, range; 0.1-20.6 ng/ml) and 1.3±0.9 ng/ml in patients and control subjects, respectively ($p=0.018$). Mean of log FGF23 was 2.48 ±1.19 pg/ml. Significant correlations were observed log FGF23 and eGFR ($p=0.025$, $r=-0.293$) and Klotho levels ($p<0.001$, $r=0.671$). No significant association was found in cardiovascular parameters and log FGF 23. Similarly, LVMI, MPI and ratio of e/e' increased with increasing tertiles of FGF 23 but not statistically significant. Mean phosphate, iPTH and Klotho concentrations significantly increased with increasing tertiles of FGF23 ($p=0.034$, 0.044, <0.001, respectively).
Conclusions: FGF23 levels are high in pediatric CKD patients. Further prospective studies consisting of larger pediatric patient population are needed to investigate the association between echocardiographic parameters and elevated FGF 23 levels.

P296 - Use of Cinnacalcet in children with Chronic Kidney Disease – A single centre experience

SHEETAL BHOJANI, ANGELA LAMB, IAN RAMAGE, JIM BEATTIE
ROYAL HOSPITAL FOR SICK CHILDREN, GLASGOW

Introduction: Secondary hyperparathyroidism is a major issue in children with chronic kidney disease (CKD). It is characterised by increased parathyroid hormone (PTH), causing metabolic bone disease. The UK Renal Association suggests maintaining PTH levels less than twice the upper limit of normal range. The calcium sensing receptor (CaSR) regulates the secretion of PTH. Calcimimetic agents (like Cinacalcet) which increase the sensitivity of the CaSR to extracellular calcium ions and inhibit the release of PTH, have been used in patients with renal osteodystrophy. We looked at the use of Cinacalcet in CKD patients in our tertiary renal unit
Material and methods: We retrospectively identified all patients started on Cinacalcet. Their demographic and clinical details were collected from the case notes and the electronic CKD database.
Results: We identified 8 patients on cinacalcet treatment. 2 patients had started treatment less than 3 months ago and therefore were excluded. The average age of remaining 6 patients was 6 yrs (range 2 months to 15 years). 3 (50 %) patients were on haemodialysis (HD) and 3 (50 %) were on no dialysis at the time of initiation of treatment. The male

female ratio was 5:1. The initial dose was 0.5 mg/kg and it ranged from 0.5 mg/kg to 3 mg/kg during the course of the treatment. There was a 42 % reduction in PTH levels noted. The calcium phosphate product was unchanged. Duration of treatment ranged from 3 – 27 months. In 2 patients the treatment was stopped, 1 after 18 months due to improvement in PTH levels and the 2nd underwent a renal transplant; in others the treatment is still ongoing. There were no side effects noted

Conclusions: Calcimimetic agents are useful in reducing PTH levels in CKD patients with or without dialysis. We did not see any side effects of cinacalcet although the long term effect on growth is yet to be determined.

P297 - Which equation to estimate Glomerular Filtration Rate in renal hyperfiltrating children?

LUCIANO SELISTRE[1], LUCIANO SELISTRE[2], LUCIANO SELISTRE[3], VANDRÉA CARLA DE SOUZA[1], LAURENCE DUBOURG[1], LAURENCE DUBOURG[4], LAURENCE DUBOURG[5], LAURENCE DUBOURG[6], PIERRE COCHAT[1], PIERRE COCHAT[4], PIERRE COCHAT[5], PIERRE COCHAT[6], DAVID SAITOVITCH[2], IVAN CARLOS FERREIRA ANTONELLO[2], AOUMEUR HADJ-AISSA[1], AOUMEUR HADJ-AISSA[5], BRUNO RANCHIN[4], OLGA DOLOMANOVA[1]

[1]*EXPLORATION FONCTIONNELLE RéNALE ET MéTABOLIQUE, GROUPEMENT HOSPITALIER EDOUARD-HERRIOT, HOSPICES CIVILS DE LYON*

[2]*PONTIFICIA UNIVERSIDADE CATóLICA DO RIO GRANDE DO SUL, BRAZIL*

[3]*UNIVERSIDADE DE CAXIAS DO SUL, BRAZIL*

[4]*CENTRE DE RéFéRENCE DES MALADIES RéNALES RARES, SERVICE DE NéPHROLOGIE ET RHUMATOLOGIE PéDIATRIQUES, HOSPICES CIVILS DE LYON, LYON, FRANCE*

[5]*UNIVERSITé CLAUDE-BERNARD LYON 1, LYON, FRANCE*

[6]*FRE 3310, CNRS, UNIVERSITé CLAUDE-BERNARD LYON 1, LYON, FRANCE*

Introduction: Monitoring renal function is crucial in pediatric patients with glomerular hyperfiltration: the use of plasma creatinine (PCr) to estimate glomerular filtration rate (GFR, mL/min per 1.73 m²) is hampered by its lack of reliability and data on the performance of cystatin C (CystC) are sparse. The aim of this study was to evaluate the performance of CysC-based, PCr-based, and combined (CysC+PCr) equations in hyperfiltrating children.

Material and methods: We assessed the performance of 6 GFR estimating equations eGFR) in hyperfiltrating patients: i) CysC-based equations: Filler, le Bricon, ii) PCr-based equations: bedside Schwartz, Schwartz-Lyon, iii) combined equations: CKiD and Zapitelli; using inulin clearance (mGFR) as the reference method. The agreement between eGFR and mGFR was assessed using bias (eGFR-mGFR) and 30 % accuracy.

Results: 37 patients (52 measurements) aged 2–18 years (11.3±4.2) with various systemic disease (liver transplantation (9), glomerulonephritis (8), uropathy (5) glycogen-storage diseases (4), others (11)) and a GFR ≥135 were studied. Mean GFR was 152.7±16.8 [135–201]). The bias (ml/min per 1.73 m2 [IC 95 %]) were of −7 (−1,-14), -28 (−21,-35), -10 (−2,-18), -18 (−10,-26), -27 (−21,-32), -23 (−15,-30), for the Filler, Bricon, bedside Schwartz, Schwartz-Lyon, CKiD, and Zappitelli equations, respectively. The ability to classify hyperfiltration patients by areas under the ROC curves was better for Filler, bedside Schwartz and Schwartz-Lyon (0.81, 0.75 and 0.70) than for the others (0.63, 0.64, and 0.65 for Bricon, CKiD, and Zappitelli respectively). The 30 % accuracies were 96 %, 77 %, 96 %, 86 %, 88 %, and 83 % for the Filler, Bricon, bedside Schwartz, Schwartz-Lyon, CKiD, and Zappitelli equations, respectively. The performance of Filler equation was significantly better for all the studied parameters.

Conclusions: The Cyst C based Filler equation which is 1) simple to use and 2) a reliable equation in hyperfiltrating children should be used when hyperfiltration is suspected.

P298 - Schwartz formula: is one K coefficient enough for all children?

VANDRÉA CARLA DE SOUZA[1], VANDRÉA CARLA DE SOUZA[2], MURIEL RABILLOUD[4], MURIEL RABILLOUD[5], PIERRE COCHAT[1], PIERRE COCHAT[2], PIERRE COCHAT[3], PIERRE COCHAT[6], LUCIANO SELISTRE[1], LUCIANO SELISTRE[7], LUCIANO SELISTRE[8], BRUNO RANCHIN[2], AOUMEUR HADJ-AISSA[1], AOUMEUR HADJ-AISSA[3], BEHROUZ KASSAI[6], BEHROUZ KASSAI[9], ULLA BERG[10], MARIA HERTELIUS[10], LAURENCE DUBOURG[1], LAURENCE DUBOURG[2], LAURENCE DUBOURG[3], LAURENCE DUBOURG[6]

[1]*EXPLORATION FONCTIONNELLE RéNALE ET MéTABOLIQUE, GROUPEMENT HOSPITALIER EDOUARD-HERRIOT, HOSPICES CIVILS DE LYON*

[2]*CENTRE DE RéFéRENCE DES MALADIES RéNALES RARES, SERVICE DE NéPHROLOGIE ET RHUMATOLOGIE PéDIATRIQUES, HOSPICES CIVILS DE LYON, LYON, FRANCE*

[3]*UNIVERSITé CLAUDE-BERNARD LYON 1, LYON, FRANCE*

[4]*HOSPICES CIVILS DE LYON, SERVICE DE BIOSTATISTIQUE, F-69003, FRANCE*

[5]CNRS, UMR5558, LABORATOIRE DE BIOMéTRIE ET BIOLOGIE EVOLUTIVE, EQUIPE BIOSTATISTIQUE-SANTé, F-69100, FRANCE
[6]FRE 3310, CNRS, UNIVERSITé CLAUDE-BERNARD LYON 1, LYON, FRANCE
[7]PONTIFICIA UNIVERSIDADE CATóLICA DO RIO GRANDE DO SUL, BRAZIL
[8]UNIVERSIDADE DE CAXIAS DO SUL, BRAZIL
[9]INSERM CIC 201, EPICIME, UMR 5558, SERVICE DE PHARMACOLOGIE CLINIQUE, LYON, FRANCE
[10]DEPT OF CLINICAL SCIENCE, INTERVENTION AND TECHNOLOGY, DIVISION OF PEDIATRICS, KAROLINSKA INSTITUTET, KAROLINSKA UNIVERSITY HOSPITAL HUDDINGE, STOCKHOLM, SWEDEN

Introduction: The equations used to estimate glomerular filtration rate (GFR, mL/min per 1.73 m²) based on plasma creatinine (PCr) have been recommended by guidelines. In 2009, Schwartz et al. updated the traditional Schwartz equation to IDMS-standardized creatinine assay, but they cannot demonstrate K coefficient variation with puberty as previously proposed. We aimed 1) to determine the usefulness of using different coefficients according to age and gender for the bedside Schwartz formula (Schwartz-Lyon formula) and 2) to validate them in an external population, and 3) to compare the performance of these 2 revisited Schwartz formulae.
Material and methods: A linear mixed effects model was used to determine coefficients according to age and sex in a French cohort of 360 children and adolescents aged 1–18 yrs (190 males, 965 measurements, GFR=86.0±34). We model the inulin clearance (mGFR) according to the ratio of height over PCr. These coefficients were validated in a Swedish cohort of 109 children and adolescents (55 males, GFR=66.0± 37), aged 4–17.9 years.
Results: We found two coefficients (k=36.5 for boys> 13 years of age and 32.5 for others) for the Schwartz-Lyon formula. In the Swedish cohort, the performance of Schwartz-Lyon assessed by the mean ratio eGFR/mGFR (expressed in mL/min per 1.73 m²±SD) for all patients, children, and adolescents was 0.96 ±0.19, 1.04 ±0.22, 0.92 ±0.16 respectively. These results are significantly better than those of the 2009-Schwartz formula (p=0.018) in children, but comparable for adolescents.
Conclusions: The good performance of the bedside Schwartz and the Schwarz-Lyon formulas and their simplicity to use in clinical practice are strong arguments to recommend these formulas in routine in children and adolescents. The best performance of Schwartz-Lyon less than 13 years of age was probably linked to the specific lower k coefficient used in that population.

P299 - RISK FACTORS FOR DEVELOPMENT OF CHRONIC KIDNEY DISEASE IN CHILDREN WITH NEUROGENIC BLADDER

MAGDALENA DROZYNSKA-DUKLAS[1], PIOTR CZARNIAK[1], MICHAŁ MATERNIK[1], KATARZYNA KRZEMINSKA[1], LESZEK KOMASARA[2], PIOTR CZAUDERNA[2], ALEKSANDRA ZUROWSKA[1]
[1]DEPARTMENT OF PEDIATRIC AND ADOLESCENT NEPHROLOGY AND HYPERTENSION, MEDICAL UNIVERSITY OF GDANSK
[2]DEPARTMENT OF PEDIATRIC SURGERY & UROLOGY, MEDICAL UNIVERSITY OF GDANSK

Introduction: Children with neurogenic bladder due to myelomeningocele are at increased risk for chronic kidney disease (CKD). Nephroprotective measures with clean intermittent catheterization (CIC) and anticholinergic drugs are standard treatment used to decrease the incidence of CKD. The aim of the study was to assess the risk factors for kidney damage in this group of patients.
Material and methods: 115 patients with MMC were included. The stage of CKD was classified according to estimated GFR (Shwartz formula), presence of albuminuria and results of imaging tests. Logistic regression analysis was used to select the risk factors, including: duration of CIC and anticholinergic therapy, presence of urinary tract infections (UTI, vesicoureteral reflux (VUR) in 1st year of life, history of recurrent UTIs, urodynamic results in 1st year of life and presence of paraplegia.
Results: CKD was diagnosed in 43,5 % children. The majority presented with CKD stage I (80 %). Children who did not develop CKD were without paraplegia (p=0,009), had a negative history of UTI (p=0,003) and no VUR in 1st year of life (p=0,0039). Neither duration of CIC (p=0,431), anticholinergic therapy (p=0,258) nor urodynamic findings (LPP> 40 cm) in first year of life (p=0,194) significantly influenced the development of kidney damage. The presence of UTI in first of life (OR=3,2), recurrent UTIs (OR=3,53), paraplegia (OR=2,66) and the presence of VUR in first year of life (OR= 2,99) were the risk factors for CKD.
Conclusions: 1. Children with neurogenic bladder due to MMC are still at increased risk for kidney damage, despite early introduction of nephroprotective therapy with CIC and anticholinergic drugs. 2. Paraplegia, the presence of UTI and VUR in the 1st year of life and recurrent UTIs are risk factors for CKD in MMC patients.

P300 - HELICOBACTER PYLORI SEROPOSITIVITY IN CHILDREN WITH CHRONIC RENAL FAILURE

GURKAN GENC[1], GONUL CALTEPE[2], OZAN OZKAYA[1], HULYA NALCACIOGLU[1], MURAT HOKELEK[3], AYHAN GAZI KALAYCI[2]

[1]ONDOKUZ MAYIS UNIVERSITY FACULTY OF MEDICINE, PEDIATRIC NEPHROLOGY DEPARTMENT
[2]ONDOKUZ MAYIS UNIVERSITY FACULTY OF MEDICINE, PEDIATRIC GASTROENTEROLOGY DEPARTMENT
[3]ONDOKUZ MAYIS UNIVERSITY FACULTY OF MEDICINE, MICROBIOLOGY AND CLINICAL MICROBIOLOGY DEPARTMENT

Introduction: Gastrointestinal symptoms are frequently seen in patients with chronic renal failure secondary to uremia. We aimed to investigate the prevalence of gastrointestinal symptoms and Helicobacter pylori (HP) seropositivity reliability in these patients.
Material and methods: The study involved 33 patients with end-stage renal disease and 33 age and sex-matched healthy controls. Serological, endoscopic and demographic features of patients were determined and gastrointestinal symptoms were questioned.
Results: Twenty seven peritoneal dialysis and 6 hemodialysis patients were included in the study. The HP seropositivity was 51.5 % and 60.6 % in uremic children and normal control respectively (p=0.46). Twenty patients underwent esophagogastroduodenoscopy and 30 % of them were shown HP on biopsy. Dyspepsia was observed in 42.4 % of all patients. In patients with dyspepsia, HP seropositivity was 57.1 % and biopsy proven HP was 36.4 %. There was no association between dyspepsia and HP seropositivity (p=0.579) Biopsy proven HP was determined in 60 % of patients with positive serology and in one with negative serology.
Conclusions: Gastrointestinal symptoms are common among dialysis patients and Hp infection is high also in childhood. It is required to eradication in all uremic patients who are candidates for transplantation. HP serology can be used as a screening test in these patients but reliability of this test is lower than expected.

P301 - Nutrition status of Greek Children with advanced stages of Chronic Kidney disease

AGGELIKI APOSTOLOU[1], NIKOLETA PRINTZA[2], THOMAIS KARAGIOZOGLOU- LAMPOUDI[1], JOHN DOTIS[2], FOTIOS PAPACHRISTOU[2]
[1]CLINICAL NUTRITION LAB, NUTRITION DEPT ALEXANDER TECHNOLOGICAL EDUCATION INSTITUTE, THESSALONIKI, GREECE
[2]1ST PEDIATRIC DEPARTMENT, ARISTOTLE UNIVERSITY, THESSALONIKI, GREECE

Introduction: Introduction: Malnutrition is a major problem among children with Chronic Kidney Disease(CKD) and it is essential to be recognized as early as possible. In this study we aimed to assess malnutrition in children with advanced stages of CKD.
Material and methods: Material and Methods: Nutrition status of 30 children (age: 1–16 y) with CKD stages III, IV (group A) and on peritoneal dialysis (PD, group B) was evaluated. Malnutrition risk was assessed by Smart score (SSc). Z-scores for weight, height, body mass index (BMI), mid upper arm muscle circumference (MUAMC), mid upper arm circumference (MUAC), triceps skinfold (TSF) were calculated. Bioimpedance analysis (BIA) measurements for phase angle (PA), body cell mass (BCM) and Fat Free Mass Index (FFMI) were performed. Three day energy and protein intake as well as biochemical indexes were evaluated. All patients were on regular dietitian advice and PA and SSc were recorded in clinics.
Results: Results: Median z-zcores for height, weight, BMI, MUAC and TSF were −1.205, -1.135, -0.600, -0.680 and +1.560 respectively. Intake/requirements ratio (mean) was 89.2 %, while mean protein intake was 1.95gr/kgr. Mean value for SSc and PA were 5.21±2.38 and 4.21±1.16 respectively. PA was below the 3rd percentile in 7/30 (23.5 %) children. SSc was inversely correlated to PA (r=−0.567, p<0.001), MUAMC (−0.498, p <0.05), FFMI (r=−0.673, p<0.001), mean energy (r=−0.624, p<0.001) and protein intake (r=−0.421, p<0.05). No significant differences regarding anthropometry or BIA parameters were found between groups A and B.
Conclusions: Conclusions: A considerable proportion of children with advanced CKD are undernourished. Regular dietitian evaluation using new tools as SSc and PA may early identify patients at risk of or with malnutrition.

P302 - Longitudinal study of bone strength using two imaging techniques in children with Chronic Kidney Disease

NIKOLETA PRINTZA[1], CHRYSA GKOGKA[1], ATHANASIOS CHRISTOFORIDIS[1], EIRINI KAZANTZIDOU[2], KONSTANTINOS KOLLIOS[3], FOTIOS PAPACHRISTOU[1]
[1]1ST PAEDIATRIC DEPARTMENT, ARISTOTLE UNIVERSITY
[2]RADIOLOGY DEPARTMENT, IPPOKRATION GENERAL HOSPITAL, THESSALONIKI
[3]3RD PEDIATRIC DEPARTMENT, ARISTOTLE UNIVERSITY

Introduction: Children with chronic kidney disease (CKD) are at high risk of developing impaired bone mass. This 2-year prospective study investigated changes of bone mass in children with CKD in relation to the type of intervention using two imaging techniques: Dual energy X-ray Absorptiometry (DXA) and Quantitative UltraSonography (QUS).

Material and methods: Thirty-three patients with CKD (18 boys and 15 girls, mean age: 10.37±3.37 years) completed a two-year follow-up. Measurements of Bone Mineral Density (BMD) by DXA at lumbar spine and hip and Speed of Sound (SOS) by QUS at radius and tibia were performed at the begging and at the end of the study. Patients' cohort consisted of 14 patients with chronic kidney disease stage 3–4 not treated with dialysis (CKD group), 5 patients on peritoneal dialysis treatment (PD group) and 14 patients after kidney transplantation (KT group).

Results: BMD measurements did not show any significant changes in CKD and PD patients during the study. There was a reduction in BMD measured at lumbar spine, femoral neck and total hip in KT patients that was approaching significance (0.14±1.41 vs −0.46±1.26, p=0.074; -0.33± 1.13 vs −1.95±2.15, p=0.080 and −0.46±1.36 vs −1.96± 2.66, p=0.060; respectively). During the 2 years follow-up, SOS measurements at radius decreased significantly in PD patients (−0.74±1.32 vs −2.44±1.85, p=0.008), whereas SOS measurements at tibia significantly improved in KT patients (−0.46±1.14 vs −1.01±1.31, p=0.004). Finally, no significant changes in QUS parameters were recorded for patients in CKD group.

Conclusions: Patients after kidney transplantation show deterioration in BMD values, probably reflecting the effect of steroid administration in contrast with a significant improvement in QUS parameters reflecting the reversal of secondary hyperparathyroidism. Patients in dialysis show significantly decreased QUS measurement associated with increased parathormone values.

P303 - Investigation of Effects of Prenatal and Postnatal Exposure of Wireless Comunication Devices on Rat Kidneys.

AYÇA ESRA KUYBULU[1], FARUK OKTEM[2], RECEP SUTCU[3], IBRAHIM METIN CIRIS[1], SELCUK COMLEKCI[1], EFKAN UZ[1]

[1]*SÜLEYMAN DEMIREL UNIVERSITY FACULTY OF MEDICINE*

[2]*BEZMİ ALEM VAKIF UNİVERSİTY FACULTY OF MEDICINE*

[3]*KATIP CELEBI UNİVERSİTY FACULTY OF MEDICINE*

Introduction: The aim of this study was to investigate wireless electromagnetic field (EMF) with a internet frequency of 2450 Hz, for a long time exposure induced oxidative stres and apoptosis on kidney tissues of pre- and postnatally exposed male Wistar rats.

Material and methods: The study was conducted in three groups of rats which were prenatal, postnatal and control groups. Mothers of rats in the prenatal group from the first day of pregnacy until delivery for 1 h/day; rats in the postnatal group until 12 weeks of the birth, were subjected to the 2450 MHz EMF in same conditions. The control group consisted of sham exposed group. At the 12 weeks of age whole rats in all groups were sacrified. Oxidative stress markers and histopathological findings for apoptosis were studied.

Results: Renal tissue malondialdehyde levels and total oxidative status of prenatal exposure group were high (P<0.05), total antioxidative status and superoxide dismutase levels were low(P<0.05). Glutathion peroxidase levels did not differ between groups. Urine N-acetyl-β-D-Glucoseaminidase/creatinine ratio was significantly higher in pre- and postnatal exposure groups (P<0.001). Hematoxylin-eosin stained kidney tissues are all normal in control group, whereas tubular injury was detected in some of specimens in postnatal exposure goups. Evaluation of Bcl-2, Bax staining specimens with image-J analyse program showed low intensity staining with Bax at cortical areas in prenatal exposure group, high intensity staining with Bcl-2 at cortical and medullary areas of prenatal group (P<0.05, P<0.05, P<0.05). Bcl2/Bax staining intensity ratio in medullary and cortical areas was higher in prenatal exposure group (P<0.05, P<0.05).

Conclusions: Prenatal exposure to 2450 MHz EMF of Wistar rats cause development of chronic stres, and increase oxidative stres. Balance between apoptotic and anti-apoptotic factors returned in favors of antiapoptotic factors, and it might stimulates proliferation and in long term some histological changes and induction of malignancies may be trigerred.

P304 - The effects of β-glucan on kidney injury in rats induced by 2.45-GHz radiation from wireless communication devices

FARUK OKTEM[1], AYÇA ESRA KUYBULU[2], RECEP SUTCU[3], OZGUR FEDAKAR[2]

[1]*BEZMİ ALEM VAKIF UNIVERSITY FACULTY OF MEDICINE*

[2]*SÜLEYMAN DEMIREL UNIVERSITY FACULTY OF MEDICINE*

[3]*KATIP CELEBI UNİVERSİTY FACULTY OF MEDICINE*

Introduction: There is widespread use of 2.45-GHz irradiation-emitting devices in industrial, medical and domestic application. The aim of the present study was to investigate the effect of 2.45-GHz electromagnetic radiation (EMR) on the oxidant status of kidney and to examine the effects of β-glucans against the renal oxidative injury.

Material and methods: Thirty-two male Wistar albino rats were randomly divided into four equal groups: cage control; sham exposed; EMR; and EMR+β-glucan. A 2.45-GHz EMR emitted device from the experimental exposure was

applied to the EMR group and EMR+β-glucan group for 60 min daily, respectively, for 4 weeks. β-glucan was administered via gavage at a dose of 50 mg/kg/day to the EMR+β-glucan group before each exposure to radiation. The activities of antioxidant enzymes, superoxide dismutase (SOD), glutathione peroxidase (GSH-Px), catalase (CAT), total antioxidant capacity (TAC) and total oxidative status (TOS), as well as the concentration of malondialdehyde (MDA) were measured in homogenates of the kidney tissue. Urinary N-acetyl-β-D-glucosaminidase (NAG, a marker of renal tubular injury) excretion and morphological changes of kidney tissue were evaluated.

Results: Exposure to 2.45-GHz EMR caused a significant increase in renal MDA levels, TOS activity, and urinary NAG excretion ($P<0.05$). Also, the activities of TAC, SOD and GSH-Px increased in kidney tissues. But renal CAT levels did not chance. Systemic β-glucan didn't reversed the elevation of MDA levels and antioxidant activities caused by EMR. There were a significant histopathological changes in EMR exposed rats more than those of the control groups. But β-glucan did not reduce the EMR-induced oxidative kidney damage both at the biochemical and histological levels.

Conclusions: The present study demonstrated the role of oxidative mechanisms in 2.45-GHz EMR-induced renal tubular damages and β-glucan could not ameliorate kidney injury.

P305 - Renin-angiotensin-aldosterone system blockers in diabetic nephropathy: the role of epithelial to mesenchymal transition

SáNDOR KőSZEGI[1], NóRA FANNI BáNKI[1], LáSZLó WAGNER[3], ÁDáM HOSSZú[1], LILLA LéNáRT[1], RENáTA GELLAI[1], TIVADAR TULASSAY[2], ANDREA FEKETE[1]
[1]*SE-MTA „LENDULET" DIABETES RESEARCH GROUP SEMMELWEIS UNIVERSITY*
[2]*1ST DEPARTMENT OF PEDIATRICS SEMMELWEIS UNIVERSITY*
[3]*DEPARTMENT OF TRANSPLANTATION AND SURGERY SEMMELWEIS UNIVERSITY*

Introduction: In diabetic nephropathy (DN) the renin-angiotensin-aldosterone system (RAAS) is activated. The elevated renal angiotensin II induces the epithelial to mesenchymal transition (EMT), which is a key element of renal fibrotic transformation. Here we investigated the development of EMT in diabetes and after various RAAS inhibitor treatments.

Material and methods: After 5 weeks of streptozotocin (65 mg/bwkg ip.) induced diabetes male Wistar rats were treated for 2 weeks with ACE inhibitor enalapril, ARB losartan or aldosterone-antagonists spironolactone or eplerenone. Untreated diabetic and healthy animals served as controls (n=6/group). Mesangial matrix expansion, vascular hyalinisation and intersititial fibrosis were analyzed on PAS and Masson stained kidney sections. Renal αSMA protein level and localization were examined byWestern blot and immunofluorescent staining.

Results: Diabetes induced significant mesangial matrix expansion, vascular hyalinisation and interstitial fibrosis, which all were ameliorated by the various RAAS blockers. In parallel the increased renal αSMA level in diabetes was lowered by RAAS inhibitor treatments. While in controls αSMA was only visible around the vessels, in diabetes intraepithelial and glomerular signal was also detectable. Different RAAS blockers minimized αSMA staining in these structures.

Conclusions: EMT could play a role in the development of DN. Inhibition of this process could serve as a new therapeutic target of RAAS blockers.

P306 - Serum fetuin-A in children with chronic kidney disease

CIRO CORRADO[1], CARMELINDA CANALE[1], ALESSANDRA ANZELMO[1], MARIA MICHELA D'ALESSANDRO[1], SILVIO MARINGHINI[1], ELISA DI MARCO[2]
[1]*PEDIATRIC NEPHROLOGY*
[2]*DIPARTIMENTO DEI SERVIZI, UOC PATOLOGIA CLINICA*[a]

Introduction: Vascular diseases are a major cause of morbidity and mortality in chronic kidney disease (CKD). Vascular calcification begins in the first decade of life in children with CKD and is regulated by inducers and inhibitors factor, Fetuin-A (Fet-A) being the major inhibitor

Material and methods: We measured Fet-A, using ELISA kit, in 21 children (Group A) with CKD (III-IV stage), in 9 children on dialysis (Group B) and in 30 health children (Group C) comparable for sex and age, used as control group. Fet-a values were correlated with clinical (weight, BMI, blood pressure values) and biochemical parameters (calcium, phosphorus, Vit D, osteocalcin, PTH, Hb, serum albumin and cholesterol, ferritin, PCR).

Results: Fet-A serum concentrations were not related to age and gender in all group. Fet-A levels in group A were significantly higher as compared to group B and C (45+−13.9 vs 24.2+−10.8 ng/ml and 45+−13.9 vs 34.2+−8.1 ng/ml respectevely; $p<0.001$). On the contrary Fet-A was lower in dialysis patients as compared to CKD children and control group. Fet-A showed a significant correlation with PCR and ferritin. No correlation with indexes of bone-turnover was found.

Conclusions: Our data showing lower Fet-A levels in dialysis patients, are similar to those published by Schaible et all (2012), but in contrast to other data of Shroff et al (2008). In our population we observed higher Fet-A levels in CKD children. This condition, in our opinion, could preserve this group of patients from vascular calcifications. We plan to measure aortic pulse wave velocity and carotid intima-media thickness in our patients.

P307 - ASSESSMENT OF NUTRITIONAL STATUS AND VOLUME DISTRUBUTION OF CHILDREN WITH CHRONIC KIDNEY DISEASE

DILEK YILMAZ[1], FERAH SÖNMEZ[1], SACIDE KARAKAŞ[2], ÇIĞDEM YENISEY[3]
[1]*DIVISION OF PEDIATRIC NEPROLOGY, DEPARTMENT OF PEDIATRICS, ADNAN MENDERES UNIVERSITY, AYDIN, TURKEY*
[2]*DEPARTMENT OF ANATOMY, ADNAN MENDERES UNIVERSITY, AYDIN, TURKEY*
[3]*DEPARTMENT OF BIOCHEMISTRY, ADNAN MENDERES UNIVERSITY, AYDIN, TURKEY*

Introduction: Malnutrition is well-described serious risk factor for morbidity and mortality in chronic kidney disease (CKD) of children. On the other hand, the determination of volume distribution abnormalities are difficult.The aim of this study was to investigate the nutritional status and volume distrubution of children with CKD in late stages
Material and methods: Anthropometric measurements were done and serum albumin, prealbumin, transferrin, RBP-4, IGF-1, zinc, leptin, urea, creatinine, cholestrol, Na, K, Ca, P ve PTH, ALP, bicarbonate, hemoglobin, Fe, B12, folate, ferritin, CRP, fibrinojen TNF-alfa levels were investigated. Student's t-test, Mann–Whitney U test and Krusgall Wallis test were used for statistically analysis.
Results: Total 52 children with CKD (stage III-IV (n=24), PD (n=16), HD (n=12)) and healthy children (n=46) were included to the study. SDS values of weight, height, body mass index, triceps scinfold thickness and mid arm circumference of CKD children were lower than the control group. BIA fat mass and body cell mass in CKD were found significantly decreased and fat free mass was found significantly increased than the control group. No difference was found in phase angles between two groups. Serum albumin, transferin, RBP-4, leptin, folate and zinc levels in CKD were significantly lower than the healthy children. Prealbumin, IGF-1, fe, B12 levels were not found different between two groups. The inflamation parameters as, serum TNF-alfa, ferritin and fibrinojen levels were higher in CKD than healthy children. BIA ICF was higher in CKD than the control. However, TBW and ECF were not different.
Conclusions: We think that, using of BIA with anthropometric measurements for nutritional assesment in CKD children might be helpful. In addition, visceral proteins, leptin and serum micronutrients should be measured for nutritional assesment of CKD. We also observed that inflamation had an important contribution in malnutrition in CKD of children.

P308 - Advanced Oxidation Protein Products and Advanced Glycation End Products in Children/ Adolescents With Chronic Renal Insufficiency

PODRACKá LUDMILA[1], ŠEBEKOVá KATARINA[2], HEDVIG JURAJ[1], KLENOVICSOVA KRISTINA[3], HEIDLAND AUGUST[4]
[1]*DEPT. PEDIAT. UNIV. CHILDRENś HOSPT., KOŠICE, SLOVAKIA*
[2]*INSTITUTE OF MOLECULAR BIOMEDICINE, COMENIUS UNIVERSITY, BRATISLAVA, SLOVAKIA 2*
[3]*DEPARTMENT OF CLINICAL AND EXPERIMENTAL PHARMACOTHERAPY, SLOVAK MEDICAL UNIVERSITY, BRATISLAVA, SLOVAKIA 3*
[4]*DEPARTMENT OF INTERNAL MEDICINE, UNIVERSITY OF WUERZBURG, WUERZBURG, GERMANY 4*

Introduction: Advanced oxidation protein products (AOPPs) represent dityrosine-containing cross-linked protein modifications formed mainly via myeloperoxidase reaction, supposed to accelerate the uremia-associated atherogenesis and renal fibrosis.
Material and methods: In a cross-sectional study, we investigated the accumulation of AOPPs and advanced glycation end product (AGE)-specific fluorescence corrected for albumin in children/adolescents with chronic renal failure (CRF, n =42), end-stage renal disease (ESRD, n=12), kidney transplanted patients (Tx, n=16), and age-matched healthy controls (n =38).
Results: AOPP levels were 2.4-fold higher in the CRF and ESRD patients, and 1.6-fold higher in the transplanted subjects when compared with the controls ($P<0.001$). In comparison with healthy controls, AGE levels rose 2-fold in the CRF, 7-fold in the ESRD, and 5-fold in the kidney transplanted children/adolescents, ($P<0.001$). Patients with cardiovascular affliction presented with higher AGE levels than those without diagnosed cardiovascular disease($P<0.02$). In patients with stabilized renal function, AOPP and AGE levels did not change significantly during 12 months.
Conclusions: Pattern of accumulation of AOPP and AGE in children/adolescents with chronic renal disease differs. Accelerated rise in AOPP levels in some children/adolescents in predialysis stage of chronic renal insufficiency, inadequate to deterioration of renal function, might require further attention. This study was supported by the Agency of the

Ministry of Education of the Slovak Republic for the Structural Funds of the European Union, Operational Program Research and Development (Contract No. 034/2009/2.1/OPR&D) and by VEGA project No. 1/0715/11

P309 - ENTERAL FEEDING IN CHILDREN OVER TWO YEARS OF AGE WITH CHRONIC KIDNEY DISEASE-MORE THAN ONE GAIN?

HELEN E JONES, LESLEY REES
GREAT ORMOND STREET HOSPITAL FOR CHILDREN NHS FOUNDATION TRUST, LONDON, UK

Introduction: To determine whether commencing enteral feeding in children over two years of age with chronic kidney disease(CKD) improves nutritional status and growth.
Material and methods: Single centre retrospective audit of nutrition and growth in pre-pubertal children with CKD who started enteral feeding (nasogastric or gastrostomy) when over two years of age.
Results: So far we have identified 18 children, 50 % male, mean age 7.1(2.1-13.3) years and GFR 16(4–47)ml/min/1.73 m2. Nine were on dialysis at initiation of enteral feeding and four commenced dialysis during the first year of enteral feeding. The mean HtSDS and BMISDS were −2.61 and −0.79 at the start of enteral feeding, -2.38 and 0.71 after 12 months (p=NS for HtSDS, p=0.0005 for BMISDS) and by 24 months (n=11)(6 children transplanted before 2 years and 1 was no longer receiving enteral feeds) the mean HtSDS and BMISDS were −2.2 and 1.13 (p=NS for HtSDS, p=0.0009 for BMI SDS). The feeds provided a mean of 53 kcal/Kg and 1.2 g protein/Kg. Albumin improved from a mean (inter-quartile range) of 34.8 (31–42)g/L pre-enteral feeding to 37.8(35–42)g/L at 1 year and 39.3(37–40.8)g/L at 2 years after starting enteral feeds (p=0.44 and 0.12).
Conclusions: Establishing enteral feeding in children with CKD beyond two years of age resulted in a small increase in HtSDS and serum albumin, although this did not reach statistical significance. However, given the association of poor growth and, in particular, hypoalbuminaemia with morbidity and mortality, improving nutrition by means of enteral feeding in this cohort may impact on their long term survival. On the other hand, the increase in BMI SDS was significant, so, knowing the current obesity epidemic, care must be taken not to provide excess calories.

P310 - Rare congenital disorders and syndromes – frequent cause of chronic kidney disease (CKD) in children

TOMASZ JARMOLIńSKI[1], DARIUSZ RUNOWSKI[2], MARCIN ZANIEW[3], BOżENA JACHIMIAK[2]
[1]*DEPT. OF PEDIATRICS, REGIONAL HOSPITAL, MIęDZYRZECZ, POLAND*
[2]*DEPT. OF PEDIATRIC NEPHROLOGY, DISTRICT HOSPITAL, GORZóW, POLAND*
[3]*DISTRICT CHILDREN'S HOSPITAL, POZNAń, POLAND*

Introduction: Progress in medical genetics and dysmorphology resulted in a growing incidence of rare congenital diseases which ultimately lead to CKD. The aim of the study was to analyze the prevalence and outcome of congenital disorders and syndromes in children with CKD treated at Department of Nephrology and Dialysis, District Children's Hospital, Szczecin, Poland (previous place of work of the authors).
Material and methods: We reviewed medical records of all CKD (stage 3–5) patients (pts) aged 0–18 yrs who were treated in years 2000–2010. Twenty-two pre-dialysis and 54 dialyzed pts were identified and included for analysis. Results of renal replacement therapy were also evaluated.
Results: 57 cases (75 %) of inherited diseases as a cause of CKD were found. Thirty-eight pts were in stage 5 and 19 pts in stage 3–4 CKD. Among them 22 pts (29 % of all children with CKD) had „rare" disease or syndrome (16 on dialysis/6 in pre-dialysis group), which included the following diagnoses: congenital nephrotic syndrome in 4 pts (4/0), familial CAKUT in 3 (2/1), VATER association in 2 (1/1), Wolf-Hirschhorn syndrome in 2 (1/1) and single cases of Alport (1/0), Arnold-Chiari (1/0), Bardet-Biedl (0/1), Boichis (1/0), Goldenhar (0/1), Hinman (1/0), Marfan (1/0), and Ochoya syndrome (1/0) as well as aHUS with C3 mutation (1/0), familial hyperuricemia with hypertension (0/1) and nephrocalcinosis with mental retardation (1/0). Ten out of 16 pts from dialytic group received kidney transplant; 6 of them experienced severe complications (3 pts lost their graft and 1 died). Total mortality for this group of CKD caused by rare diseases was estimated to be as high as 23 % (5 children died).
Conclusions: The prevalence of rare congenital disorders and syndromes is surprisingly high in pediatric population with CKD and the outcome in this group seems to be worse than for other causes of CKD.

P311 - Validation of Jaffe creatinaemia in extreme low birth weight neonates: can we go for a pooled approach?

ANNE SMITS[1], RACHEL VIEUX[2], JEAN-MICHEL HASCOET[2], MARIE-CHRISTINE BUCHWEILLER[2], MAISSA RAYYAN[1], KAREL ALLEGAERT[1]
[1]*NEONATAL INTENSIVE CARE UNIT, UNIVERSITY HOSPITALS LEUVEN, LEUVEN, BELGIUM*
[2]*DEPARTMENT OF NEONATOLOGY, MATERNITE REGIONALE UNIVERSITAIRE, NANCY, FRANCE*

Introduction: Serum creatinine (Scr) is routinely used as biomarker in extreme low birth weight (ELBW) neonates to assess renal function. In this study, we aimed to cross-validate center specific Jaffe neonatal Scr datasets.
Material and methods: From 2 published Jaffe Scr datasets [(1) Vieux et al. Pediatrics 2010; (2) George et al. Pediatr Nephrol 2011], patients with the same clinical characteristics (i.e. birth weight <1000 grams and gestational age 27–31 weeks) were included. Scr at postnatal age (PNA) day 1,2,7,14,21 and 28 were compared using Mann Whitney U test.
Results: Data of 159 patients (73 in cohort 1; 86 in cohort 2) were collected. Both cohorts did not differ significantly in gender, birth weight, intra-uterine growth restriction and ibuprofen use. There was as significant difference in median oxygen therapy duration and postnatal steroid use. Median Scr values of cohorts 1 and 2 were respectively 100 μmol/L versus 68,95 μmol/L on day 1; 94 vs 88,4 on day 2; 71 vs 70,28 on day 7; 58 vs 62,76 on day 14; 53 vs 56,58 on day 21 and 49 vs 50,39 on day 28. Scr measurements on PNA day 1 ($p<0,0001$) and day 14 ($p=0,0038$) differed significantly between both groups. In cases with ibuprofen exposure (26 in cohort 1; 35 in cohort 2) median Scr values differed significantly on day 1, but not on days 2,7,14, 21 and 28.
Conclusions: Despite the use of the same (Jaffe) quantification technique, Scr measurements during the first day of life differed significantly between both cohorts of ELBW neonates, reflecting individual adaptation of renal function during the first 24 hours of life. Scr measurements after 24 hours, were comparable between both cohorts. This allows pooling for the development of Scr reference values based on age and weight within the total neonatal population.

P312 - Neonatal and long term evolution of children diagnosed with life threatening severe kidney malformation

FERNANDEZ CAMBLOR CARLOTA, NAVARRO TORRES MERCEDES, ESPINOSA ROMAN LAURA, PEñA CARRION ANTONIA
HOSPITAL INFANTIL "LA PAZ"

Introduction: Objective: Describe neonatal and long term evolution of patients ante-natally diagnosed with life threatening severe kidney malformation.
Material and methods: 16 patients (8♂ 8♀) diagnosed via intrauterine US between 1986 and 2008 with severe isolated renal malformations (12 structural malformations y 4 autosomal recessive polycystic kidney disease); half also had oligohydramnios. The parents chose not to terminate the pregnancies
Results: Intrauterine PUV ablation was performed in one case. Labour occurred at a gestational age of 32–41 weeks, half of the births were pre-term and half of the cases were caesarian deliveries. 1 ARPKD patient died due to pulmonary hypoplasia, renal insufficiency and hypertension 2 months after birth; 10/16 patients presented respiratory pathology in the neonatal period, 5 required mechanical ventilation for 15±19 days (3–50). 5/16 had hypertension and 7/16 acute renal insufficiency, conservatively treated in all cases. After a mean follow-up of 12.5±6 years (4–22 yrs), 7/15 patients continue to receive conservative treatment, with the following CKD distribution: Stage 1: 1, Stage 2: 1, Stage 3: 2, Stage 4: 3. Substitutive treatment has become necessary in 8 patients; mean age on initiating dialysis was 2±3.2 years (0.2-9.4 yrs) with kidney transplantation at a mean age of 3.6±3 years of age (1.8-10.33 yrs). The graft is functioning in all cases. Only one patient has a slight psychomotor developmental delay, one developed diabetes mellitus post-transplant and two have developed Perthes' disease.
Conclusions: Intrauterine diagnosis of renal malformation and/or oligoamnios is not correlated with the actual post-birth outcome. Mortality rate is 6 %, renal transplantation within 10 years of birth is 53 % and 47 % have only required conservative treatment. Ante-natally diagnosed severe renal malformation requires evaluation by an experienced, combined nephro-urological and neonatological team so as to offer the parents the best possible advice regarding the child's short and long-term prognosis.

P313 - Final height in children with chronic kidney disease (CKD) and liver transplant treated with growth hormone

FERNANDEZ CAMBLOR CARLOTA, NAVARRO TORRES MERCEDES, ESPINOSA ROMAN LAURA, PEñA CARRION ANTONIA
HOSPITAL INFANTIL "LA PAZ"

Introduction: Objetive: To study final height in in children with chronic kidney disease (CKD) and liver transplant treated with growth hormone.
Material and methods: Retrospective analysis of 16 patients (10♂, 6♀) with a liver transplant of 5.7±3.1 (0.9-10.5) years follow-up+CKD: Cr-EDTA estimated GFR 56±16 ml/min /1.73 m2 (30–78)+height≤−2 SD and /or growth rate<P25 for their age and gender. Age at initiating rhGH treatment 12.4±2.2 years (8.4-15.5). Prednisone dose: 0.2±0.19 mg/48 hours. rh-GH treatment duration: 3.7±3.2 years (1.5-9.1 yrs)
Results: Significant ($p<0.05$) increase in SD height from an initial −3.5±1.1 at initiating treatment to −2.9±1.2 after 1 year of treatment and −2.5±1.3 after 2 years of treatment,

with an increase in growth rate from an initial 4.3±2.2 cm/year to 8.3±2 after 1 year and 7.3±1.1 after 2 years of rhGH treatment (p<0,05). There were no significant changes in PTH levels or GFR in the first 2 years of treatment. There was a significant increase (p<0. 05) in IGF-1 level. No patient showed thyroid alteration, increase of Hb A1C, intracraneal hypertension, limp or hepatic rejection. There was no difference in the response to treatment by gender, age at initiatining treatment, GFR, rhGh doses or inicial SD height Mean adult height was 160±7.7 cm (149–174 cm) in males and 155±7.6 (146–163) in females, representing respective differences of −4.9±4,4 y −8±9.2 cm with their midparental height. Before treatment patients had −3.5±1.1 SD mean height reaching a final mean height of −1.8±1.3 SD

Conclusions: rhGh treatment is effective, regardless of age or GFR at initiating treatment. The response of treatment continues after the first year of treatment There was no evidence of hepatic rejection during treament and no significant change in GFR

P314 - Young women on dialysis are at relatively high risk of death from infections

JUDITH L. VOGELZANG[1], KARLIJN J. VAN STRALEN[2], JAAP W. GROOTHOFF[1], KITTY J. JAGER[2]
[1]*PAEDIATRIC NEPHROLOGY, EMMA CHILDREN'S HOSPITAL ACADEMIC MEDICAL CENTRE, AMSTERDAM, THE NETHERLANDS*
[2]*DEPARTMENT OF MEDICAL INFORMATICS, ERA-EDTA REGISTRY, ACADEMIC MEDICAL CENTRE, AMSTERDAM, THE NETHERLANDS*

Introduction: Few data exist on non-cardiovascular mortality in young patients on dialysis or with a kidney transplant. Previous research showed that young women on dialysis have lost their survival advantage compared to men. We therefore evaluated whether mortality from infections and malignancies was increased as compared to the general population in male and female RRT patients below 40 years of age.

Material and methods: The study cohort consisted of patients from the ERA-EDTA Registry who started dialysis or received a transplant between 1993–2004 (follow-up till Jan 1st 2009). Causes of death among the patients were compared to the general population. Age-specific mortality rates per 1000 person-years and mortality rate ratios were calculated. To identify those at highest risk of death among dialysis patients and transplant recipients we calculated hazard ratios.

Results: Men and women on dialysis <40 years had an over 500- and 300-fold increased risk of infectious mortality, respectively. Dialysis patients aged <19 years had a higher risk of infectious death than the general population aged >80 years. Female sex, and diabetes and multisystem disease as primary renal disease were associated with an increased risk of infectious mortality among those <40 years. The prevalence of multisystem disease was 2–3 times higher in women than in men <40 years. Women had a lower risk of death from malignancies than men. Cancer as cause of ESRD was associated with an increased risk of malignant mortality among those <40 years.

Conclusions: Patients <40 years on dialysis have a relatively high risk of infectious mortality. Dialysis patients <19 years even had a higher risk of infectious death than the general population aged >80 years. Female dialysis patients in the fertile age group, especially those with multisystem disease as primary renal disease, deserve special attention because of their relatively very high risk of infectious death.

P315 - FACTORS AFFECTING THE CARDIAC FUNCTIONS AND DETERIORATION OF RENAL FUNCTIONS IN CHILDREN WITH CHRONIC RENAL FAILURE

MUHLIKE GÜLER, NERMIN UNCU, BANU ACAR, F. ŞEMSA ÇAYCI, GÖKÇE GÜR, NILGÜN ÇAKAR
ANKARA CHILDREN'S HEMATOLOGY AND ONCOLOGY HOSPITAL

Introduction: Cardiac functions alter during the course of renal failure. To investigate the affects of hypertension, anemia and biochemical indices on LVMI and progression of renal failure in children with grade 2–4 renal failure.

Material and methods: Twentyone (13 male, 8 female) predialytic children were evaluated with instant and 24 hour ABPM along with LVMI and obtaining CBC and other biochemical factors by giving an interval of one year.

Results: Left ventricular hypertrophy (LVH) was detected in 16/21 children (76,1 %) at the start of the study. The LVMI were found 48,8±12,74 g/m2.7. Fifteen children were evaluated after one-year follow up and among those, LVH was detected in 11 with LVMI 42,83±9,66 g/m2.7 . Hypertension was detected in 5 patients (23,8 %) by instant measurements, although one patient (4,8 %) had normal measurements by ABPM. By ABPM, systolic hypertension was detected in 6(28,57 %) and diastolic hypertension in 8 children (38,09 %). At the beginning, a positive correlation between LVMI and cholesterol level and relative body mass index, and a negative correlation between LVMI and albumin was found. After one-year of follow up LVMI increased significantly, showing a negative correlation with GFR, albumin and hemoglobin levels. LVMI at the beginning showed a positive correlation between instant BP measurements and by ABPM night time significant diastolic BP levels and night time diastolic loading levels. After one-

year of follow up, change in LVMI values, did not show a correlation between instant BP measurements, but a correlation was found between LVMI changes and day time significant systolic BP and day time significant arterial BP levels and night time significant diastolic BP levels($p<0,05$)
Conclusions: Night time diastolic BP levels, night time diastolic loading and daytime systolic BP levels have been associated with changes in LVMI. Low levels of hematocrite, albumin and GFR and relative body mass index are associated with LVH.

P316 - EFFECTS OF WHOLE BLOOD VISCOELASTICITY ON CARDIAC FUNCTION AND CEREBRAL BLOOD FLOW IN THE CHILDREN WITH CHRONIC KIDNEY DISEASE

NECLA BUYAN[1], MELTEM AKCABOY[1], TAYFUN GOKTAS[2], SERDAR KULA[3], BIJEN NAZLIEL[4], NILGUN CAKAR[5], NERMIN UNCU[5], BULENT CELIK[6], AZIME SEVCAN BAKKALOGLU[1]
[1]*GAZI UNIVERSITY DEPARTMENT OF PEDIATRIC NEPHROLOGY*
[2]*GAZI UNIVERSITY DEPARTMENT OF PHYSIOLOGY*
[3]*GAZI UNIVERSITY DEPARTMENT OF PEDIATRIC CARDIOLOGY*
[4]*GAZI UNIVERSITY DEPARTMENT OF NEUROLOGY*
[5]*MINISRTY OF HEALTH ANKARA CHILDREN'S HOSPITAL*
[6]*GAZI UNIVERSITY FACULTY OF HEALTH SCIENCES*

Introduction: Changes of whole blood viscoelasticity (WBV) is associated with cardiovascular and cerebrovascular complications among the patients with chronic kidney disease (CKD). Aim of the study is to investigate the effects of WBV on cerebral and cardiovascular risks associated with CKD and to compare the impact of HD and PD treatments on WBV.
Material and methods: The study group consisted of 40 patients aged between 8–18 years (13.88±3.02 years) [20 patients with stage III-IV CKD (pre D), 10 on PD, 10 on HD] and 21 healthy control subjects (12.90 ±3.03 years). Fasting blood samples were obtained 24 hrs after the last session in HD patients and early in the morning before dialysis fluid instillation in PD patients. In addition to hematologic and biochemical variables, echocardiographic findings and middle cerebral artery blood flow velocity (MCABFV) were examined by transcranial doppler USG.
Results: WBV values of patients (pre D, PD and HD groups) were significantly lower than control group (4.23, 4.18, 3.86 spoise versus 6.08 spoise respectively, $p<0.05$). It seemed that statistically lower values of Htc, total protein, albumin ($p<0.05$) and higher values of ferritin ($p<0.05$) in all patient groups might result in low WBV levels. In patient groups, myocardial thickness, left ventricular mass index, mitral E and A values were found higher than those in controls ($p<0.05$). No statistically significant difference was present in MCABFV between patient and control groups. Also blood viscosity did not have any effect on MCABFV in studied patient subgroups and in controls.
Conclusions: Although there have been some data supporting the relationship between hyperviscosity and cerebrovascular as well as cardiovascular events in CKD patients, no correlations were found among those parameters in this study. We believe that successful anemia management and adequate dialysis treatment is crucial to achieve well-maintained cardiovascular and cerebrovascular functions in pediatric CKD patients.

P317 - The new ERA-EDTA coding system for coding causes of renal failure

FRANZ SCHAEFER[1], KITTY JAGER[2], CHRISTOPHER REID[3], KEITH SIMPSON[4]
[1]*DEPARTMENT OF PEDIATRIC NEPHROLOGY, UNIVERSITY HOSPITAL, HEIDELBERG, GERMANY*
[2]*ERA-EDTA REGISTRY, DEPT. OF MEDICAL INFORMATICS, AMC, UNIVERSITY OF AMSTERDAM, THE NETHERLANDS*
[3]*DEPARTMENT OF PAEDIATRIC NEPHROLOGY, EVELINA CHILDREN'S HOSPITAL, GUYS & ST THOMAS NHS FOUNDATION TRUST, LONDON, UNITED KINGDOM*
[4]*RENAL UNIT, GLASGOW ROYAL INFIRMARY, GLASGOW, UNITED KINGDOM*

Introduction: In the past decades in many studies the ERA-EDTA coding system for causes of renal failure has been used. However this coding system, which has been developed in the 1970's and only updated in the 1990's, is considered outdated as it does not reflect the substantial progress in genetic and pathophysiological understanding accomplished in recent years. Also, many rarer or specific paediatric kidney diseases were not specified in the old classification system.
Material and methods: Therefore in 2006 an initiative by the ERA-EDTA was started to develop a completely new coding system. Paediatric and adult nephrologists have worked together to define 274 unique codes for patients with kidney disease.
Results: These codes have now been finalized. It includes specific codes for hereditary kidney diseases such as Denys-Drash syndrome, Bardet-Biedl syndrome and Finnish type nephropathy, and improved specification for more common kidney diseases, e.g. distinguishing steroid-sensitive and steroid-resistant nephrotic syndrome. The classification system is not limited to disorders leading to end-stage renal

disease but provides a comprehensive catalogue of paediatric and adult kidney diseases. Another improvement of the new coding system is that it can be mapped to the ICD-10 codes and the SNOMED-ICT coding system. The diagnoses will also be mirrored in upcoming ICD-11 codes which are currently under development. To facilitate the use of the new PRD coding system a look-up tool has been developed, allowing easy searching for the new codes, including links to the OMIM website. This can be found at www.era-edta-reg.org. Furthermore, Excel forms and a PDF document including detailed information are available on this website.
Conclusions: Both ESPN and IPNA are endorsing the use of the new coding system. The ESPN/ERA-EDTA Registry as well as other pediatric renal databases are planning to implement the new coding system.

P318 - HIGHER PRECISION OF URINARY PROTEIN/CREATININE RATIO COMPARED WITH 24 HOURS PROTEIN EXCRETION IN KIDNEY DISEASES

GIANLUIGI ARDISSINO, FRANCESCA TEL, SARA TESTA, STEFANIA ROTONDO, LUCIANO SANGALETTI, PAOLO VERCELLONI, LUISA NAPOLITANO
CENTRO PER LA CURA E LO STUDIO DELLA SINDROME EMOLITICO-UREMICA, FONDAZIONE IRCCS CA' GRANDA OSPEDALE MAGGIORE POLICLINICO MILANO

Introduction: Proteinuria, an important biomarker in all nephropathies, is commonly measured as urinary protein excretion on 24-hour timed collection (PE24hrC) a time consuming, burdensome, often unreliable method. In the pediatric setting, the urinary protein-over-creatinine ratio (uPr/uCr) on spot samples is widely employed as surrogate marker of PE24hrC but, to the best of our knowledge, the reliability of uPr/uCr has only been compared with PE24hrC assuming the latter as a gold standard rather then analysing respective precision and accuracy. The present study compares the precision (degree to which repeated measurements under unchanged conditions show the same results) of the two methods of assessing proteinuria (PE24hrC vs uPr/uCr) in a selected group of patients with stable renal disease with the working hypothesis that the most precise method is the one with lowest coefficient of variation (CV).
Material and methods: Six patients with longstanding and well documented stable renal disease (hypodisplasia, FSGS and HUS in remission) were provided written instruction on how to perform 4 sets of urine sampling within a short period of time. Each set included a 24hrC and 4 urine samples collected any time during the day in different days across the urine collection (total of 120 determinations). The mean CV of proteinuria was calculated for the PE24hrC and for uPr/uCr as single sample as well as for the mean of 2, 3 and 4 samples assuming that, in patients with stable disease, the CV of proteinuria, with any method, should approach 0, by definition.
Results: The mean CV for PE24hrC was 33.9 while for uPr/uCr it was 32.2, 32.8, 27.3 and 23.9 % for 1, 2, 3 and 4 sampling, respectively.
Conclusions: The best method for assessing proteinuria in patients with kidney diseases, as to precision, is uPr/uCr and, even on a single sample it has a higher precision than PE24hrC. However the mean of 4 samples has the lowest CV and therefore the highest precision.

P319 - Organisation of a programme for therapeutic patient education for paediatric patients with chronic kidney diseases in a Paediatric Nephrology Unit - Toulouse France.

BANDIN FLAVIO, RUDZKY CHRISTELLE, BARBA NADINE, BROCHARD KARINE, GARNIER ARNAUD, DECRAMER STéPHANE
DEPARTMENT OF PAEDIATRIC NEPHROLOGY, HôPITAL DES ENFANTS, TOULOUSE, FRANCE

Introduction: The Paediatric Nephrology Unit of the Children's Hospital, Toulouse launched in 2006 a therapeutic patient education (TPE) programme for its chronic kidney diseases and organ transplant patients. In 2011 one hundred seventy-two patients were included (88 male, 84 female) with 151 patients in the age range from 6–20 and 21 patients were younger than six. Thirty three patients were kidney transplant patients. TPE was proposed by the reference paediatric nephrologists. All patients (the parents for children under 6) attended to a minimum of 3 h of individual TPE sessions per year.
Material and methods: The TPE programme was organised in 4 individual sessions (45 minutes/session) per year, given by a specifically trained, for-this-purpose, team of nurses and physicians. The first step in the TPE programme is a meeting between a nurse and the patient (parents) to collect information of how the patient understands about the disease, the treatment and the impact in the current life of patient and his family. This information is combined with the medical records to propose a TPE programme. In the follow-up sessions we evaluated systematically the knowledge acquired by the TPE programme, the therapeutic compliance (drugs and dietetics measures) and bio-clinical outcomes (laboratory findings, blood pressure, …). The patients' satisfaction was evaluated once a year.
Results: Results indicate a gain in knowledge mainly on important issues (better understanding of the treatment and

safety skills). The TPE programme improved compliance. Patient satisfaction towards the TPE programme was high.
Conclusions: The TPE programme for chronic kidney diseases and kidney transplant patients improves patient knowledge, compliance and management of disease.

P320 - Inappropriate left ventricular mass in children with chronic renal insufficiency

CHINALI MARCELLO[2], MATTEUCCI MARIA CHIARA[1], RINELLI GABRIELE[2], WUEHL ELKE[3], SCHAEFER FRANZ AND ESCAPE TRIAL NETWORK[3]
[1]*BAMBINO GESù CHILDREN'S HOSPITAL, IRCCS, ROME, ITALY, DEPARTMENT OF PEDIATRIC NEPHROLOGY AND UROLOGY,ROME ITALY*
[2]*BAMBINO GESù CHILDREN'S HOSPITAL, IRCCS, ROME, ITALY, DEPARTMENT OF PEDIATRIC CARDIOLOGY AND CARDIAC SURGERY,ROME ITALY*
[3]*UNIVERSITY OF HEIDELBERG, DIVISION OF PEDIATRIC NEPHROLOGY, CENTER FOR PEDIATRICS AND ADOLESCENT MEDICINE, HEIDELBERG GERMANY*

Introduction: We have previously shown in a small sample of CKD children (Raimondi F et al, Ped Nephrol), that left ventricular (LV) mass exceeding the amount needed to sustain cardiac workload (i.e. inappropriate LV mass, iLVM) is associated with abnormalities in cardiac function. In the present studies we analyze the prevalence inappropriate LV mass in a large population of children with predyalitic CKD enrolled in the ESCAPE trial.
Material and methods: Complete anthropometrics, biochemical profile and echocardiograms were obtained in 105 children with pre-dialysis CRI (mean age 13±4 yrs). LV dimensions and wall thicknesses were measured from the M-mode, LV volume and long-axis dimension from the 2D, blood pressure from 24-hour ambulatory recordings. Endocardial shortening, ejection fraction, LV mass index, relative wall thickness, circumferential wall stress, and excess of LV mass (as ratio of observed LV mass to value predicted from body size, gender, and cardiac workload) were analyzed.
Results: Prevalence of iLVM was significantly (14 %) in the population, although significantly lower than the prevalence of LV hypertrophy (31 %). Interestingly, a significant number of patients with iLVM did not show clear cut left ventricular hypertrophy, suggesting only a fair overlap between the two populations. Patients with iLVM showed more concentric LV geometry paired with significantly lower LV ejection fraction, lower midwall fractional shortening and lower stress-corrected midwall shortening as compared to patients without iLVM. Reduction in systolic performance remained significant also when excluding patients with clear cut LV hypertrophy.
Conclusions: In CRI children a significant percent of patients show values of LV mass higher than those needed to sustain individual cardiac load. This condition is partially independent from the presence of LV hypertrophy and is associated with reduced systolic performance.

P321 - NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN AS AN EARLY SIGN OF DIABETIC NEPHROPATHY

ZEYNEP YURUK YILDIRIM[1], AHMET NAYIR[1], ALEV YILMAZ[1], ASUMAN GEDIKBASI[2]
[1]*ISTANBUL UNIVERSITY ISTANBUL MEDICAL FACULTY PEDAITRIC NEPHROLOGY DEPARTMENT*
[2]*BAKIRKOY DR. SADI KONUK TRAINING AND RESEARCH HOSPITAL BIOCHEMISTRY DEPARTMENT*

Introduction: Noninvasive methods to diagnose diabetic nephropathy in the early stage are needed to prevent end-stage chronic kidney disease. The aim of our study is to determine whether urinary neutrophil gelatinase-associated lipocalin (uNGAL) can be considered as an early sign of diabetic nephropathy.
Material and methods: Seventy six patients with Type 1 diabetes mellitus (DM) (mean age: 12.43±3.87 years) and 35 healthy individuals (mean age: 11.14±3.77 years) were enrolled the study. Random urine samples were obtained to measure uNGAL and creatinine (Cr) values. Urine NGAL was measured by ELISA. Within the DM group, patients were divided into two subgroups according to presence of microalbuminuria and three subgroups according to the duration of diabetes (0–2 years, 2–5 years and over 5 years).
Results: Mean uNGAL level and uNGAL/creatinine (uNGAL/Cr) in diabetic patients were found to be higher than in the control group (uNGAL: 100.16±108.28 ng/ml vs 21.46±18.59 ng/ml, and uNGAL/Cr: 118.93-117.97 ng/mg vs 32.1±51.48 ng/mg; respectively) (p=0.0001). Using a cutoff of 36.3 ng/ml for uNGAL for diagnosis of diabetic nephropathy, sensitivity and specificity were 94.7 % and 94.3 % respectively. Using a cutoff of 34.88 ng/mg Cr for uNGAL/Cr for diagnosis of diabetic nephropathy, sensitivity and specificity were 81.5 % and 88.6 %, respectively. No significant differences were determined in uNGAL levels and uNGAL/Cr between the subgroups according to duration of diabetes, but uNGAL and uNGAL/Cr values were significantly higher in each group when compared to the control group. No significant differences in uNGAL levels and uNGAL/Cr were found between the subgroups according to glycemic control levels. Although there was no statistical difference in uNGAL values between two groups, it was higher in group with microalbuminuria. Additionally, positive correlation was found between urinary microalbumin and uNGAL (r=0.344 p=0.002).

Conclusions: Our results suggest that uNGAL and uNGAL/Cr values indicate kidney damage, while normal microalbumin levels do not exclude diabetic nephropathy in children.

P322 - ROLE OF IL-17 IN THE PATHOMECHANISM OF RENAL FIBROSIS

LEONóRA HIMER[1], BEáTA SZEBENI[1], ERNA SZIKSZ[1], DOMONKOS PAP[2], SHINOBU SAIJO[3], ÉVA KIS[2], ÁGNES PRóKAI[2], NóRA FANNI BáNKI[2], MAGDOLNA KARDOS[4], PéTER DEGRELL[5], ANDREA FEKETE[2], KRISZTINA RUSAI[2], TIVADAR TULASSAY[2], ÁDáM VANNAY[1]

[1]*RESEARCH LABORATORY OF PAEDIATRICS AND NEPHROLOGY, HUNGARIAN ACADEMY OF SCIENCES, BUDAPEST, HUNGARY*

[2]*FIRST DEPARTMENT OF PAEDIATRICS, SEMMELWEIS UNIVERSITY, BUDAPEST, HUNGARY*

[3]*CENTER FOR EXPERIMENTAL MEDICINE, INSTITUTE OF MEDICAL SCIENCE, UNIVERSITY OF TOKYO, JAPAN*

[4]*SECOND DEPARTMENT OF PATHOLOGY SEMMELWEIS UNIVERSITY, BUDAPEST, HUNGARY*

[5]*SECOND DEPARTMENT OF MEDICINE AND NEPHROLOGICAL CENTER, UNIVERSITY OF PéCS, HUNGARY*

Introduction: Chronic kidney disease (CKD) is a major public health problem worldwide. Regardless of the initiating cause, the mechanism of organ fibrosis is similar in the different CKDs and has an inflammatory component. Previously, epithelial-mesenchymal transition (EMT) – as the mechanism which is responsible for the generation of the majority of myofibroblasts – was thought to play an important role in renal fibrosis. However, in the last few years the in vivo existence of EMT was questioned. Here we investigated the in vivo presence of EMT and the possible role of interleukin (IL)-17 – the main cytokine secreted by Th17 cells – in this process.

Material and methods: We evaluated the renal level and localization of IL-17 and IL-17R in a mouse model of ureteral obstruction (UUO). For this purpose immunohistochemical staining and flow cytometry were used. The in vitro effects of IL-17 on the different signaling pathways were tested on HK-2 and renal proximal tubular epithelial cells (PTECs) by flow cytometry. The in vivo effects of IL-17 on PTECs were studied in ureter obstruated wild-type (WT) and IL-17 knockout (KO) animals by flow cytometry.

Results: The number of IL-17 producing T-cells and IL-17R positive epithelial cells elevated 5 days after UUO. After IL-17 treatment of HK-2 cells we found increased phosphorylation of Erk1/2, Jnk1/2, Smad2/3 signaling pathways and the mesenchymal transition of PTECs. After UUO we found increased phosphorylation of Smad2/3 and elevated amount of αSMA and vimentin in the PTECs of WT mice. The levels of these markers were less increased in the kidneys of IL-17KO mice.

Conclusions: Our results demonstrate the existence of in vivo EMT and the impact of IL-17 in this process. However, further experiments are needed to elucidate the importance of in vivo EMT in the mechanism of renal fibrosis.

P323 - Complications in children with chronic kidney disease

DUšAN PARIPOVIć[1], RADOVAN BOGDANOVIć[2], MIRJANA KOSTIć[1], EMILIJA GOLUBOVIć[3], BILJANA MILOšEVIć[4], ALEKSANDRA PARIPOVIć[2], IVANIšEVIć IVANA[1], AMIRA PECO-ANTIć[1]

[1]*UNIVERSITY CHILDREN'S HOSPITAL, BELGRADE, SERBIA*

[2]*INSTITE FOR MOTHER AND CHILD HEALTH, BELGRADE, SERBIA*

[3]*MEDICAL FACULTY OF UNIVERSITY OF NIS, NIS, SERBIA*

[4]*MEDICAL FACULTY OF UNIVERSITY OF NOVI SAD, NOVI SAD, SERBIA*

Introduction: The aim of the study was to analyze clinical characteristics and complications in pediatric patients with chronic kidney disease (CKD) in Serbia.

Material and methods: Data about pediatric patients with CKD (stages 2–5) for 2010. were retrospectively collected. Staging of CKD was performed according to KDOQI guidelines. Glomerular filtration rate (GFR) was estimated using Schwartz formula.

Results: 179 patients (61 % female) were included in the study. Median age was 12.3 years (interquartile range IQR 5.8-15.6). Congenital anomalies of kidney and urinary tract (CAKUT) were the leading causes of CKD (60 %), followed by hereditary nephropathies (17 %) and glomerular diseases (12 %). Median eGFR was 54 (IQR 31–70) ml/min/1.73 m2. Median height percentile was 22 (IQR 3–59). Short stature (defined as a height standard deviation score below −2) was present in 23 %. Growth hormone therapy was used in 20 %. Median weight percentile was 32 (IQR 6–64). Underweight (defined as a weight below 3rd percentile) was observed in 20 %. Prevalence of anemia was 23 %, proteinuria 63 %, and acidosis 25 %. Antihypertensive medications were prescribed to 70 %. 14 % reported a family history of CKD, 37 % hypertension, and 22 % diabetes mellitus.

Conclusions: CAKUT were the most frequent causes of CKD. CKD complications including short stature, malnutrition, hypertension, anemia, proteinuria, and acidosis were recognized as common among described group.

P324 - PREDICTIVE VALUE OF SERUM CYSTATIN C AND CYSTATIN C BASED GFR FORMULAS IN DEVELOPMENT OF REFLUX NEPHROPATHY

SEVGI YAVUZ, ALI ANARAT, AYSUN KARABAY BAYAZIT
CUKUROVA UNIVERSITY

Introduction: Reflux nephropathy (RN) is a deleterious complication of vesico-ureteral reflux (VUR). In this prospective study we investigated the predictive value of cystatin C in development of RN.
Material and methods: Ninethy-three (35 boys and 58 girls) children aged 3,5 to 17,5 years with primary VUR were enrolled into the study. Microalbuminuria (urinary microalbumin≥30 mg/g creatinine) was regarded as the major indicator of reflux nephropathy and patients were divided into two groups according to the presence of microalbuminuria (MA). Renal function tests, urine chemistry and Cystatin C levels were all analysed. Glomerular filtration rates (GFR) of the patients were calculated according to Schwartz, two Cystatin-C based formulas (Hoek and Larsson) and also creatinine clearence (Ccr).
Results: Serum cystatin C levels were statistically higher in MA(+) group (p=0,000). GFR values calcaluted according to four different formulas were significantly lower in MA(+) group (p=0,000). There was a positive correlation between Ccr, Schwartz and cystatine C based formulas (p=0,000).
Conclusions: Cystatine C might be a useful marker for predicting RN in VUR. Cystatine C based GFR formulas (Hoek and Larsson) might be a practical alternative for Schwartz and Ccr particularily in patients with abnormal body composition and who are not appropriate for 24-hours urine collection.

P325 - End-stage renal disease in Slovak children: Roma are at risk

GABRIEL KOLVEK, LUDMILA PODRACKA
SAFARIK UNIVERSITY

Introduction: Ethnic differences in the occurence of end-stage renal disease (ESRD) are reported on various populations across the world, but the evidence on Roma fully lacks. The aim of this study was to explore the relative risk (RR) of ESRD for Roma children who constitute a major minority in Slovakia.
Material and methods: Ethnicity was assessed in all children (aged 0–14; n=44) who underwent renal replacement therapy (RRT) in Slovakia during the years 2005–2009. Rates of ESRD among Roma and non-Roma based on RRT data were calculated as well as the RR of Roma for ESRD. The latter was repeated after standardization for differences in age of both populations.
Results: Roma represented 25,0 % (n=11) of all RRT patients. The RR of ESRD for Roma was 1.56, compared to the majority population. After age-standardization the RR for Roma was 1.72. Congenital anomalies (36.4 %) and hereditary nephritis (27.3 %) were the most common reasons of ESRD in Roma. Hereditary nephritis was significantly more common in Roma compared to the majority population (p=0.015).
Conclusions: This study shows that the risk for ESRD is significantly higher for Roma than for non-Roma. A genetic propensity of Roma to renal failure might partially explain the higher risk. Moreover, consanguinity and low birth weight, which are significantly more common in Roma, may add to this higher risk too.

P326 - USE OF METHOXY POLYETHYLENE GLYCOL-EPOETIN BETA IN TREATMENT OF ANAEMIA IN CHRONIC KIDNEY DISEASE PATIENTS– A CASE CONTROL STUDY

ANGELA LAMB, SHEETAL BHOJANI, LEAH KRISCHOCK, IAN RAMAGE
ROYAL HOSPITAL FOR SICK CHILDREN, GLASGOW

Introduction: The optimal haemoglobin (Hb) level for chronic kidney disease (CKD) patients in not known. NKF-KDOQI guidelines define anaemia as an Hb level below the 5th percentile for age and gender in children with CKD. In 2011 UK NICE Anaemia Management in CKD guidelines suggested an optimal Hb of 100 to 120 g/L in children>2 years of age and Hb of 95 to 115 g/L<2 years of age. Impaired erythropoietin synthesis by the diseased kidneys is a major factor in the anaemia of CKD. Erythropoiesis-Stimulating Agents (ESA) is used for anaemia in CKD. Methoxy polyethylene glycol-epoetin beta (MPG-EPO), a continuous erythropoetin receptor activator, has a longer half life and is less painful subcutaneous injection.
Material and methods: We prospectively looked at 13 patients who were treated with MPG-EPO (cases) and compared them to 14 patients who were treated with non MPG-EPO ESA (controls) over a period of 7 months. Their clinical and demographic details were obtained from the case notes.
Results: We followed up 13 cases on MPG-EPO and 14 controls on non MPG-EPO ESA for a period of 7 months. The mean age was 10.5 years for cases and 8.4 years for controls. The sex ratio was comparable in the 2 groups. Among the cases, there were 2 patients on peritoneal dialysis (PD), 6 post renal transplant and 5 conservatively treated CKD patients (CONS). In the control group, 4 patients on PD, 3 on haemodialysis and 7 CONS. After 7 months of treatment, the rise in

Hb was comparable in the 2 groups. No side effects of MPG-EPO were observed.
Conclusions: Patients on MPG-EPO have a rise in Hb similar to the standard non MPG-EPO ESA. The MPG-EPO patients received less number of injections therefore improving the patient compliance and the overall treatment cost. There were no side effects observed.

P327 - A reliability assessment of the new Schwartz formula (2009) in children with GFR>60 ml/min/1.73 m2

ZACHWIEJA KATARZYNA[1], KOROHODA PRZEMYSŁAW[3], KWINTA-RYBICKA JOANNA[1], MIKLASZEWSKA MONIKA[1], MOCZULSKA ANNA[1], BUGAJSKA JOLANTA[2], BERSKA JOANNA[2], DROżDż DOROTA[1], PIETRZYK JACEK A.[1]
[1]*PEDIATRIC NEPHROLOGY DEPARTMENT UJMC*
[2]*DEPARTMENT OF LIPID BIOCHEMISTRY UJMC*
[3]*ELECTRONIC DEPARTMENT UNIVERSITY OF SCIENCE AND TECHNOLOGY, KRAKOW*

Introduction: The aim of the study was to assess the reliability of formulae used to calculate eGFR in a group of children with GFR above 60 ml/min/1.73 m2.Those analyzed included 3-marker formula by Schwartz et al. (GFR3M); the simplified formula by Schwartz et al. (GFRKR); and our formula based on serum cystatine C (GFRC), all compared to iohexol plasma disappearance method (GFRIOH).
Material and methods: The study group consisted of 265 children (age range 2–18; mean 12.1),with correct hydration. We present average eGFR values in ml/min/1.73 m2 accordingl to formulas, mean differences and squared correlation coefficient (R2) for all patients.
Results: Mean Values±SD: GFR3M=90,5±17 GFRKR= 84,8±20,1 ; GFRC=109,5±20,1; GFRIOH=111,9±26,2 Mean difference: GFRIOH -GFR3M: 21,5±19,1; GFR IOH - GFR KR: 27,2±21,6; GFR IOH- GFR C: 2,62± 23,3 R2 (GFR IOH vs. GFR 3 m): 0,5 (p=0,000); GFR IOH vs GFR KR:0,38 (p=0,000); GFR IOH vs GFR C:0,36 (p=0,000). The patients were divided into two groups: a) those with a significant underestimation between the GFR result for GFRKR in relation to GFRIOH (with GFRIOH/GFRKR ratio >1.5: N=65 children, mean GFRIOH - GFRKR: 53.4±15.7) and b) those with good agreement in GFR results (GFRIOH/GFRKR between 0.67 and 1.5; mean GFRIOH-GFRKR:18.7±15.5). The patient groups did not differ statistically in terms of age, body mass and height. A significant tendency for greater discrepancy in GFR estimation according to GFRKR and GFRIOH, and GFR3M and GFRIOH, was observed at higher GFR values. The best agreement with the referential GFRIOH method was exhibited by our cystatine C formula, independent of body mass, height and age.
Conclusions: 1. The Schwartz et al. formula can significantly underestimate real GFR in children with GFR>60 ml/min/1.73 m2>2 yrs, especially at high GFR values. 2. Our own GFR estimation formula using cystatine C is the most precise formula for assessing eGFR in children>2 yrs.

P328 - Overhydration and arterial blood pressure in children on renal replacement therapy.

TATIANA PANKRATENKO[1], KHADIZHA EMIROVA[2], DMITRIY ZVEREV[2], TATIANA ABASEEVA[1]
[1]*MOSCOW REGIONAL SCIENTIFIC-RESEARCH CLINICAL INSTITUTE NAMED AFTER M.F. VLADIMIRSKII*
[2]*ST VLADIMIR PEDIATRIC CLINICAL HOSPITAL*

Introduction: Arterial hypertension is a common complication in children on renal replacement therapy (RRT). It may be caused by fluid overloud. A multifrequency bioimpedance tool (body composition monitor, BCM)allows to measure overhydration quantitatively and to assess its' influens on arterial blood pressure (ABP).
Material and methods: With the aim to evaluate the hydration status and its' influence on ABP in children on RRT, repeated monthly body composition monitoring with contemporary assessment of the systolic and diastolic ABP (SABP, DABP) was performed in 33 children with ESRD aged 4–17 years, 11 (5 males) on hemodialysis (HD), 22 (13 males) on peritoneal dialysis (PD) in the single dialysis center. PD patients were measured with full abdomen. HD patients were measured before the midweek session. Mild overhydration was defined as the excess of 7-15 %, severe overhydration – as the excess of>15 % of the extracellular fluid. ABP >95 centile for the age and sex regarded as elevated.
Results: At the first investigation, the prevalence of the mild overhydration was 27,2 % in HD and 36,4 % in PD patients (p=NS), the severe overhydration was found in 45,5 % HD and 40,9 % PD patients(p=NS). The prevalence of the elevated SABP was 0 % in the euvolemic (n=7), 40 % in both mildly and severely overhydrated children (n=25, p= 0,04). There were positive correlations of the overhydration and SABP (r=0,41, p=0,016), the overhydration and DABP (r=0,47, p=0,006). During the observation period of 1–24 (median 7) months, the overhydration reduced in 19 previously overhydrated patients from 21,3±8,9 % to 7,6±7,8 % (p=0,000). In these patients, the SABP decreased from 132±25 mm Hg to 120±25 mmHg (p=0,006), the DABP from 82±15 mm Hg to 69±19 mm Hg (p=0,007).
Conclusions: Overhydration is highly prevalent in children on RRT, and is associated with elevated ABP. Reduction of the overhydration may contribute to normalization of the ABP in these patients.

P329 - Encapsulating Peritoneal Sclerosis in paediatric PD patients – a survey from the European Paediatric Dialysis Working Group

RUKSHANA SHROFF[1], CONSTANTINOS STEFANIDIS[7], CLAUS PETER SCHMITT[1], SEVCAN BAKKALOGLU[4], MICHEL FISCHBACH[8], ALBERTO EDIFONTI[6], ALEKSANDRA ZUROWSKA[9], GUNTER KLAUS[5], GEMA ARICETA[11], KAREL VONDRAK[10], TUULA HOLTTA[1], ALAN WATSON[2]

[1]*GREAT ORMOND STREET HOSPITAL FOR CHILDREN*
[2]*NOTTINGHAM CHILDREN'S HOSPITAL*
[3]*CENTER FOR PEDIATRIC AND ADOLESCENT MEDICINE, HEIDELBERG*
[4]*GAZI UNIVERSITY HOSPITAL, ANKARA*
[5]*KFH PEDIATRIC KIDNEY CENTER, MARBURG*
[6]*CLINICA PEDIATRICA DE MARCHI, FONDAZIONE IRCCS POLICLINICO, MANGIAGALLI E REGINA ELENA, MILAN*
[7]*A & P KYRIAKOU, CHILDREN'S HOSPITAL, ATHENS*
[8]*HOPITAL DE HAUTEPIERRE, STRASBOUR*
[9]*GDANSK UNIVERSITY MEDICAL SCHOOL, POLAND*
[10]*UNIVERSITY HOSPITAL MOTOL PRAGUE*
[11]*HOSPITAL CRUCES, BARAKALDO, VIZCAYA*
[12]*UNIVERSITY OF HELSINKI*

Introduction: Encapsulating Peritoneal Sclerosis (EPS) is a rare but serious complication of peritoneal dialysis (PD) that is associated with significant morbidity and mortality in adults. There are only anecdotal reports in the children.

Material and methods: We performed a 10-year survey across 13 paediatric nephrology centres to determine the prevalence, potential risk factors and outcomes for EPS in children.

Results: 23 cases of EPS were reported giving a prevalence of 1 per 100 patient-years on PD. Full data are available for 19 patients who are described below. The median age at start of PD was 2.4 (0.01–19) years. The median time on PD was longer than for the remainder of the population (6.1 [1.6–10.1] vs 1.8 [0.1–77] years; $p<0.0001$). EPS was diagnosed while the child was on PD in 14 cases, one month after conversion to HD in 2, and 5 years after transplantation in 2 others. 17/18 children presented with ultrafiltration failure; all were high transporters. 14 had signs of bowel obstruction (3 complete obstruction), 6 had intra-abdominal masses, 3 bowel perforation and 7 ascites or hemoperitoneum. Abdominal ultrasound (n=7) or CT (n=9) showed bowel obstruction, abnormal peristalsis, matted bowel loops with tethering to the posterior abdominal wall, peritoneal thickening or calcification and ascites. A peritoneal biopsy was obtained in 7 children that confirmed peritoneal fibrosis, hyalinosis and calcification in all. Enterolysis was performed in 10 children, 3 requiring complete enterolysis. 13 children received immunosuppression (prednisolone in all, sirolimus and mycofenolate mofetil in 1 each), and 6 received tamoxifen. 8 required parenteral nutrition. At final follow-up 4.6 (1.1–8.2) years after EPS diagnosis, 2 patients have died, 10 have a functioning transplant and 6 are on hemodialysis (including 3 on home hemodialysis).

Conclusions: EPS is a rare but severe complication of PD in children that is potentially treatable. A prolonged time on PD is a significant risk factor.

P330 - A comparison of arteriovenous fistulas and central lines for long-term chronic haemodialysis

ALISON LT MA, RUKSHANA SHROFF, LESLEY REES
DEPARTMENT OF PAEDIATRIC NEPHROLOGY, GREAT ORMOND STREET HOSPITAL FOR CHILDREN

Introduction: Despite the fistula first initiative there is still reluctance to use arteriovenous fistulas (AVF) for children on haemodialysis (HD). Our aim was to compare outcomes of AVFs in comparison to central venous lines (CVL) in children on chronic HD in a centre where AVF is the primary choice for vascular access.

Material and methods: We retrospectively reviewed the case notes of children haemodialyzed for at least 12 months between Jan 2007 and Dec 2010 at Great Ormond Street Hospital for Children. Data collection began after creation of AVF or insertion of CVL, and the patients were grouped accordingly.

Results: Twenty patients (M:F=9:11, median age 13.2 (3–12.4) years) were dialyzed with an AVF and five (M:F=2:3, age 2.4(2.0-5.3) years) with a CVL for a median of 19.7 (16.7-25.0) and 18.5 (15.1-23.6) months respectively. The age at start of HD was 10.6 (2.0-16.3) years. Access failure within the first month was 1 per 78.8 patient months for AVF (n=5) and 1 per 15.5 patient months for CVLs (n=6, p=0.3). Failure thereafter was 1 per 131.3 patient months and 1 per 18.5 patient months for AVF and CVLs respectively (n=3 and 5 respectively; p=0.2). The annualized hospitalization rate for patients with AVFs and CVLs was 0.44 % and 3.1 % respectively in hospital due to access malfunction (p=0.004). Patients with AVFs had a lower infection rate of 0.25 per 100 patient months; CVL at 3.2 per 100 patient months (p=0.002). There was no difference in dialysis efficiency or laboratory values between AVF and CVL groups.

Conclusions: Patients with AVF spend less time in hospital than those dialyzed using CVLs and have a much lower access infection rate. Multi-centre registry data on large cohorts of children on chronic HD patients are required to better understand the outcomes from AVF use.

P331 - Determinants of exercise capacity in pediatric patients on chronic hemodialysis

FABIO PAGLIALONGA[1], AMALIA LOPOPOLO[1], VIVIANA SCARFIA[3], ANNA BRIVIO[2], ALBERTO EDEFONTI[1]

[1]*PEDIATRIC NEPHROLOGY AND DIALYSIS UNIT, FONDAZIONE IRCCS CA' GRANDA OSPEDALE MAGGIORE POLICLINICO, MILAN, ITALY*

[2]*DEPARTMENT OF PAEDIATRICS, CYSTIC FIBROSIS CENTER OF MILAN, FONDAZIONE IRCCS CA' GRANDA OSPEDALE MAGGIORE POLICLINICO, MILAN, ITALY*

[3]*NEPHROLOGY AND PERITONEAL DIALYSIS UNIT, AOU POLICLINICO VITTORIO EMANUELE, CATANIA, ITALY*

Introduction: Pediatric patients on chronic hemodialysis (HD) are at high risk of inactivity and low exercise capacity. Aim of the study was to assess the main determinants of the functional exercise capacity in a cohort of children and young adults on chronic HD.

Material and methods: Twelve patients on chronic HD, median age 15.6 years (range 9.1-26.2), underwent spirometry, 6-minute walking test (WT), chair sit-to-stand test and lower extremity strength measurement. Demographic data, anthropometry (dry weight, height, BMI, all expressed as standard deviation scores), biochemistry (serum albumin, hemoglobin, creatinine, C-reactive protein, bicarbonate), HD adequacy (spKt/V and eKt/V), left ventricular mass index and medications were also recorded.

Results: A significant correlation was found among the distance covered during the WT (median 552 m, range 186–670), the forced vital capacity (87.8 % of predicted, range 49.7-136), the forced expiratory volume in 1 second (86.7 %, range 54.7-126.7) and the peak expiratory flow (75.5 %, 49.7-105.1). All these indices were positively correlated with weight SDS (r2 from 0.48 to 0.72), serum albumin (0.35-0.59) and creatinine (0.35-0.59), and negatively correlated with weekly erythropoietin dose per kg body weight (0.44-0.70), with p values from <0.05 to <0.0001. Lower extremity strength (median 11.5 kg, range 3–15) was positively correlated with the number of stands in 1 min at the chair sit-to-stand test (median 33, range 18–47; r2 0.53, $p<0.05$) and with serum albumin (r2 0.69, $p<0.01$).

Conclusions: Since decreased body weight, serum albumin and serum creatinine and increased resistance to erythropoietin can suggest a state of protein energy wasting (PEW), our data indicate PEW as the major cause of low exercise capacity in children and young adults on chronic HD.

P332 - Chyloperitoneum associated with Peritonitis and Calcium channel blockade in an infant

TAMARA MALLETT, KARL MC KEEVER, CIARA CULLIGAN

PAEDIATRIC NEPHROLOGY UNIT, ROYAL BELFAST HOSPITAL FOR SICK CHILDREN, BELFAST, NORTHERN IRELAND

Introduction: We report the spontaneous development of chyloperitoneum associated with bacterial peritonitis and calcium channel blockade in an infant with Prune Belly Syndrome on Continuous Cycling Peritoneal Dialysis (CCPD).

Material and methods: A 7-month-old boy with Stage 5 chronic kidney disease and Prune Belly syndrome on CCPD developed chyloperitoneum in the setting of bacterial peritonitis. He presented with failure of peritoneal drainage and dialysate leucocytosis in the absence of systemic upset. Dialysate cultured Staphylococcal epidermidis. After 48 hours antimicrobial therapy the dialysate fluid became 'milky' with raised triglyceride levels indicative of chyloperitoneum. Our patient had been on Amlodipine therapy for hypertension from the age of two months. Chyloperitoneum has been described in adults.

Results: Conservative treatment with a low-fat diet supplemented with medium–chain triglycerides resulted in resolution of the chyloperitoneum within 48 hours. Two attempts to reintroduce regular feeds, after three weeks and six weeks of dietary modification respectively, was associated with rising dialysate triglyceride levels. Partial dietary modification was continued. Dialysate triglyceride levels remained elevated, however dialysate remained clear. Further episodes of Staphylococcal epidermidis peritonitis resulted in the removal of the peritoneal dialysis catheter and conversion to haemodialysis.

Conclusions: Chyloperitoneum is a rare but important complication of peritoneal dialysis which needs to be considered in children on peritoneal dialysis presenting with suspected peritonitis. Chronic chyle loss during dialysis can result in recurrent infections and malnutrition. We have reported an association between chyloperitoneum, calcium channel blockade and peritoneal dialysis catheter loss secondary to recurrent bacterial peritonitis. Calcium channel blocker induced chyloperitoneum has been described in adults, but we believe this is the first such case report in an infant. Further work should focus on the utility of dialysate triglyceride level monitoring in this population, particularly where calcium channel blockers are used.

P333 - Online hemodiafiltration in children and hypoparathyroidism: how much HDF can be too much?

THOMAS PEROUSE DE MONTCLOS, JUSTINE BACCHETTA, ANNE LAURE LECLERC, PIERRE COCHAT, BRUNO RANCHIN

HOSPICES CIVILS DE LYON AND UNIVERSITé DE LYON

Introduction: Hemodialysis was dramatically improved by the onset of hemodiafiltration (HDF) in the mid 1980's in adults. However, due to its specific technical requirements,

it is not widely used in pediatric centers. We have been using online HDF in our centre since 2009 and we have recently observed some unusually low parathyroid hormone (PTH) levels despite the accurate management of CKD-associated mineral and bone disorders (CKD-MBD) following the international guidelines.

Material and methods: We retrospectively reviewed the medical charts of the six children (median age 14.0 years, 2 boys) undergoing chronic online HDF in our centre on November 1st, 2011; we also prospectively investigated the main parameters of phosphate/calcium metabolism on a before/after session basis.

Results: We observed low PTH levels (below 80 pg/mL) in all our patients and very low levels (below 45 pg/mL) in five, two of them presenting with pathological fractures. This trend was reversed when calcium concentrations in the dialysate were decreased from 1.5 to 1.25 mmol/L. Moreover, baseline C-terminal FGF23 levels were relatively low, all being below 1600 RU/mL, and were cleared by online HDF (32 %).

Conclusions: Physicians using online HDF in pediatric populations should be aware of the risk of hypoparathyroidism and therefore closely follow-up PTH levels as well as use low-calcium dialysates in children. Given the negative impact of high FGF23 levels on global outcomes, one may hypothesize that online HDF could be associated with better outcomes in pediatric CKD, but this hypothesis deserves to be prospectively studied in the future.

P334 - Could Mini-PET and/or Double Mini-PET be used to instead of 4 hour PET to assess peritoneal permeability in children on peritoneal dialysis?

FUNDA BASTUG, ISMAIL DURSUN, JALE DURSUN, DEMET GUNAY, SIBEL YEL, RUHAN DUSUNSEL, ZUBEYDE GUNDUZ, ZUHAL TAŞCI, KENAN YILMAZ, HAKAN POYRAZOGLU, SIBEL BOLAT

ERCIYES UNIVERSITY, FACULTY OF MEDICINE, DEPARTMENT OF PEDIATRIC NEPHROLOGY

Introduction: The peritoneal equilibration test (PET) is the gold standard method for defining peritoneal membrane permeability and for prescribing peritoneal dialysis (PD) therapy on an individual basis. However, it is laborious, consumes nursing time, and requires many hours to be performed. Therefore, several authors have attempted to validate short and fast PET protocols, with controversial results. The aim of this study was to evaluate the concordance between the Mini-PET, Double Mini-PET and 4-h (classical) PET.

Material and methods: we performed a classical peritoneal equilibration test (4 hours), a Mini-PET with 3.86 % glucose PD fluid (1 hour) and Double Mini-PET, consisting of two Mini-PET, was performed consecutively (2 hour) compared UF and small solute transports obtained with the three methods.

Results: Twenty six children, 14 males, mean age 11.4± 5.6 (range 2.5-19 years), were included. Meantime on PD at time of enrollment was 35.2±24.5 months (range 6–84 months). Based on the 4-h creatinine D/P data, the number of the patients within each transport category was as follow: high, 5; average, 18; low, 3. Kappa test showed a significant concordance between standard 2.27 % PET and mini PET (0.610, p=0.000) and also moderate agreement between standard 2.27 % PET and double mini PET (1st hour)(0.403, p=0.007). Based on the 4-h glucose D/D0 data, the number of the patients within each transport category was as follow: high, 5; average, 17; low, 4. Kappa test showed a moderate agreement between standard 2.27 % PET and mini PET (0.514, p=0.000).When Pearson correlation analysis between standard 2.27 % PET, double mini PET and mini PET was performed, there were significant positive correlations between standard 2.27 % PET and mini PET, and double mini PET(1st h) and (2nd h) (r= 0.720, p=0.000, r=0.638, p=0.000, r=0.493, p=0.02, respectively). When comparing the numeric results of mini PET, double mini PET and 4 h of PET for D/PCreatinin, by simple regression analysis, we found statistically significant correlation among PETs.. Bland–Altman plots showed a high level of the agreement between the PET techniques

Conclusions: This study showed concordance between the Mini-PET, Double Mini-PET and 4-h (classical) PET. The 3.86 % mini-peritoneal equilibration test is a simple and fast method to assess free water transport. It also gives information about total UF and small solute transports and it is in good agreement with the classical peritoneal equilibration test.

P335 - Two cases of Joubert Syndrome with End Stage Renal Failure

DILEK YILMAZ[1], FERAH SÖNMEZ[1], MELIKE GÜZÜNLER[2], SEBAHATTIN ÇIRAK[3], SARAH FROST[4], INGA VATER[4], GAMZE CÖMERTPAY[5], MARISOL HEISE[5], YORCK HELLENBROICH[4], GÖKHAN UYANIK[5]

[1]*DIVISION OF PEDIATRIC NEPROLOGY, DEPARTMENT OF PEDIATRICS, ADNAN MENDERES UNIVERSITY, AYDIN, TURKEY*

[2]*DEPARTMENT OF PEDIATRICS, GEDIZ HOSPITAL, MANISA, TURKEY*

[3]*UCL INSTITUTE OF CHILD HEALTH, GREAT ORMOND STREET HOSPITAL, LONDON, UK*

[4]INSTITUTE OF HUMAN GENETICS, UNIVERSITY HOSPITAL OF SCHLESWIG-HOLSTEIN, CAMPUS LÜBECK / UNIVERSITY OF LÜBECK, GERMANY
[5]INSTITUTE OF HUMAN GENETICS, UNIVERSITY MEDICAL CENTER HAMBURG-EPPENDORF, GERMANY

Introduction: Joubert syndrome (JS) is a rare autosomal resesive devolopmental disorder of the central nervous system, characterised by brainstem and cerebellar malformations, hypotonia, ataxia, abnormal eye movements, irregular breathing pattern, mental retardation and "molar tooth sign" on magnetic resonance imaging. Sixteen causative genes have been recognized. Every single one encoding for proteins of the primary cilium or the centrosome, making Joubert Sydrome Related Disease (JSRD) part of expanding group of diseases called "ciliopathies". Renal disease and renal failure are reported in %2-20 of cases with JS. Defined renal abnormalities are cystic dysplasia and nephronophthisis.
Material and methods: In this study two cases of JS leading to end stage renal disease at ages 5.5 years and 15 months were reported.
Results: To our knowledge they are probably the youngest cases of JS with end stage chronic renal failure. In the case with nephronophthisis CEP 290 c.5668 G>T (p.G1890X) stop mutation (JBTS5) and in the case with infantile nephronophthisis INPP5E c.1303 C>G (p.R435G) homosigot (JBTS1) mutation were observed.
Conclusions: Children with Joubert Syndrome who present predominantly with mental and motor retardation, should be also followed for renal disease.

P336 - NOCARDIA ASTEROIDES PERITONEAL DIALYSIS-RELATED PERITONITIS; FIRST CASE IN PEDIATRICS TREATED WITH PROTRACTED LINIZOLID.

MOHAMED EL NAGGARI[1], IBTISAM EL NOUR[1], ZAKARIA AL MUHARRMI[2], ANAS AL WOGOUD ABDELMOGHETH[1]
[1]SULTAN QABOOS UNIVERSITY HOSPITAL; CHILD HEALTH DEPARTEMENT
[2]SULTAN QABOOS UNIVERSITY; MICROBIOLOGY DEPARTEMENT

Introduction: Peritonitis is a common problem in patients undergoing continuous ambulatory peritoneal dialysis (CAPD) and represents the most frequent cause of peritoneal catheter loss and discontinuation of dialysis. Common bacteria, particularly staphylococcal species, are the usual causative agents. Fungi and higher bacteria such as Nocardia asteroides as etiological agents have been infrequent in patients undergoing CAPD. Nocardia can enter the peritoneal cavity through the Tenckhoff catheter. The predisposing factors, treatment protocol, and whether to treat with or without catheter in situ are unanswered questions in Nocardia peritonitis.
Material and methods: Our case is 13 years old female diagnosed as diffuse global sclerosis with end stage renal failure on CAPD since 3 years. she suffers from familial leukodystrophy with cerebellar ataxia and pyramidal features. She presented with history of high grade fever leaking from the exit site of the peritoneal catheter, abdominal pain and non bloody diarrhea. On admission, patient started imprically on intraperitoneal (IP) Vancomycin, Ciprofloxacin and intravenous (IV) cloxacillin. Initial peritoneal fluid examination was turbid appearance with white sidement and high white blood cell count. Exit site showed no inflammation but marked leaking. Blood investigation showed leucocytosis with high C-Reactive protein. Amphotricin-B was added after 4 days to cover for suspected fungal peritonitis. As there is no clinical improvement; cipro replaced by IP Ceftazidime, IV cloxacilin stopped, IV Meropenem and Amikacin added. Peritoneal culture Nocardia after 12 days of incubation. Child went into cardiac arrest and septic shock. Catheter was removed. Child was managed in PICU with Continuous Veno-Venous Haemofiltration, ventilation and Inotropic support. Case was complicated with peritoneal abscess that was evacuated by ultrasound guided aspiration. Jeujonal adhesions with some feeding intolerance was treated conservatively.
Results: Linizolid was given IV for 3 months in hospital then orally for 5 months after discharge with close monitoring of side effects. Patient discharged on haemodialysis.
Conclusions: Nocardia generally present as infection unresponsive to empirical treatment and initially an apparent ‘culture-negative’ peritonitis. Diagnosis and management can be problematic due to the slow growth and difficult identification of Nocardia species. The optimal duration of treatment for Nocardia peritonitis is not known. Linizolid can be used for prolonged period in trimethoprim-sulphamethoxazole resistant cases with close monitoring of side effect.

P337 - NEW MARKERS OF ATHEROSCLEROSIS IN CHILDREN WITH END STAGE KIDNEY DISEASE

IRENA MAKULSKA, MARIA SZCZEPAńSKA, DOROTA DROżDż, DANUTA ZWOLIńSKA
1PEDIATRIC NEPHROLOGY, WROCłAW MEDICAL UNIVERSITY

Introduction: Chronic kidney disease (CKD) is characterized by a state of generalized vasculopathy caused mainly by atherosclerosis. It has recently been established that in addition to classical mechanisms, new biochemical markers of endothelial inflammation and dysfunction play a role.

The aim of the study was to assess the biochemical markers of endothelial inflammation/dysfunction: sE-selectin, MMP-9, TIMP-1, ADMA, SDMA, PAI-1 and intima-media thickness (IMT) of the carotid artery in 3 groups children.

Material and methods: 20 children (12 boys, 8 girls) mean age 14,3±2,3 years on PD (peritoneal dialysis), 20 children (10 boys, 10 girls) mean age 15,0±3,3 on HD (hemodialysis) were included in the study and compared to 26 healthy age-matched subjects. Concentrations of serum sE-selectin, MMP-9, TIMP-1, ADMA, SDMA, PAI-1, iPTH, creatinine, Ca, P, total cholesterol, HDL, LDL, CRP were measured. Intima-media thickness (IMT) of the carotid artery was assessed in all children

Results: cIMT, sE-selectin, MMP-9, TIMP-1, ADMA, SDMA, PAI-1 values were significantly higher in dialysed patients vs control group. A significant positive correlation was observed between cIMT and age, sE-selectin, ADMA, SDMA, PAI-1 and negative with MMP-9 and TIMP-1.

Conclusions: In dialysed children we can observed increased inflammation and endothelial destruction what may be caused by examined markers. The positive correlations between all endothelial markers and cIMT confirm this observation.

P338 - Haemodialysis in Infants

CATHERINE QUINLAN, MARIE BATES, AISHLING SHEILS, NIAMH DOLAN, MICHAEL RIORDAN, ATIF AWAN

THE CHILDREN'S UNIVERSITY HOSPITAL, TEMPLE STREET, DUBLIN 1, IRELAND

Introduction: Haemodialysis (HD) in infants is usually used when peritoneal dialysis (PD) has failed. The limited published data reflects its limited usage. We sought to describe our experience with haemodialysis (HD) for infants weighing less than 10 kg managed with HD for more than 6 months, outlining the morbidity, complications and outcomes for infants weighing less than 10 kg managed with HD for more than 6 months.

Material and methods: All patients weighing less than 10 kg at who were managed with HD for more than 6 months from May 2001 to 2011 were identified from the hospital database. A retrospective review of the clinical notes was conducted to collect demographic information, anthropometric data, dietary history, site and form of vascular access, details of HD prescription, complications and outcomes.

Results: Over the 10-year period 9 patients weighing less than 10 kg were haemodialysed for more than 6 months. Median age at commencement of HD was 9 months (range 4 – 19 months). Median weight SDS at commencement of HD was −2.14 (range −3.81 – -0.71) and at the end of HD was −1.56 (range −3.25 – -0.68). Median height SDS at commencement of HD was −0.61 (range −4.09 – +1.63) and at the end of HD was −1.32 (−3.15 – -0.59). Median energy intake was 96.6 kcal/kg/day and protein intake was 1.66 g/kg/day. Median number of line revisions was 0.32 line changes/patient year. Median CVC longevity was 13 months (range 2 days – 53 months). Mean rate of line infection was 0.14/patient year (range 0 – 0.63). No CVCs were removed due to infection. Median time on HD was 27 months (range 3 – 51 months). Median age at transplantation was 3.4 years.

Conclusions: Our cohort demonstrates that chronic HD, whilst not the treatment modality of choice, is a viable management option in children <10 kg where PD is not possible as a bridge to transplantation. Access issues are paramount and can be minimised with good line care. Based on these results, we conclude that the initiation of long term HD in babies weighing less than 10 kg is a safe option and we provide encouraging statistics to support the use of HD in this cohort of infants in End Stage Renal Failure.

P339 - MSC treatment decreased peritoneal fibrosis in a rat model

SEBAHAT TÜLPAR[1], FUNDA BAŞTUĞ[1], İSMAIL DURSUN[1], ESRA BALCIOĞLU[2], ZÜBEYDE GÜNDÜZ[1], SAIM ÖZDAMAR[2], SIBEL YEL[1], YASEMIN A. TORUN[3], ARZU YAY[2], RUHAN DÜŞÜNSEL[1], M. HAKAN POYRAZOĞLU[1]

[1]*DEPARTMENT OF PEDIATRIC NEPHROLOGY, ERCIYES UNIVERSITY FACULTY OF MEDICINE, KAYSERI, TURKEY*

[2]*DEPARTMENT OF HISTOLOGY AND EMBRYOLOGY, ERCIYES UNIVERSITY FACULTY OF MEDICINE, KAYSERI, TURKEY*

[3]*KAYSERI EDUCATION AND RESEARCH HOSPITAL, KAYSERI, TURKEY*

Introduction: The purpose of this study was to determine the effect of mesenchymal stem cells (MSC) transplantation on the peritoneal fibrosis and function of peritoneal membrane in rat models of sclerosing peritonitis.

Material and methods: Wistar albino female rats divided into four groups: Control (C) (n=7), chlorhexidine gluconate (CG) (n=8), MSC (n=8) and placebo (P) (n=8) groups. All rats, except for C group, were given 2 ml/200gr 0.1 % CG and 15 % ethanol dissolved in saline daily by intraperitoneal (ip) injection during four weeks. After 4 weeks, MSC group was treated with 1.5-2 million MSC per kg per rat and P group was treated with an equal volume of saline solution via ip injection. The C and CG groups were evaluated at the end of fourth week, MSC and P groups were evaluated at the end of fifth week. Peritoneal equilibrium

test was performed to all animals. The parietal peritoneum was evaluated histologically by light microscopy.
Results: D/Purea, D/Pprotein and D/PNa in the CG, MSC and P groups were significantly higher than the C group. The permeability of this solutes in the MSC group was similar to those of the CG and P groups. There was no difference between groups in terms of DD0glucose and D/Pcr. Fibrosis of the MSC group was low compared with CG group (p=0.04).No significant differences were found between the P and CG group according to fibrosis (p=0.8).
Conclusions: MSC treatment decreased peritoneal fibrosis in our rat sclerosing peritonitis model. MSC transplantation did not lead to improvement in peritoneal membrane function. Failure in peritoneal functional improvement possibly was due to there was not enough time for adequate peritoneal healing.

P340 - PATIENT AGE DETERMINES PERITONEAL DIALYSIS EVOLUTION. A SPANISH PERITONEAL DIALYSIS PEDIATRIC GROUP STUDY

ÁNGEL ALONSO, ANA SáNCHEZ, GEMA ARICETA, JESúS LUCAS, DOLORES MORALES, RAFAEL MULEY, JUAN ANTONIO CAMACHO, FERNANDO SANTOS
SPANISH PERITONEAL DIALYSIS PEDIATRIC GROUP STUDY

Introduction: Peritoneal dialysis (PD) is the initial renal substitution therapy for 30 % of end stage renal disease Spanish children and of 85 % of under three-year-olds. Excellent mid-term patient and technique survival (96.5 and 70 % respectively) makes this an ideal treatment while awaiting transplantation. Based on the greater frequency in infants we asked whether age when beginning treatment influences patient evolution
Material and methods: Children beginning PD between the years 2003 and 2010 were divided in two groups to study characteristics and evolution; Group A: 62 infants aged 1.4±0.8 years and Group B: 146 children aged 10.6± 4.4 years. Both groups were similar in so far as percentage of initially anuric patients, initial and final urine output, and blood albumin levels
Results: Duration of PD was longer in infants than in older children (17 vs. 9 months, respectively). Technique failure was more frequent in older children (40 %) than in infants (20 %), usually due to inadequate ultrafiltration while the greatest cause of failure in infants was infection or catheter problems. Infants compared to older children had a higher percentage of enteral feeding by nasogastric tube (38 vs. 3 %) or by gastrostomy (22 vs. 7 %); incidence of peritonitis (1.14 vs. 0.4 episodes/patient); number of catheter replacements and parathormone levels (374 vs. 175 pg/ml). In addition, infants, unlike older children, gained weight (delta Z score +0.94 vs. – 0.01) and height (delta Z score 0.01 vs. -0.11). Paradoxically, infants show a greater Kt/V (2.98 vs. 2.74 in older children), which was associated with decreased hypertonic glucose consumption (17 % vs. 23 %), less decrease in residual renal function and lower prevalence of hypertension (32 % vs. 67 %).
Conclusions: Age at initiating PD treatment influences technique complications and outcome. Infants have excellent survival and, despite their higher incidence of infection, show a lower risk of technique failure

P341 - PERITONEAL DIALYSIS IN CHILDREN UNDER TWO YEARS OF AGE

BORA GÜLHAN, ALI DÜZOVA, FATIH ÖZALTIN, REZAN TOPALOĞLU, SEZA ÖZEN, YELDA BILGINER, ASLI ÇELEBI TAYFUR, ÇIĞDEM YILDIZ, NESRIN BEŞBAŞ
HACETTEPE UNIVERSITY FACULTY OF MEDICINE PEDIATRIC NEPHROLOGY & RHEUMATOLOGY

Introduction: End stage renal disease (ESRD) is a devastating cause of morbidity and mortality in infants. Although peritoneal dialysis (PD) is an important treatment modality, PD experience in this age group is still limited.
Material and methods: We retrospectively analyzed medical records of all children with ESRD under two years of age who were on chronic PD treatment in our center. Peritoneal dialysis was instituted by surgical placement of swan-neck or straight catheter.
Results: Between years 1997–2012, 80 PD patients were followed. Twelve infants (4 male, 8 female) were on chronic PD treatment. Most common ESRD etiology was congenital anomalies of the kidney and urinary tract. Mean age of PD onset was 8.2 months (range 13 days-22 months) and mean dialysis duration of the patients was 28.2 months (range 2.5-73.5). In two patients, PD was initiated in newborn period and in five patients PD was initiated between 1–12 months of age. Most of the patients use biocompatible PD fluids. Seven patients suffered from 10 peritonitis episodes giving an incidence of 1 episode/33.9 patient-months. Most common microorganism was Pseudomonas aeruginosa and and 40 % of peritonitis episodes was culture-negative. Two patients suffered from exit site infection and tunnel infection, respectively. Inguinal, umbilical or abdominal hernia were observed in four patients. Mean urea Kt/V at 6 months of PD was 2.19±1.21 and at last follow-up 2.34±0.48. Mean urea Kt/V of anuric and non-anuric patients were not statistically significant. The mean erythropoietin and calcitriol dose were 130.9±71.7 IU/kg/week and 0.32±0.14 mcg/kg/day, respectively. Three patients died in first 6 months and one patient died after one year after PD.

Conclusions: Peritoneal dialysis is a preferable and safe method of renal replacement modality in this age group of children.

P342 - Implantation of permanent catheter for hemodialysis in child with serious chest deformation due to meylomeningocele – case report

PIOTR MACIEJASZ[1], MARIA DZIERZEGA[2], MONIKA MIKLASZEWSKA[3], KATARZYNA ZACHWIEJA[3], DARIUSZ CHMIEL[2], DOROTA DROZDZ[3], JACEK A PIETRZYK[4]

[1]*INTENSIVE CARE DEPARTMENT OF CHILDREN'S UNIVERSITY HOSPITAL IN KRAKOW*

[2]*THE PEDIATRIC EMERGENCY MEDICINE DEPARTMENT OF JAGIELLONIAN UNIVERSITY COLLEGIUM MEDICUM*

[3]*PEDIATRIC NEPHROLOGY AND DIALYSIS DEPARTMENT JAGIELLONIAN UNIVERSITY COLLEGIUM MEDICUM, CRACOW*

[4]*PEDIATRIC NEPHROLOGY AND DIALYSIS DEPARTMENT JAGIELLONIAN UNIVERSITY COLLEGIUM MEDICUM, CRACOW*

Introduction: In children with myelomeningocoele (MMC) there is a great risk of development of end-stage kidney disease due to the neurogenic bladder and chronic reflux nephropathy. When the patients are dialysis dependent the vascular or peritoneal access insertion is necessary.

Material and methods: The presentation of the technically complicated implatation of the permanent HD catheter in 11 years old girl with lumbo-sacral MMC with ventriculoperitoneal shunt on the left. The child has the end stage renal failure due to neurogenic bladder and chronic reflux nephropathy (the both sides vesicoureteral refluxes of V grades were found). The girl was qualified for the insertion of permanent catheter for HD. Because of the coexisting hydrocephalus and the large chest deformation, the operation procedure of insertion of dialysis access was supposed to be difficult and challenging. The risk of chronic subsequent respiratory insufficiency after the muscular laxation and tracheal intubation was estimated to be more than 60 % . Due to severe chest malformation, small abdomen with small peritoneal cavity volume and the body weight of 12 kg the creation of arterio-venous HD fistula and peritoneal dialysis were contraindicated. The operation method: The operation field was prepared with lidocain, the child was entered into general anesthesia with midazolam, nitrogen monoxide and fentanyl without intubation. The Trendelenburg position was done, the head was turned backward and left (it was very difficult to obtain such position due to chest deformation), by Seldinger method the catheter was successfully inserted to the right jugular vein and placed into right atrium using ultrasound and fluroscopic guidance.

Results: The catheter is now used for performing HD sessions.

Conclusions: The insertion of permanent catheter into right jugular vein is possible in children with a seriously body deformation using the combination of modified local and general anesthesia. The adequate nephrologist-surgeon and anesthesiologist cooperation is extremely important.

P343 - Intradialytic cycling: preliminary results in a pediatric population

FABIO PAGLIALONGA[1], AMALIA LOPOPOLO[1], VIVIANA SCARFIA[3], ANNA BRIVIO[2], ALBERTO EDEFONTI[1]

[1]*PEDIATRIC NEPHROLOGY AND DIALYSIS UNIT, FONDAZIONE IRCCS CA' GRANDA OSPEDALE MAGGIORE POLICLINICO, MILAN, ITALY*

[2]*DEPARTMENT OF PAEDIATRICS, CYSTIC FIBROSIS CENTER OF MILAN, FONDAZIONE IRCCS CA' GRANDA OSPEDALE MAGGIORE POLICLINICO, MILAN, ITALY*

[3]*NEPHROLOGY AND PERITONEAL DIALYSIS UNIT, AOU POLICLINICO VITTORIO EMANUELE, CATANIA, ITALY*

Introduction: Intradialytic exercise has been well investigated in adults on chronic hemodialysis (HD), but very scarce data exist in the pediatric population. Aim of the study was to assess the feasibility, acceptability, safety and efficacy of intradialytic exercise in children and young adults on HD.

Material and methods: The program consisted of 30 minute-sessions of intra-HD cycling by means of a cycloergometer, 2 to 3 times per week for 3 months. The following parameters were assessed at the beginning and at the end of the study period: distance at the six-minute walking test (WT), indices of respiratory function (FVC, FEV1, PEF, MEMF), number of stands in 1 minute at the chair sit-to-stand test, lower extremity strength (LES), anthropometry (weight, weight gain/month, height, height velocity, BMI), skinfold thickness (MAMC AMA, AFA), daily energy and protein intake, dialysis adequacy (spKt/V. eKt/V), incidence of symptomatic sessions, biochemistry (hemoglobin, albumin, creatinine, BUN, bicarbonate, calcium, phosphate, C-reactive protein, PTH) and left ventricular mass index.

Results: Preliminary data are available for 6 patients, median age 14.5 years (range 9.1-26.3). One of them underwent kidney transplantation during the study period. All the remaining 5 patients completed the protocol and showed a good acceptance of the program. No adverse events occurred; the incidence of symptomatic sessions was lower, although not significantly, during the study period than in the 3 months preceding the study (10 % vs 30 %). All the

patients showed a significant improvement in the WT (median change +25 m, range 10–45, $p<0.05$), chair test (+5 stands, 2–10, $p<0.05$) and LES (+3.5 kg, 0.3-7, $p<0.05$). Among the other parameters, only preHD serum albumin and postHD serum creatinine did improve (+ 0.4 g/dl and +0.3 mg/dl, respectively).

Conclusions: In conclusion, a program of 30 minute-intradialytic cycling is feasible, well-accepted and safe in pediatric patients on chronic HD, and lead to a significant improvement of exercise capacity.

P344 - Single-needle hemodialysis combined with plasma exchange in a child with difficult vascular access

ANTONIETTA BIASUZZI, FABIO PAGLIALONGA, GIANLUIGI ARDISSINO, SARA TESTA, ALBERTO EDEFONTI

PEDIATRIC NEPHROLOGY AND DIALYSIS UNIT, FONDAZIONE IRCCS CA' GRANDA OSPEDALE MAGGIORE POLICLINICO, MILAN, ITALY

Introduction: The procedure of single-needle plasma exchange (PEX) has never been described in the literature

Material and methods: We report on a 9 year old child treated with PEX combined with single-needle hemodialysis (HD). The child, a 18 kg female, was treated with peritoneal dialysis since the age of 6 months because of ESRD secondary to factor H deficient hemolytic uremic syndrome (HUS), and shifted to HD at 7 years due to ultrafiltration failure. An arterovenous fistula was prepared, which allowed for the placement of a single needle; due to central venous thrombosis secondary to repeated catheterization in the first years of life, no other access suitable for the extracorporeal circuit could be obtained. Because of the hyperimmunization status secondary to previous HUS-related blood transfusions and a failed renal transplant, a desensitization program with PEX, immunoglobulins and rituzimab was planned. The single-needle HD circuit was connected with the standard PEX circuit. Gambro AK 200 Ultra machine was used for HD and Baxter BM 25 device for PEX. HD was performed by a 0.6 sqm polyamide membrane, while Gambro PF2000N (0.3 sqm) was used as plasmafilter. The HD circuit was connected first and the ultrafiltration started. When cardiocirculatory parameters were stabilized, PEX arterial and venous line were connected at the HD venous port and venous expansion chamber respectively and PEX started. HD and PEX Qb were 100 and 60 ml/min respectively. No supplemental heparin was added to the circuit, compared to the usual HD dose.

Results: Two sessions were performed in two consecutive days. Ultrafiltration was 1250 ml in the first session and 600 ml in the 2nd one; spKt/V and eKt/V were 1.98 and 1.71 respectively. No significant adverse effects were observed.

Conclusions: In conclusion, single-needle HD can be safely performed in association with standard PEX in children with difficult venous access.

P345 - USE OF TESIO CATHETERS IN INFANTS AND CHILDREN RECEIVING CHRONIC HEMODIALYSIS

ANTONINO MUSUMECI[1], FRANCESCA NUZZI[2], UGO GRAZIANO[3], SALVATORE FERRAIUOLO[3], GIOVANNI SEVERINO[3], MARIA TERESA SARAVO[2], CARMINE PECORARO[2]

[1]*DEPARTMENT OF CARDIOLOGY, UNIVERSITY FEDERICO II, NAPLES, ITALY*

[2]*DEPARTMENT OF NEHROUROLOGY, CHILDREN'S HOSPITAL SANTOBONO, NAPLES, ITALY*

[3]*DEPARTMENT OF SURGERY, CHILDREN'S HOSPITAL SANTOBONO, NAPLES, ITALY*

Introduction: Tesio Catheters (TC) were first used in adults as a dual-catheter system with two independent single-lumen catheters into the right internal jugular vein. TC have been associated with improved Qb compared with other catheter types and recirculation rates less than 5 %. The recent availability of pediatric-sized TC has further expanded the hemodialysis catheter options available for children. We report the experience with TC survival rates, complications and effect on dialyisis adequacy in a series of children on HD of a single pediatric hemodialysis center

Material and methods: From january 2003 to December 2011, 49 children underwent chronic hemodialysis for ESRD: 25 (16 boys) of them (50 %) received TC as central vascular access; mean age 2.8 years; range 0.5-11.9 years. Primary renal diseases that caused ESRD were: Renal HypoDysplasia (11), Focal Segmental Glomerulo Sclerosis (6), Diffuse Mesangial Sclerosis (3), Oto-Branchio-Renal Syndrome (1), Wolff-Hirschon Syndrome (1), Middle Aortic Syndrome (1), Atypical Haemolitic Uremic Syndrome (1), Oxalosis (1). In infants there was inability to perform peritoneal dialysis. Indications for central venous catheter use in these patients included: low body size (weight range: 3 to 19 Kg) (n=17); main neurological complications (n=4); need for daily hemodialysis (n=1); periferal venous vessel exhaustion (n=3).TC were inserted with ultrasound guidance into the right internal jugular vein on general anesthesia by vascular surgeon in our institution.

Results: Four patients received a single TC-10,5 F, in them hemodialysis was performed with a double alternate blood pump; in the remaining 21 patients twin single lumen TC 6.5 F and 10 F, in 19 and in 2 patients respectively, were inserted. Only in one case a mild right pleural effusion developed as complication. Until now 31 interventions in 25 children have been performed: 6 patients needed of removal with replacement of TC because of a) increase of

body height with relative shortness of TC (n=3); failure because of thrombosis (n=2); dialysis inadequacy (n=1). Our procedure for the management of TC includes disinfection of the exit site weekly, oral warfarin and in situ urokinase and heparine to maintain lumen patency, without side effects. 3 episodes of TC and one tunnel and/or exit site sepsis occurred over 25 months mean follow up (range: 3–87 months). Monthly single poolKt/V was>1.5 in all patients indicating adequate dialysis. Due to lack of pain related to venipuncture and the confidence in one's movements, patient and parents compliance was very good.

Conclusions: Use of TC in children on chronic HD is very limited, our excellent experience also in children weighing less than 10 Kg is unique. We conclude that TC are a reliable, effective in term of dialysis adequacy and low infection long term vascular access in infants too.

P346 - Vitamin D Status in Children Undergoing Haemodialysis in Ireland

CHIA WEI TEOH, AISHLING SHEILS, NIAMH DOLAN, MICHAEL RIORDAN, MARY WALDRON, ATIF AWAN
THE NATIONAL CENTER FOR PAEDIATRIC NEPHRO-UROLOGY AND TRANSPLANTATION, THE CHILDREN'S UNIVERSITY HOSPITAL, TEMPLE STREET, DUBLIN 1, IRELAND

Introduction: Patients with end-stage renal disease undergoing haemodialysis are at risk of hypovitaminosis D, contributing to the development of secondary hyperparathyroidism. The extent of vitamin D deficiency in children undergoing haemodialysis is poorly studied. There is no data on vitamin D status of children undergoing haemodialysis in Ireland. We assessed vitamin D status of children undergoing haemodialysis in our tertiary nephrology unit. We intend to use this data in future studies to assess efficacy of vitamin D supplementation in this population.

Material and methods: Eight boys and two girls (9 Caucasians, 1 South Asian) undergoing haemodialysis at our center had serum 25(OH)-Vitamin D, PTH, alkaline phosphatase, calcium and phosphate levels measured in March 2012. Serum 25(OH)-Vitamin D levels were measured by automated chemi-luminescence immunoassay (Roche/Elecsys). Serum 25(OH)-Vitamin D levels of <12.5 nmol/L were defined as severe deficiency; 12.6-37.4 nmol/L as mild deficiency; 37.5-75 nmol/L as insufficiency (KDOQI Clinical Practice Guidelines for Bone Metabolism and Disease in Children with Chronic Kidney Disease).

Results: Mean age of our patients was 8.91 years (age range 6 months to 17 years). Of the ten patients, seven (70 %) were deficient/insufficient in 25(OH)-vitamin D (two severely deficient, two mildly deficient, three insufficient) while three (30 %) had adequate 25(OH)-Vitamin D levels. Nine patients were on alfacalcidol. Eight patients were on fortified feeds including vitamin D3. PTH levels range from 3–1055 ng/L (median 125 ng/L). Mean serum calcium, phosphate and alkaline phosphatase levels were 2.455 ±0.145 mmol/L, 1.434 ±0.53 mmol/L and 316 ±232.9 U/L respectively. We found no correlation between 25(OH)-vitamin D levels, serum calcium, phosphate, alkaline phosphatase and PTH levels.

Conclusions: In our haemodialysis population, 70 % were vitamin D deficient/insufficient, 29 % of whom were severely deficient. We have started cholecalciferol supplementation and await data of separate analysis of 25(OH)-vitamin D2 and 25(OH)-vitamin D3 which we will present later.

P347 - The performance of acute peritoneal dialysis treatment in neonatal period

CANER ALPARSLAN, ONDER YAVASCAN, ALKAN BAL, ENGIN KOSE, ALI KANIK, NEJAT AKSU
TEPECIK TRAINING AND RESEARCH HOSPITAL, PEDIATRIC NEPHROLOGY, IZMIR, TURKEY

Introduction: The aim of this retrospective study was to evaluate our neonatal intensive care unit (NICU) patients characteristics treated with acute peritoneal dialysis (PD) and their risk factors for mortality. We also wanted to share our experience of the application of PD in neonates who required less than 60 ml of dwell volume and their PD-related problems as well as special solutions for these problems.

Material and methods: This study included 27 infants treated in our NICU between February 2008 and December 2011. We retrospectively analysed of these patients' records. The percutaneous PD catheter was placed by us. Peritoneal dialysis procedure was made either by manual technique or automated PD. Statistical evaluation was made by using chi-square and student's t-tests.

Results: In these 27 neonates, the average gestational age and birth weight were 35.18±4.02 weeks and 2534.62 ±897.41 grams (g), respectively. The mean PD duration time was 6.11±6.30 days. Of these, 10 patients were treated by manual technique [mean birth weight: 1584±528.60 g (min: 1000 g., max:2500 g.)] whereas 17 patients treated with automated system [mean birth wieght: 3093.82±504.45 g (min: 2100 g., max: 3800 g.)]. Among 27 neonates, 16 patients died. Metabolic disease and prematurity were the most frequent causes of death (in 9 patients). Eight out of 14 premature neonates and 8 out of 13 mature neonates died. Overall mortality rate was 59.25 %. Eleven patients survived. Peritoneal dialysis related complications were seen in 7 patients (peritonitis in 3 patients, obstruction in 3 patients and leakage in 1 patient).

Conclusions: In conclusion, currently performed conventional peritoneal dialysis technique is less effective and troublesome for low-birth weight infants. These centers should create their solutions to accommodate problematic patients in PD treatment to improve outcome in this special population.

P348 - Arteriovenous fistula as vascular access for hemodialysis in children (36 years' experience in the academic hospital of Tours)

AURELIE DAVOURIE-SALANDRE[1], SYLVIE CLOAREC[1], ANNE LETOUZE[2], LUC TURMEL-RODRIGUES[3], STEPHANE BENOIT[1], ELODIE MERIEAU[1], HUBERT NIVET[1]
[1]*PEDIATRIC NEPHROLOGY, CHRU TOURS, FRANCE*
[2]*PEDIATRIC SURGERY, CHRU TOURS, FRANCE*
[3]*CARDIO-VASCULAR RADIOLOGY, ST GATIEN HOSPITAL, TOURS, FRANCE*

Introduction: The autogenous arteriovenous fistula (AVF) appeared to be the first choice of vascular access for haemodialysis in children.
Material and methods: This retrospective study was carried out over a 36 year period (1975–2011) in the pediatric nephrology unit of Tours, France. The aim of this study was to describe the changes in AVF creation, indications, techniques and in the management of side-effects over time.
Results: Ninety-six patients were included with a sex ratio of two. The mean age at AVF creation was 9.6 years. There was an interval of at least one month between AVF creation and the first cannulation. One hundred-twenty-seven AVFs were created, which results in an average of 1.4 AVF per patient. The number of AVFs per child decreased over time. More intervention was necessary to obtain a functional AVF in little children. 10 had to be superficialized before use (7,8 %), 10 never functioned (7,8 %), 5 were never used due to a successful peritoneal dialysis or because of preemptive transplantation. The radial-cephalic AVF was preferentially performed. One hundred-thirty-five complications occurred during follow up. The management of the majority of complications were performed by required interventional radiology from 2002. Stenosis (68,5 %) was the most frequent complication in our population and was cured by dilation in 50.8 % of the cases. Very few infections were observed and they disappeared with the abandonment of the prostheses after 1994. Twenty-three were ligated including 19 after successful renal transplantation. Four children (19 %) developed left ventricular hypertrophy after AVF creation.
Conclusions: AVF is the first choice vascular access for children undertaking chronic hemodialysis in view of the low rate of severe complications. AVF can be done in small children as well. Interventional radiology is essential and effective for the treatment of complications.

P349 - IS INFLAMMATION IN CHILDREN AND YOUNG ADULTS ON CHRONIC HEMODIALYSIS REALLY PREVALENT?

FABIO PAGLIALONGA[1], AMEDEA SILVIA TIRELLI[2], MASSIMO CONESE[3], ALBERTO EDEFONTI[1]
[1]*PEDIATRIC NEPHROLOGY AND DIALYSIS UNIT, FONDAZIONE IRCCS CA' GRANDA OSPEDALE MAGGIORE POLICLINICO, MILAN, ITALY*
[2]*LABORATORY OF CLINICAL PATHOLOGY, FONDAZIONE IRCCS CA' GRANDA OSPEDALE MAGGIORE POLICLINICO, MILAN, ITALY*
[3]*DEPARTMENT OF BIOMEDICAL SCIENCES, UNIVERSITY OF FOGGIA, FOGGIA, ITALY*

Introduction: Only a few studies have investigated the inflammatory state in pediatric patients on chronic hemodialysis (HD). Aim of this study was to assess the prevalence of inflammation in children and young adults undergoing chronic HD, by means of a microchip array technology.
Material and methods: Twelve cytokines and growth factors (IL2, IL4, IL6, IL8, IL10, VEGF, IFNγ, TNFα, IL1α, IL1β, MCP1, EGF) were assessed in 22 patients on HD, median age 15.1 years (range 2.5-28.4), at the beginning and at the end of a standard mid-week dialysis session, and in 76 age-matched controls, median 19.7 years (0.7-29.4). The following parameters were also assessed: preHD C-reactive protein, white cell count, creatinine, BUN, hemoglobin, bicarbonate, parathyroid hormone, postHD creatinine, albumin and BUN, and spKT/V and eKt/V.
Results: Patients on HD had higher IL6 values than controls, 2.3 (0.8-13.7) vs 1.1 pg/ml (0.01-22), and lower levels of IL4, IL8, IFNγ and EGF. Five patients (22.7 %) had IL6 values higher than the 95° centile of controls (3.9 pg/ml). No correlation between IL6 and the above-mentioned laboratory parameters was found. Dialysis caused a significant increase of IL8, IL10 and IFNγ. Limiting the analysis to the 15 patients and 25 controls younger than 18 years, we found that HD children had higher levels of IL6 (median 2.5 vs 1.0 pg/ml) and TNFα (5.4 vs 2.7 pg/ml) than controls, and lower levels of IL2, IL8, IL1β and EGF. Values of IL-6 and TNFα higher than 95° centile were observed in 20 % and 40 % of HD patients respectively.
Conclusions: In conclusion, based on a comprehensive panel of growth factors and cytokines, high values of IL6 and TNFα, and the increased cytokine levels due to the dialysis procedure "per se", suggest the presence of chronic inflammation in children and young adults on chronic HD. The clinical significance of this data requires further investigation.

P350 - Body composition monitoring derived urea distribution volume allows for correct estimation of Kt/V in children on hemodialysis

ARIANE ZALOSZYC[1], MICHEL FISCHBACH[1], BETTI SCHAEFER[2], RéMI SALOMON[3], PATRICK NIAUDET[3], CLAUS PETER SCHMITT[2]
[1]*NEPHROLOGY DIALYSIS TRANSPLANTATION CHILDREN'S UNIT, UNIVERSITY HOSPITAL HAUTEPIERRE, STRASBOURG, FRANCE*
[2]*CENTER FOR PEDIATRIC AND ADOLESCENT MEDICINE, UNIVERSITY OF HEIDELBERG, GERMANY*
[3]*PEDIATRIC NEPHROLOGY, HôPITAL NECKER-ENFANTS MALADES, PARIS, FRANCE*

Introduction: Urea kinetic modeling (Kt/V) is used for dialysis dose assessment. Modern hemodialysis measure ionic dialysance online to continuously monitor the achieved Kt/V. The latter depends on the correct input of the volume of total body water, i.e. the urea distribution volume (V). V can be assessed by anthropometric equations, and by body composition monitoring (BCM®), which yielded excellent accordance with gold-standard dilution methods in adults.
Material and methods: We now compared the V determined by BCM to the V obtained from the modified equation of Mellits-Cheek, and from the Watson, Hume-Weyers and Morgenstern formula in 24 pediatric hemodialysis patients from three pediatric hemodialysis centers. Mean age was 15.8(2.4-26.1) years. 512 BCM measurements were performed. Moreover, we compared Kt/V derived from on-line clearance measurements using V values assessed by BCM and by the Kt/V calculated from pre- and post-dialytic urea of 65 hemodialysis sessions using the single pool second generation Daugirdas equation.
Results: Mellits-Cheek and Hume-Weyers formula significantly overestimated V by BCM by a mean of 11(−3-35) and 11(−11-42)% (both $p<0.001$), independent of age. Watson formula overestimated V by 31(2–148)% ($p<0.001$), with an overestimation rate of 115(96–148)% in children below 5 and 19(4–56)% in patients above 16 years of age (both $p<0.001$). In contrast, V calculated by the Morgenstern equation was similar to V by BCM throughout the entire age range, with a mean difference of 0.8(−14-17)% (p=n.s.). Online Kt/V determination based on V by BCM were similar and highly correlated with the Daugirdas Kt/V ($r=0.74$; $p<0.001$).
Conclusions: V measured by BCM is highly correlated with V calculated by the Morgenstern equation, the only equation validated in children on dialysis, but not with other anthropometric equations. BCM derived V allows for correct online determination of Kt/V in children on hemodialysis.

P351 - chyloperitoneum in an infant on chronic peritoneal dialysis

JUSTINE LANNEAU, IULIA STOICA, ELENA TUDORACHE, AURéLIEN GALERNE, TIM ULINSKI, BILAL AOUN
PEDIATRIC NEPHROLOGY UNIT, TROUSSEAU HOSPITAL, APHP, PARIS

Introduction: Chyloperitoneum is a rare complication in children on chronic peritoneal dialysis. It can be secondary to traumatic insertion of dialysis catheter. Diagnosis is made by detecting elevated triglyceride levels in the dialysate.
Material and methods: We report a 3-month old infant on chronic ambulatory peritoneal dialysis for ESRD secondary to posterior uretheral valves and dysplastic kidneys. Peritoneal dialysis was started at D15 of life. One episode of peritonitis due to stenotrophomonas maltophilia was treated with intraperitoneal antibiotics. At the age of 2 months, we performed Nissen fundoplication and gastrostomie due to nutritional problems. Four weeks after the surgical intervention, we noticed milky colored dialysate, which was found to be due to very high triglyceride levels suggesting the diagnosis of chyloperitoneum.
Results: A low-fat diet supplemented with medium-chain triglycerides was started. Within 48 hours dialysate color normalized and, due to weight loss we decided to re-introduce normal diet only one week later without reappearance of chyloperitoneum.
Conclusions: Despite being a rare complication in PD infants, it should be considered rapidly as a differential diagnosis of peritonitis. Early exclusion of long chain fatty acids from the diet may be helpful to rapidly reduce chyloperitoneum and can avoid the use of more aggressive treatment such as octreotide.

P352 - Immunoadsorption in pediatric patients

THERESA KWON[1], ARNAUD GARNIER[2], GWENAELLE ROUSSEY[1], CHRISTINE PIETREMENT[1], VERONIQUE BAUDOUIN[1], ANNE MAISIN[1], STEPHANE DECRAMER[2], MARIE-ALICE MACHER[1]
[1]*NEPHROLOGIE PEDIATRIQUE, HOPITAL R. DEBRé, ASSISTANCE PUBLIQUE-HôPITAUX DE PARIS*
[2]*NEPHROLOGIE PEDIATRIQUE, HOPITAL DES ENFANTS, TOULOUSE*
[3]*NEPHROLOGIE PEDIATRIQUE, CHU NANTES*
[4]*PEDIATRIE, CHU DE REIMS*

Introduction: Immunoadsorption (IA) finds incremental implementation in the treatment of autoimmune disorders as well as for kidney transplant indications. As opposed to plasmapheresis, IA allows a more specific but also a probably more effective clearance of circulating

immunoglobulins without the side effects associated with the substitution of fresh frozen plasma or albumin. Few data are available in children.

Material and methods: We report a series of 128 sessions in 10 patients in 2 centers.

Results: Age range was from 26 months to 16 years old. Indications were acute humoral renal allograft rejection (4 patients, 35 IA), steroid resistant focal segmental glomerulosclerosis on native kidneys (2 patients, 79 IA), recurrent nephrotic syndrome after renal transplantation (2 patients, 13 IA), severe autoimmune thrombopenia in lupus (1 patient, 1 IA), typical HUS with severe neurological involvement (1 patient, 5 IA) and myasthenia gravis (1 patient, 12 IA). IA devices were a regenerable Ig column of polyclonal anti-IgG antibodies for one center and protein A regenerable Immunosorba column for the second one. Anticoagulation consisted in citrate and continuous heparin. Results: 7 incidents were reported during the 128 sessions, 2 were technical, 1 had allergic reaction, 2 had minor signs of hypocalcemia, 1 symptomatic hypotension and 1 fistula hematoma. IA allowed significant decrease of creatinine level in 3 out of 4 patients with acute humoral rejection, 1 patient obtained complete remission of a nephrotic syndrome recurrence after renal transplantation. The patients with neurologic HUS and autoimmune thrombopenia did not improve, but the patient with myasthenia gravis was dramatically improved with significant decrease in the anti-acetylcholine receptor antibodies.

Conclusions: IA is efficient in adult and children. The low extra corporeal volume of the device allows a safe treatment in children, as we did with a patient weighing 12 kg. IA should be considered as an option for apheresis in pediatric patients.

P353 - Benefits of Chronic Eculizumab Treatment in a Female Patient With Atypical Hemolytic Uremic Syndrome (aHUS) Receiving Long-term Dialysis

CHRISTOPH LICHT[1], ELIZABETH HARVEY[1], MASAYO OGAWA[2]
[1]*DIVISION OF NEPHROLOGY, THE HOSPITAL FOR SICK CHILDREN AND UNIVERSITY OF TORONTO, TORONTO, ON*
[2]*ALEXION PHARMACEUTICALS INC., CHESHIRE, CT, USA*

Introduction: aHUS is a rare, systemic disease of chronic uncontrolled complement activation and thrombotic microangiopathy (TMA). Over one-third of patients die or progress to ESRD with the first clinical manifestation, despite plasma exchange/infusion (PE/PI). aHUS patients, including those requiring dialysis, are at continuous risk of clinical complications from ongoing TMA.

Material and methods: Case update of an18-year-old female with aHUS receiving PE/PI since infancy (De, et al. 2010). The patient initiated eculizumab in a clinical study (NCT00844428): 900 mg weekly for 4 weeks, 1200 mg on week 5 and every 2 weeks thereafter. We assessed clinical outcomes in this dialysis patient following chronic treatment with the terminal complement inhibitor, eculizumab.

Results: The patient presented with low platelets, hypertension and renal insufficiency (complement Factor H mutation S1191L). aHUS was diagnosed aged 8 months; the infant received PI, corticosteroids, and antihypertensives. Hematologic parameters were maintained with PI. However, ongoing TMA and severe renal injury sequelae from infancy led to progressive deterioration of renal function and subsequently ESRD (aged 12 years). After long-term peritoneal dialysis/PI, the patient transitioned to eculizumab (aged 16 years). PI was discontinued; dialysis was maintained. Prior to eculizumab initiation, platelets were normal (178x109/L); eGFR (8 mL/min/1.73 m2) and hemoglobin (79 g/L) were low. During eculizumab treatment, there were no further TMA complications. By Week 52, platelets remained normal (160x109/L), eGFR was at 7.7 mL/min/1.73 m2, and hemoglobin increased (97 g/dL, despite reducing darbepoietin alfa). Blood pressure decreased (from 139/74 to 109/60 mmHg (antihypertensives unchanged). Alkaline phosphatase, a marker of bone metabolism in chronic renal dysfunction, improved from 297 U/L to 181 U/L. The patient reported increased energy and substantially less fatigue.

Conclusions: Despite PI intervention, this aHUS patient progressed to ESRD and long-term dialysis. Following initiation of eculizumab, systemic complement-mediated TMA was inhibited and the patient experienced no further TMA complications. Normal platelets were maintained, anemia and hypertension improved and overall well-being was substantially enhanced.

P354 - Sonographic Measurement of Peritoneal Thickness and Association with Peritoneal Transport Characteristics in Pediatric Patients on CAPD

AYSUN ÇALTIK, SARE GÜLFEM AKYÜZ, MEHMET BÜLBÜL, ÖZLEM ERDOGAN, GÜLAY DEMİRCİN
DR SAMI ULUS CHILDREN HOSPITAL

Introduction: Peritoneal dialysis (PD) has been an effective and successful therapy for end-stage renal disease (ESRD). However, effectiveness of PD doesn't remain for life-long. The peritoneal membrane failure is especially observed in long term PD patients. We hypothesize that there are easier methods needed for following long term PD patients and ultrasonography can be used for this objective.

Material and methods: We recruited two groups of patients (ages 3–18), 20 who have with ESRD ongoing PD for at least 24 months. The control group 20 non-ESRD children patients didn't have ongoing PD yet. None of the participating patients had peritonitis the preceding 3 months and none had a history of abdominal surgery, malignancy. We measured the sonographic thickness of parietal peritoneum and Doppler indexes of superior mesenteric artery (SMA) by trans-abdominal ultrasonography.
Results: The sonographic peritoneal thickness measurements were found significantly thicker in PD group than control predialysis group. We found that relation between the duration of PD and thickness of the peritoneum is linear and statistically significant (p=0,008). We categorized all 20 patients into rapid transporters and slow transporters respectively for creatinine (D4/P >0,64; D4/P <0,64) and glucose (D4/D0 <0,32; D4/D0>0,32). Patients have rapid transporter peritoneal membrane for both of creatinine and glucose which were found significantly thicker than slow transporters. In Doppler indexes of superior mesenteric artery no statistical difference were found between two groups. Doppler indexes showed significantly smaller Vmax and RI for slow transporters than rapid transporters for glucose (D4/D0), however, no significant difference for creatinine (D4/P).
Conclusions: Our study illustrated the sonographic thickness of the parietal peritoneum which is associated with the duration of PD and transport characteristics. The Doppler indexes of SMA had no association with PD duration. Ultrasonography is non-invasive, practical and useful for following PD patients.

P355 - Variability of pulse wave velocity during hemodialysis session in children undergoing chronic hemodialysis

NUR CANPOLAT[1], CENGIZ CANDAN[2], MEHMET TASDEMIR[1], SENNUR ERKUT[1], LALE SEVER[1], SALIM ÇALIŞKAN[1]
[1]*ISTANBUL UNIVERSITY, CERRAHPASA MEDICAL FACULTY, DEPARTMENT OF PEDIATRIC NEPHROLOGY*
[2]*ISTANBUL MEDENIYET UNIVERSITY, GÖZTEPE EDUCATION AND RESEARH HOSPITAL, DEPARTMENT OF PEDIATRIC NEPHROLOGY*

Introduction: The central pulse wave velocity (PWV) has been recognized as a gold standard for the determining of arterial stiffness that is associated with structural and functional changes within vessel wall. However, PWV may be affected by the alterations in blood pressure (BP) and volume status. The aim of this study was to evaluate possible changes of PWV between before and after hemodialysis (HD) session in children undergoing chronic HD.

Material and methods: A total of ten anuric patients on chronic HD, ages ranging from 5.7 to 17.7 years, were examined in the second weekly HD session. Volume status was assessed by clinical observation and multi-frequency bioelectrical impedance analysis (BIA). For each patient, brachial artery BP, aortic (carotid-femoral) PWV and BIA were performed immediately before (pre) and 30 minutes after (post) the end of dialysis session.
Results: All patients were receiving HD thrice weekly; and the mean single pool Kt/V was 1.83±0.35. As compared to before HD session, five patients exhibited a significant decrease in PWV after HD (6.15±0.43 vs. 5.72±0.78 m/s, p=0.039); in contrast, the remaining five patients exhibited a significant increase in PWV (5.30±0.51 vs. 6.26±0.87 m/s, p=0.043). In the patients with decreased PWV, there were significant differences in both systolic and diastolic BPs between pre-session and post-session (146±19 vs. 118±8.5 mmHg and 103±14 vs. 81±3.4 mmHg, respectively, p=0.042 for both); however, in the patients with increased PWV, there were no differences in BPs between pre-session and post-session (138±9.3 vs. 137±27 mmHg and 86±11 vs. 84±25 mmHg, respectively). In the patients with decreased PWV, the change of systolic BP was significantly correlated with the changes of ECW (r=0.975, p=0.005); however neither BPs nor PWV were associated with the changes of ECW in the patients with increased PWV.
Conclusions: Despite the limited number of patients, our findings suggest that changes in volume status and blood pressure appear to be the main factors affecting PWV; however, volume status may not be sufficient to explain all alterations in PWV.

P356 - Chronic PD in Lebanese infants and young children of families with low socioeconomic status

BILAL AOUN[1], TIM ULINSKI[2], MANAL DAHROUJ[1], SALAH TERMOS[1], GHINWA KALKAS[1], HASSAN FAKHOURY[1], CLAUS PETER SCHMITT[3]
[1]*RAFIC HARIRI UNIVERSITY HOSPITAL, DEPARTMENT OF PEDIATRICS, BEIRUT, LEBANON*
[2]*ARMAND-TROUSSEAU UNIVERSITY HOSPITAL, DEPARTMENT OF PEDIATRIC NEPHROLOGY, PARIS, FRANCE*
[3]*DIVISION OF PEDIATRIC NEPHROLOGY, CENTER FOR PEDIATRIC AND ADOLESCENT MEDICINE, UNIVERSITY OF HEIDELBERG, HEIDELBERG, GERMANY*

Introduction: The association between economic status with clinical outcome in health and disease are complex and multifaceted. At present it is unclear whether this holds true in pediatric PD patients. A recent analysis from Brazil has shown that educational level and geographic factors are associated with risk for the first peritonitis independent of

the socioeconomic status in adult population. Thus, we conducted a retrospective survey on Lebanese children on chronic peritoneal dialysis (CPD).

Material and methods: Four patients who fulfilled the inclusion criteria (low educational and low socioeconomic status and minimum six months on CPD) were included. All were evaluated at one and six months post PD for weight, height, calcium, and phosphorus, haemoglobin (Hb), creatinine (Cr) and PTH levels. A technical service was available to evaluate the PD related technical problems, and phone calls were reported. The numbers of peritonitis episodes were reported.

Results: The patients' age was (1–13 yrs), improvement in height was noted in all patients. 14 calls have been identified by the technical service,4 calls by the same parents due to alarm in drainage phase. Other ten calls due to sleeping position causing compression of the catheter. All calls could be managed by phone between parents and technical service. Hb at one month was (7.5- 11 g/dl) vs (11.5-13 g/dl) at 6 months. PTH level at one month was (150–1085 pg/ml) vs (300–520 pg/ml) at 6 months. As for calcium at one month (6.3-9.5 mg/dl) vs (9–9.5 mg/dl) at 6 months. Phosphorus at one month (2.1-8.2 mg/dl) vs (5.5-7 mg/dl) at 6 months. Creatinine level at one month 2.5-10 mg/dl vs 3–6.5 mg/dl at 6 months

Conclusions: Improvement in all parameters was noticed, with absence of peritonitis episodes. Thus, PD can be performed successfully, regardless educational and economical status.

P357 - UK Paediatric Renal Transplantation: A review of changing practice and improved outcomes

LISA MUMFORD[1], STEPHEN MARKS[2], NIAZ AHMAD[3], HEATHER MAXWELL[4], JANE TIZARD[5]
[1]*NHS BLOOD AND TRANSPLANT*
[2]*GREAT ORMOND STREET HOSPITAL*
[3]*LEEDS GENERAL INFIRMARY*
[4]*GLASGOW ROYAL HOSPITAL FOR SICK CHILDREN*
[5]*BRISTOL ROYAL HOSPITAL FOR CHILDREN*

Introduction: This review reports the outcomes of paediatric renal transplantation in the United Kingdom (UK) over the last 20 years and describes the changes in clinical practice and organ allocation that may have contributed to the improvements observed.

Material and methods: Data obtained from the UK Transplant Registry on 2,566 paediatric renal transplants from deceased and living donors performed between 1991 and 2010 were analysed. The Kaplan-Meier method was used to estimate graft survival following transplant. Transplants performed since 1986 were included in the survival analysis to enable 20 year outcomes to be reported. Cox multiple regression analysis was used to identify factors associated with improvements in graft survival.

Results: There has been a decrease in the number of deceased donors after brain death (DBD) aged less than 50 years leading to fewer DBD paediatric renal transplants. An increase in living donor renal transplants has helped to maintain level of activity. Significant improvements in HLA matching have been achieved; 85 % of patients received 000 or favourable (0 DR and 0/1 B) mismatches in 2010 compared with 21 % in 1991. As a consequence, median waiting time has increased from 125 days in 1999 to 319 days in 2010, but children still maintain a significant priority over adults who wait a median of 1153 days. Triple drug therapy with steroid, azathioprine and ciclosporin was used for the majority of patients prior to 2001, when tacrolimus replaced the use of ciclosporin in most regimens. Paediatric renal transplant outcome has improved significantly with most of the improvement explained by a reduction in early graft loss. One year DBD kidney graft survival for those transplanted from 2006–2010 was 95 %, compared with 71 % for those transplanted from 1986–1990. Twenty year DBD kidney graft survival is 37 % compared with 48 % following living donor transplant. Changes in immunosuppression regimens and improvements in HLA matching in part explain the improvements in one year graft survival.

Conclusions: Donor demographics, HLA matching, median waiting time and immunosuppression in paediatric renal transplantation have changed markedly over the last 20 years. Better HLA matching and advances in immunosuppression have contributed to improved outcomes.

P358 - Successful outcome of first paediatric renal transplant for HIV associated nephropathy

RUKSHANA SHROFF[1], MIGNON MCCULLOCH[2], VAS NOVELLI[1], DELANE SHINGADIA[1], MARGARET CLAPSON[1], MAMTA JAGANI[1], SUSAN PATEY[1], NIZAM MAMODE[3], NEIL SEBIRE[1], SUZANNE BRADLEY[1], STEPHEN MARKS[1]
[1]*GREAT ORMOND STREET HOSPITAL FOR CHILDREN*
[2]*EVELINA CHILDREN'S HOSPITAL*
[3]*GUY'S AND ST THOMAS' NHS FOUNDATION TRUST*

Introduction: Classical HIV-associated nephropathy (HIVAN) was first described before the advent of highly active anti-retroviral therapy (HAART) in late stages of HIV disease with high viral load and low CD4+ cell count. Renal transplantation guidelines for adults with HIVAN have been developed with comparable patient and graft survival. We report the successful outcome of living related renal transplantation in an 8 year old girl (AB; name changed) on haemodialysis due to HIVAN.

Material and methods: AB is a vertically HIV-infected girl who presented aged 5.5 years with lymphocytic interstitial pneumonitis and CDC stage 1. She had good CD4 counts and was not initially commenced on HAART but subsequently developed acute renal failure and renal biopsy confirmed HIVAN. Hemodialysis and HAART (Lopinavir/ritonavir, lamivudine and abacavir) were started at 6.5 years.
Results: Pre-transplantation screening showed an undetectable HIV-1 viral load and CD4 counts of 43 % (=1990/mm3). She underwent living related renal transplantation from her 56-year old maternal grandmother (mismatch 1,1,1; donor and recipient both CMV negative and EBV positive). There was a historical B-cell positive cross-match, and she was therefore treated as a 'high-risk' transplant using induction therapy with basiliximab, tacrolimus, mycophenolate mofetil and steroids. HAART (Lopinavir/ritonavir, abacavir and lamivudine) was continued together with isoniazid, azithromycin, co-trimoxazole and fluconazole prophylaxis. Currently, she is 6-months post-transplant with excellent allograft function - plasma creatinine 50 -55 μmol/l; estimated glomerular filtration rate 85-90mls/min/1.73 m2. She has mild hypertension requiring one antihypertensive agents and low-grade albuminuria (25 mg/mmol). Therapeutic tacrolimus levels are achieved with once-daily tacrolimus given 4-days per week only. Protocol biopsy at 6 weeks shows mild chronic changes, no donor specific antibodies and normal transplant renal ultrasound. She has an undetectable HIV-1 viral load, good CD4+ counts of 240/mm3 and no HIV-related complications.
Conclusions: This is the first reported case of successful renal transplantation in a child with HIVAN in the UK. Adult experience suggests higher risk of rejection and careful monitoring for long-term HIV-associated complications.

P359 - Transplant Nephrectomy for the Failing Renal Allograft: predictors and outcomes

INES VERGARA[1], MARINA MUÑOZ[1], SUSAN MINSON[1], MARTIN MRAZ[1], ROBERT W VAUGHAN[2], RUKSHANA SHROFF[1]
[1]RENAL UNIT, GREAT ORMOND STREET HOSPITAL FOR CHILDREN, LONDON, UNITED KINGDOM
[2]CLINICAL TRANSPLANTATION LABORATORY GUY'S, KING'S AND ST THOMAS' HOSPITAL MEDICAL SCHOOLS, LONDON, UNITED KINGDOM

Introduction: Children returning to dialysis after graft loss are an increasing proportion of any end-stage renal disease population. Factors predictive of graft nephrectomy in children are not described.
Material and methods: We performed a retrospective case-note review of all renal allograft failure presenting over a 10 year period (2002–2011) in children under 18 years of age. Cases of allograft failure in the first month post-transplant were excluded. For the purpose of this study allograft failure was defined as commencement of dialysis, listing for deceased donor transplant or commencing work-up for live related transplant.
Results: 34 children (18 males) developed graft failure after a median of 4.3 (range 0.2-15) years post-transplantation. 18 (53 %) children required graft nephrectomy. The median age at transplant, underlying diagnoses, modality of renal replacement therapy pre-transplantation, number with pre-emptive and living donor transplants and HLA match were comparable between groups. The median graft survival was 1.08 [0.2-10.6] and 7.5 [1.5-15.0] years in the nephrectomy and non-nephrectomy groups. The time to development of graft failure was significantly shorter in those who required a nephrectomy (p=0.04; Hazard Ratio 4.2, 95%CI 0.07-0.94). 12 of 18 (66 %) children who underwent nephrectomy had fever and graft tenderness but the non-nephrectomised patients were all asymptomatic. CRP was higher in the nephrectomy group (67 [5–219] vs 6 [5–69] mg/L; p=0.0003). 12/18 (66 %) showed acute T-cell medicated rejection on histology. The presence and class of donor specific antibodies was comparable between groups. At final follow-up of children still under paediatric care (n=18), 14 are on dialysis and 4 have a functioning transplant (78 % and 22 % of nephrectomy group respectively).
Conclusions: Early graft failure, clinically symptomatic rejection and raised CRP were strongly predictive of the need for graft nephrectomy in children. There was no difference in HLA sensitization between groups.

P360 - KIDNEY TRANSPLANTION IN PEDIATRIC PATIENT : SEVENTEEN YEAR EXPERIENCE IN HOTEL DIEU DE FRANCE

CHEBL MOURANI, BERNARD GERBAKA
HOTEL DIEU DE FRANCE (HDF)

Introduction: During the period from September 1993 to March 2010, 69 kidney transplant in children and adolescents less than 18 year old were performed in our department. We report in this abstract: immunosuppression protocols, medical and surgical complications (including rejection episodes), graft and patient survival. Kidney transplant in pediatric patients were realized by the same surgeon, 46 in the familial group and 13 in the cadaveric group. Ten were realized outside Lebanon (Irak or Pakistan or India) due to the possibility to realize there a commercial kidney transplant.
Material and methods: Immunosuppression protocole has been modified along those seventeen years. Induction therapy includes serum antilymphocyte+ciclosporine+azathioprine and prednisone. Since 2000, azathioprine was replaced

by mycophenolate mofetil and since January 2005 ciclosporine was replaced by tacrolymus. Seven deaths occurred in both groups, 3 in the familial group (lymphoma and non compliance) and 3 in the cadaveric group (lymphoma, internal hemorrhage). At the moment of kidney transplant, mean age in the familial groups was 10 years (2 – 16 Y), eleven years in the cadaveric group (10 – 14 Y) and eleven in the commercial group (10 – 13). Surgical procedure was performed by intraperitoneal approach in the first five patients less than 15 Kgs. In all the others the extraperitoneal approach was performed.

Results: Medical complications were mainly infections or rejections. The most frequent bacterial infection was UTI (27 episodes). Ten episodes of cytomegalovirus infection occurred with favourable outcome, one death occurred due to severe CMV infection.36 episodes of rejection occurred: 7 episodes in the commercial group, 16 in the familial group and 13 in the cadaveric group. All these rejections responded to 3 pulses of Solumedrol, Only one patient was resistant to corticosteroid and responded to OKT3 and plasma exchange.At the end of the study, 9 patients returned to dialysis, 5 in the cadaveric group and 2 in the familial group and 2 in the commercial. In the cadaveric group loss of the allograft was due to hemolytic uremic syndrome, oxalosis, mesangial proliferation, adenoblastoma and chronic rejection (one case each). In the familial group, chronic rejection in one (after 15 years) and oxalosis in the other case. Mean serum creatinine is 110 μmol/l in the familial group, 120 μmol/l in the cadaveric group and 326 μmol/l in the commercial group.

Conclusions: After seventeen year experience in kidney transplant, we believe that kidney transplant remains the optimal treatment for terminal renal failure even for children weighing less than 15kgs.No difference in graft and patient survival in both cadaveric and familial group. Medical complications are rejection or infection and the incidence are similar in both group. The follow-up of pediatric patients with kidney transplant revealed different positive effects on growth, regular school attendance and psychomotor development. At the end of the study : 24 are at school, 12 in the university, 4 in specialized school and 9 are active workers.

P361 - PRE-EMPTIVE KIDNEY TRANSPLANTATION IN SMALL ARPKD PATIENTS, WITH AN ADULT SIZE KIDNEY (ASK) COMBINED WITH UNILATERAL NATIVE NEPHRECTOMY: A CASE SERIES.

RWG VAN ROOIJ-KOUWENHOVEN, EM DORRESTEIJN, AA PRYTULA, GC MADERN, CEJ SLOOTS, K CRANSBERG

ERASMUSMC-SOPHIA CHILDREN'S HOSPITAL

Introduction: Autosomal Recessive Polycystic Kidney Disease (ARPKD), defined by bilateral renal cysts and congenital hepatic fibrosis, occurs in 1:20.000 of births. Its inheritance is autosomal recessive, with the responsible PKHD1-gene on chromosome 6p12. Patients with ARPKD often develop end-stage renal disease (ESRD) at young age. They are prone to growth retardation, due to a combination of renal insufficiency and intolerance of enteral feeding caused by their enormous native kidneys, which can easily weigh 400-500gr each. The size of these native kidneys hamper the transplantation of an ASK into these children. Hypovolemia or hypotension in a small recipient of an ASK can cause ATN, graft thrombosis and permanent graft non-function and should be strictly avoided in these patients.

Material and methods: We present three ARPKD patients with ESRD, aged 26, 33 and 36 months, body weight 9.9, 14.7 and 15.5 kg, respectively, pre-emptively transplanted, with an ASK from a living donor. In the same surgical procedure right-sided nephrectomy was performed immediately prior to transplantation in the right iliac fossa. Vascular anastosmoses were made on aorta and inferior vena cava. Ample fluid infusion during surgery and early post-transplant period was applied to induce a relative state of intravascular hypervolemia. A central venous and an arterial line allowed continuously monitoring. Hyperhydration was continued for at least 6 months post-transplantation. Thrombosis prophylaxis included continuous intravenous heparin for the first two weeks followed by oral acetylsalicylic acid until three months post-transplant.

Results: All children had an uncomplicated post-operative period and their renal function remains excellent one year post-transplant; eGFR>100 ml/min/1.73 m2.

Conclusions: Unilateral native nephrectomy allows renal transplantation with an adult size kidney in small children with ARPKD in a pre-emptive setting.

P362 - ENHANCED SENSITIVITY TO CYCLOSPORINE-INDUCED SUPPRESSION OF INTRACELLULAR INTERLEUKIN-2 EXPRESSION IN VIVO IN PAEDIATRIC VS. ADULT RENAL TRANSPLANT RECIPIENTS

BILLING HEIKO[1], SOMMERER CALAUDIA[2], GIESE THOMAS[3], ZEIER MARTIN[2], MEUER STEPHAN[3], CZOCK DAVID[4], BURKHARD TÖNSHOFF[1]

[1]*DEPARTMENT OF PAEDIATRICS I, UNIVERSITY CHILDREN'S HOSPITAL HEIDELBERG*

[2]*DEPARTMENT OF MEDICINE, DIVISION OF NEPHROLOGY, UNIVERSITY HOSPITAL HEIDELBERG*

[3]*DEPARTMENT OF IMMUNOLOGY, UNIVERSITY HOSPITAL HEIDELBERG*

[4]*DEPARTMENT OF CLINICAL PHARMACOLOGY AND PHARMACOEPIDEMIOLOGY, UNIVERSITY HOSPITAL HEIDELBERG, GERMANY*

Introduction: Pharmacodynamic monitoring can provide information on biologic effects of drugs. A new method to measure effects of calcineurin inhibitors by quantification of IL2, IFNg and GMCSF (residual gene expression) has been established to estimate the degree of immunosuppression with cyclosporine (CsA). Many drug targets and enzymes are developmentally regulated (Kearns GL, NEJM 349, 2003). In vitro data indicated age-dependency of CsA-induced IL2 suppression (1). We investigated a potential developmental regulation of NFAT-regulated-gene expression in response to CsA in pediatric vs. adult renal transplant recipients.
Material and methods: Prospective study of stable 184 renal allograft recipients, age<18y, 18-59y and≥60y (N=31, 98, 55). CsA concentrations were measured before and 2-hours (C2) after drug intake. IL2, INFg and GMCSF-expression was measured in PMA/ionomycin-stimulated peripheral blood lymphocytes by PCR. Differences between groups were analyzed by the Kruskal Wallis test and Dunn's test and the influence of age and CsA concentrations by multiple linear regression analysis.
Results: Patients <18y C2 was significantly lower (289 vs. 456 and 524 μg/L, p<0.01). Residual biomarker expression was inversely correlated to C2 (25 % vs. 14 % and 11 %, p< 0.01). IL2 expression in relation to CsA C2 showed a higher sensitivity to CsA in patients <18y, the suppression of INFg, GMCSF was comparable. Age showed an independent effect on residual IL-2 expression, but not on IFN-g or GM-CSF expression. Predicted IL-2 expression at C2 in different age groups is depicted in Fig. 1. An "age effect" is apparent at lower C2 concentration, but appears irrelevant at higher drug concentration.
Conclusions: The observed age-dependency of residual IL2 expression indicates, after correction for concentration effects, a significantly stronger suppression of IL2 in patients<18 years, indicating a higher sensitivity towards CsA. The overall suppression of residual gene expression in response to CsA was comparable among age groups.

P363 - Effect on an everolimus- vs. MMF-based steroid-free immunosuppressive regimen on longitudinal growth in paediatric renal transplant recipients: a case–control study

BILLING HEIKO[1], BURMEISTER GRETA[2], PLOTNIZKI LUKASZ[1], AHLENSTIEL THURID[2], HÖCKER BRITTA[1], TÖNSHOFF BURKHARD[1], PAPE LARS[2]
[1]DEPARTMENT OF PAEDIATRICS I, UNIVERSITY CHILDREN'S HOSPITAL HEIDELBERG, GERMANY
[2]DEPARTMENT OF PEDIATRIC NEPHROLOGY, HANNOVER MEDICAL SCHOOL, HANNOVER, GERMANY

Introduction: Concerns have been raised that mTOR inhibitors such as sirolimus or everolimus (EVR) might interfere with longitudinal bone growth. Two previous clinical studies are difficult to interpret because of concomitant administration of glucocorticoids and inclusion of late pubertal patients. We therefore undertook a case–control study over 2 years in steroid-free paediatric patients after renal transplantation (RTx).
Material and methods: Data of 15 patients on an EVR/low-dose cyclosporin A (CsA)-based regimen (EVR-group, median age 5.4 [1.0 – 13.7] years, were compared to a matched cohort of 15 patients on an MMF-based regimen in conjunction with tacrolimus (n=10) or CsA (n=5) (MMF-group, age 8.3 [2.8 – 15.6] years. The matching criteria were (i) age at RTx, (ii) age at study entry, and (iii) estimated glomerular filtration rate (eGFR). Data documentation and analysis were performed within the CERTAIN Registry (Cooperative European Pediatric Renal Transplant Initiative; www.certain-registry.eu).
Results: Median height SDS at baseline were comparable (EVR-group, -1.25 [−3.40 to 1.28] SDS; MMF-group, -0.97 [−2.80 to 0.74] SDS; P=0.16). One year after steroid withdrawal, mean height SDS in the EVR-group increased to −0.60 [−2.40 to 0.93] SDS compared to −1.24 [−2.60 to 1.80] SDS in the MMF-group (P=0.26). The respective height data 2 years after steroid withdrawal were −0.62 [−2.20 to 0.96] SDS in the EVR-group vs. 1.01 [−2.30 to 4.30] SDS in the MMF-group (P=0.46). The percentage of patients experiencing catch-up growth (increase of height SDS≥0.5 in 2 years) were similar in the EVR-group (5/11, 45 %) and the MMF-group (6/10, 60 %). Transplant function remained stable in both groups during the 2 year follow-up.
Conclusions: These data demonstrate that longitudinal growth 2 years after steroid withdrawal in an EVR-treated cohort is comparable to that of a matched cohort treated with MMF. Hence, EVR does not appear to negatively impact growth in children after RTx.

P364 - IVIG and Rituximab for Treatment of Chronic Antibody-mediated Rejection in Pediatric Renal Transplantation: A Prospective Pilot Study with a 2 Year Follow-up

BILLING HEIKO[1], RIEGER SUSANNE[1], SÜSAL CANER[2], WALDHERR RÜDIGER[3], OPELZ GERHARD[2], WÜHL ELKE[1], TÖNSHOFF BURKHARD[1]
[1]DEPARTMENT OF PAEDIATRICS I, UNIVERSITY CHILDREN'S HOSPITAL HEIDELBERG
[2]INSTITUTE OF IMMUNOLOGY, DEPARTMENT OF TRANSPLANTATION IMMUNOLOGY, UNIVERSITY OF HEIDELBERG
[3]INSTITUTE FOR CLINICAL PATHOLOGY, HEIDELBERG, GERMANY

Introduction: Chronic antibody-mediated rejection (CAMR) is the major cause of late renal allograft loss. No

established treatment exists for CAMR. We report on an antihumoral regimen consisting of high-dose intravenous immunoglobulin G (IVIG) and rituximab.

Material and methods: Twenty patients with CAMR were treated with IVIG (4 x 1 g/kg body weight per dose) and rituximab (1 x 375 mg/m² body surface area). Response to therapy was defined as a reduction of the loss of GFR by at least 30 %. eGFR data were smoothed by the LOESS procedure (SAS 9.2) to reduce bias due to outliers. DSA were quantified with the Luminex-based bead array technology.

Results: Loss of eGFR decreased significantly from 7.6 ml/min/1.73 m² (range, -29.2 to 1.9) 6 months prior to therapy to 2.1 ml/min/1.73 m² (range, -15.0 to 7.6; P=0.006) 6 months after intervention. Fourteen patients (70 %) responded: 9 of 9 patients (100 %) without and 5 of 11 (45 %) with transplant glomerulopathy (P=0.014). During 2 years of follow-up, the respective mean loss of eGFR in each of the four 6-month periods remained significantly lower than that prior to intervention (Fig. 1).No patients had pre-existing anti-HLA DSA. At the time of index biopsy de novo anti-HLA DSA were found in 16/20 (80 %) patients. 13/20 patients (65 %) had DSA against HLA class II. HLA class I DSA declined in response to antihumoral therapy by 54.4 % (p=0.027) and HLA class II DSA by 47 % (p=0.040) at 12 months. The percentage of C4d positivity in PTC decreased from 40±18.5 % in the index biopsy to 11.6±12.2 % (P=0.002) in the follow-up biopsy. In four of nine biopsies (44 %) C4d turned negative.

Conclusions: Antihumoral treatment with IVIG and rituximab significantly reduces or stabilizes the progressive loss of transplant function in paediatric patients with CAMR over 2 years, apparently by lowering DSA and reducing intrarenal complement activation. This protocol may represent a significant advance in the management of this common and often difficult-to-treat posttransplant complication.

P365 - USE OF ANTI-C5 ANTIBODY TO TREAT A PLASMAPHERESIS-RESISTANT ACUTE HUMORAL REJECTION IN A PEDIATRIC KIDNEY RECIPIENT

GIULIA GHIRARDO[1], ELISA BENETTI[1], FRANCESCA POLI[2], ENRICO VIDAL[1], EMANUELE COZZI[3], LUISA MURER[1]

[1]PAEDIATRIC NEPHROLOGY, DIALYSIS AND TRANSPLANT UNIT, DEPARTMENT OF PAEDIATRICS, PADUA GENERAL HOSPITAL, UNIVERSITY OF PADUA, ITALY

[2]IRCSS "CA GRANDA FUNDATION", POLICLINICO HOSPITAL, MILAN, ITALY

[3]CLINICAL AND EXPERIMENTAL TRANSPLANTATION IMMUNOLOGY, DEPARTMENT OF MEDICAL AND SURGICAL – AZ OSPEDAL.- UNIVERSITY OF PADUA, ITALY

Introduction: Even if kidney graft survival has improved during the last decades, highly immunized waitlisted patients are an emerging problem.

Material and methods: We describe a caucasian 17-year old male, transplanted at three years of age, who lost his first graft due to chronic allograft nephropathy. While on the waiting list, he presented a progressive rise in Panel Reactive Antibodies levels (PRA 99.61 %). The patient received a desensitization protocol based on plasmapheresis (PP), immunoglobulins and Rituximab, with minor response (post desensitization PRA 75 %). He was enrolled in a National Protocol for organs allocation to immunized patients and received his second non-living HLA-compatible kidney transplant at the age of 16. He had prompt function of his allograft. On postoperative day 30 he developed a biopsy-proven antibody-mediated rejection (AMR). Post-transplant immunological monitoring showed donor-specific anti-DQ5 antibodies (DSA) that were already present at the time of transplantation. The patient received three methylprednisolone pulses and 45 PP sessions, starting with daily sessions, gradually reduced to twice per week. A stabilization of creatinine levels was observed, but a raise in creatinine and DSA levels occurred after PP's frequency reduction. PP sessions were then enhanced; a second graft biopsy demonstrated a persistent C4d positive AMR. Therefore, the option of receiving Eculizumab, an anti-C5 monoclonal antibody, was offered. Eculizumab was administered starting with two weekly infusions, followed by two infusions every two weeks; PP was discontinued.

Results: After the fourth infusion graft function was normal and a third percutaneous biopsy showed the resolution of AMR. Taking into account graft function stabilization and the improvement of histological features, Eculizumab infusions were continued.

Conclusions: Eculizumab allowed our patient to stop PP therapy. One year after transplantation, in a monthly infusion regimen, graft function is still normal and stable. Anti C5 therapy may represent an effective therapeutic option also in pediatric patients with persistent PP-resistant AMR.

P366 - Can pre-implantation biopsies predict renal allograft function in paediatric renal transplant recipients ?

ALISON LT MA[1], ISMAIL MOHAMED[2], NEIL SEBIRE[3], STEPHEN D MARKS[1]

[1]DEPARTMENT OF PAEDIATRIC NEPHROLOGY, GREAT ORMOND STREET HOSPITAL FOR CHILDREN

[2]DEPARTMENT OF TRANSPLANT SURGERY, GUY'S HOSPITAL, LONDON

[3]DEPARTMENT OF PATHOLOGY, GREAT ORMOND STREET HOSPITAL FOR CHILDREN

Introduction: Pre-implantation renal transplant biopsies are a valuable tool in delineating objective information about the donor organ, which can be important in understanding the aetiology of chronic changes subsequently in renal transplant biopsies. We aim to determine the utility of pre-implantation biopsies to predict long term renal allograft outcome in paediatric renal transplant recipients (RTR).
Material and methods: Single centre retrospective review performed on all patients who underwent pre-implantation renal transplant biopsies from 2003 to 2011 with evaluation of the clinical characteristics of recipients, the presence of delayed graft function (DGF) and renal allograft function in the immediate and subsequent post-transplantation period.
Results: 32 (57 % male) patients aged 1.5 - 16 (median 10.2) years of whom 56 % received deceased donor renal transplants (DD) and had pre-implantation biopsies performed during the study period with follow-up of 6 to 78 (median 33) months. The characteristics between DD and living donors (LD) were similar with donor age of 30–50 (median 41.3) and 34–51 (median 45.3) years. There was no significant difference between the histological findings of LD and DD. 47 % (15) of biopsies were reported as showing minor chronic vascular changes while three were reported with moderate to severe vascular changes. 9 % of patients displayed DGF and 21 % had acute rejection episodes. The presence of pre-existing vascular changes did not appear to be related to DGF. No correlation was observed between renal allograft function and the presence of minor vascular changes at 3, 6 and 12 months post transplant.
Conclusions: 46 % of pre-implantation renal transplant biopsies displayed minor vascular changes. These minor histological changes did not show major impact on subsequent renal allograft function in paediatric RTR but helped delineate changes which could be of donor or recipient origin. We would recommend the routine practice of pre-implantation biopsies in children, which provides important baseline information of the graft with implications on the subsequent medical treatment for paediatric RTR.

P367 - Anemia In Pediatric Renal Allograft Recipients

ASLI KAVAZ[1], Z. BIRSIN ÖZÇAKAR[1], BURCU BULUM ÖZTÜRK[1], BEYZA DOĞANAY[2], MESİHA EKİM[1], F.FATOŞ YALÇINKAYA[1]
[1]*ANKARA UNIVERSITY SCHOOL OF MEDICINE, PEDIATRIC NEPHROLOGY*
[2]*ANKARA UNIVERSITY SCHOOL OF MEDICINE, DEPARTMENT OF BIOSTATISTICS*

Introduction: The aim of the study was to determine the incidence and etiology of anemia in pediatric renal allograft recipients.
Material and methods: Between March 2008-January 2012, we had followed 28 renal transplant patients (16 M - mean age 14.1 ±7.3 years). The median duration of follow up was 24.1 ±11.48 months (5–46). Anemia was defined according to K/DOQI guidelines as Hb is less than the fifth percentile of the normal, adjusted for age and sex.
Results: The mean Hb levels of all patients were 11.95± 1.88 mg/dl (4.8-16.2). During the study period 14 patients (50 %) developed anemia. The median onset of anemia was 5.3±5 months (1–16) after transplantation. Seven patiens (50 %) developed anemia in first 3 months, two (14.2 %) between 3–6 months and five patients after six months of transplantation. The most frequent causes of anemia were bone marrow supression (35 %), iron deficiency (28.6 %) and parvovirus enfection (14.28 %). Erythropoietic stimulating agents were used in 42.85 % of the patients, 35.7 % were treated with iron and 12.5 % with folate supplementation. Immunsupresive drug dose was reduced in 35.7 % of the patients.
Conclusions: Anemia is one of the most common problems seen in children with kidney transplantation. There may be various causes of anemia in these patients, the etiology should be found and the patients should be treated according to the underlying causes.

P368 - Bone and Mineral Metabolism Disorders In Pediatric Renal Allograft Recipients

ASLI KAVAZ[1], Z.BİRSİN ÖZÇAKAR[1], BURCU BULUM ÖZTÜRK[1], BEYZA DOĞANAY[2], MESİHA EKİM[1], F.FATOŞ YALÇINKAYA[1]
[1]*ANKARA UNIVERSITY SCHOOL OF MEDICINE, PEDIATRIC NEPHROLOGY, ANKARA, TURKEY*
[2]*ANKARA UNIVERSITY SCHOOL OF MEDICINE, DEPARTMENT OF BIOSTATISTICS*

Introduction: The aim of the study was to determine the incidence and outcome of bone and mineral metabolism disorders in pediatric renal allograft recipients.
Material and methods: Between March 2008-January 2012, we followed 28 renal transplant patients (16 M - mean age 14.1 ±7.3 years). The median duration of follow up was 24.1 ±11.48 months (5–46). Bone and mineral metabolism disorders was defined according to K/DOQI guidelines.
Results: During the study period all of the patients (100 %) had at least one bone and mineral metabolism disorder. The mean serum vitamin D levels were 21.64± 11.63 ng/ml (4.2-87.4). All of the patients had vitamin D metabolism disorder; 43.8 % deficiency and 57.2 % had insufficiency of vitamin D. Four patients (14.3 %) had hyperphosphatemia, 3 (10.7 %) hypophosphatemia,

1(3.5 %) hypocalcemia and 1 (3.5 %) had hyperparathyroidism. According to bone mineral densitometry results the mean z scores of all patients were −0.53±1.27 (−3.63 – 1.22). Only two (7.8 %) patients had osteopenia. None of our patients had bone fracture. All of our patients were treated with vitamin D supplementation.

Conclusions: Successful kidney transplantation corrects many of the metabolic abnormalities associated with the bone and mineral metabolism. Despite a well functioning graft all of our patients have Vitamin D metabolism disorders. All patients with renal transplantation should be checked routinely for vitamin D abnormalities.

P369 - Metabolic Disorders In Pediatric Renal Allograft Recipients

ASLI KAVAZ[1], Z.BİRSİN ÖZÇAKAR[1], BURCU BULUM ÖZTÜRK[1], BEYZA DOĞANAY[2], MESİHA EKİM[1], F.FATOŞ YALÇINKAYA[1]

[1]*ANKARA UNIVERSITY, SCHOOL OF MEDICINE, PEDIATRIC NEPHROLOGY, ANKARA, TURKEY*

[2]*ANKARA UNIVERSITY, SCHOOL OF MEDICINE, DEPARTMENT OF BIOSTATISTICS*

Introduction: The aim of the study was to evaluate the metabolic disorders in pediatric renal allograft recipients.

Material and methods: Between March 2008-January 2012, we followed 28 renal transplant patients (16 M- mean age 14.1 ±7.3 years). The median duration of follow up was 24.1 ±11.48 months (5–46).

Results: At the beginning of the study 39.3 % of the patients were underweight, 53.6 % were normal and 7.1 % were overweight. At the end of the study 21.4 % of the all patients were underweight, 64.3 % were normal, 10.7 % were overweight and 3.6 % were obese.The mean body mass index of all patients at the beginning and the end of the study were 16.64±3.22 (11.54-27.21) and 19.93 ±3.81 (13.85-30.59). During the study period 18 patients (64.2 %) had dyslipidemia. High LDL and TG levels were observed 25 % and 64.2 of all patients, respectively. Low HDL levels was observed 3.5 % and high TG with low HDL levels were observed 28.7 % of all patients. Omega-3 was given in one patient and 12 patients were treated with theurapeutic life style changes. Diabetes mellitus (DM) was seen 4 of the renal recipients and all of them were treated with insulin. The mean duration of insulin treatment was 12.25 ±7.8 months (5–23) and it was withdrawn in all patients at the end of the study.

Conclusions: Metabolic disorders are common after kidney transplantation. Pediatric renal allograft recipients should be screened periodically for metabolic disorders.

P370 - CONVERSION OF PROGRAF ® TO ADVAGRAF ® IN PEDIATRIC KIDNEY TRANSPLANT

LAURA ESPINOSA[1], CARMEN GARCÍA MESEGUER[1], ANGEL ALONSO[1], CARLOTA FERNÁNDEZ CAMBLOR[1], MARTA MELGOSA[1], MERCEDES NAVARRO[1], ARMANDO CAMPOS[2], ANTONIO CARCAS[2]

[1]*PEDIATRIC NEPHROLOGY. HOSPITAL UNIVERSITARIO LA PAZ. MADRID*

[2]*CLINICAL PHARMACOLOGY. HOSPITAL UNIVERSITARIO LA PAZ. MADRID*

Introduction: To study the tacrolimus levels in stable kidney recipient children after Prograf ® to Advagraf ® conversion and assess the clinical and biochemical impact at 6 months follow up.

Material and methods: Prograf® to Advagraf® conversion study, performed in 21 patients (12.8±4.8 years) at a mean time from transplantation of 5.5±3.3 years. After 7 days with supervised Prograf® administration, 24-hour pharmacokinetic data sets (PKP) were obtained. Next, patients were switched to Advagraf® (ratio of 1:1 in dosing) and on day 14 a new PKP was obtained.

Results: The Cmax with Prograf ® was 16.4±5.68 ng/ml and 13.63±5.03 ng/ml with Advagraf ®. The mean AUC0-24 was 202.3±39.6 ng*h/ml with Prograf ® and 178.23±42.61 ng*hr/ml with Advagraf ® . The mean ratio AUCAdvagraf ®/AUCPrograf ® was 87. 19 % with a confidence interval 90 % to 79.91-95.13. The mean CmaxAdvagraf®/CmaxPrograf® was 81.54 % with a confidence interval of 71.6±92.87 %. The mean dose of Prograf ® prior to conversion was 0.11±0.06 mg/Kg with a preconversion tacrolimus C12 level of 6.2 ±1.34 ng/ml. Two months after switching to Advagraf ® the dose was 0.10 +0.05 mg/kg with tacrolimus C24 levels of 5.2 ±1.23 ng/ml (14 % lower). After 6 months, the Advagraf ® dosage is 0.11±0.06 mg/kg with tacrolimus C24 level of 5.8±1.4 ng/ml. The glomerular filtration rate remained stable (94.1 preconversion vs 98.8 ml/min/1.73 m2 postconversion) and there are no significant differences in uric acid level (5.3 vs 5.13 mg/dl) or magnesium (1.68 vs 1.66 mg/dl). After one year there have not been any acute rejection episodes.

Conclusions: In paediatric renal transplant recipients conversion from Prograf ® to Advagraf ® at a 1:1 ratio seems appropriate. Despite the approximately 20 % decrease in bioavailability, at 6 months there is no significant difference in dasge between drugs. Conversion to Advagraf ® has not produced any effect on graft outcome at 6 months treatment.

P371 - Primary and additional Vaccination, Screening for viruses in Renal Transplantation- A Joint Audit from 2 Paediatric Regional Centres in UK

MURALIKRISHNA BHAGAVATULA[1], JUDITH VAN DER VOORT[1], CAROL INWARD[2], AMY HAWKINS[2]

[1]CHILDREN'S HOSPITAL FOR WALES, CARDIFF, UNITED KINGDOM
[2]BRISTOL ROYAL HOSPITAL FOR CHILDREN, BRISTOL, UNITED KINGDOM

Introduction: Following renal transplantation, patients are susceptible to infections, making immunization an effective strategy in improving host immunity. Moreover, screening for viruses in transplant subjects is additional widespread clinical practice. Our aim in this audit is to review the vaccination and screening practices of 2 paediatric nephrology units in United Kingdom and compared our practices against the regional, national recommendations including RCPCH & Department of Health.
Material and methods: Data were collected retrospectively from the records of the 2 regional paediatric renal units and from primary care. Of the 34 patients who were selected randomly between 2006 and 2010, 23 had been transplanted and 11 on waiting list.
Results: Uptake of primary and booster live vaccines is below the intended 100 % target. Uptake of primary DPT, Polio and Hib vaccines is below the national target of 95 %. Similarly, uptake of primary pneumococcal, Meningococcal C and HPV vaccines is less than national uptake. Uptake of inactive booster vaccines is less than national uptake seen among paediatric population. Viral screening pre-transplant is done in 100 % for CMV and EBV, but subsequent regular screening is done only in 94 % & 74 % of sero-negative patients respectively. Screening during immediate post- transplant period for CMV is done in 70 %, EBV in 52 % and BKV in 9 % of children which his below recommended of 100 %.
Conclusions: Uptake of primary immunizations overall among renal transplant patients is suboptimal. Cover for booster doses of live and inactive vaccines is below the national uptake. Antibody screen for selective viruses has been good pre-transplantation but post-transplant viral screening needs further attention. Liaison with primary care and education of patients and parents might improve immunization uptake. Nurses with expertise and experience in pre-transplant workup and post transplant monitoring have already contributed to improved vaccination uptake and pre and post transplant monitoring.

P372 - KIDNEY TRANSPLANT IN A PATIENT WITH ATYPICAL HAEMOLYTIC URAEMIC SYNDROME WITH HIGH LEVELS OF ANTIFACTOR H ANTIBODIES.

LAURA ESPINOSA[1], MARTA MELGOSA[1], ANTONIA PEñA[1], ANGEL ALONSO[1], CARLOTA FERNÁNDEZ CAMBLOR[1], MARGARITA LOPEZ TRASCASA[2], PILAR SANCHEZ CORRAL[2], MERCEDES NAVARRO[1]
[1]PEDIATRIC NEPHROLOGY. HOSPITAL UNIVERSITARIO LA PAZ. MADRID
[2]INMUNOLOGY. HOSPITAL UNIVERSITARIO LA PAZ. MADRID

Introduction: Recurrence of atypical haemolytic uremic syndrome (aHUS) is frequent after renal transplantation
Material and methods: A 4.5 yr-old boy was admitted to hospital in 2007 with hallmark signs of aHUS, being treated with plasma exchange (PE) and dialysis and obtaining clinical improvement after 1.5 months. 20 days later there was recurrence, treated with PE and peritoneal dialysis. After 9 months on dialysis he recovered renal function, maintaining CKD stage 2 during 2 years and 9 months. In 2010 he presented a new recurrence of aHUS; methyl prednisolone treatment and PE were begun but he progressed to ESRD. The patient was referred to our hospital. The C3 level was slightly low and he had antifactor H antibodies (AFH-Ab) with homozygous deletion in CFHR1/CFHR3. During the 23 months on dialysis AFH-Ab titers were above 2000 IU/ml despite different treatments (PE, rituximab and mycophenolate mofetil (MMF)). Haptoglobin remained low all the time; however the patient only presented symptoms of anemia with thrombocytopenia during a peritonitis episode; they resolved with antibiotic treatment of the infection.
Results: In 2011 he received a deceased donor kidney transplantation. Immunosuppressive treatment was rituximab and PE (1 session pretransplant and on alternate days posttransplant) with basiliximab, corticosteroids, tacrolimus and MMF. His serum Cr was 0.4 mg on day 5. After 7 PE sessions AFH-Ab levels fell to 323 IU/ml, gradually increasing to 3865 IU/ml with decreased Factor H. So, we then started cyclophosphamide IV (3 pulses monthly), without response. The patient is presently asymptomatic, with normal level of Hb, platelets, C3 and haptoglobin. After 12 months follow-up his GFR is normal and AFH-Ab titer is above 3000 IU/ml.
Conclusions: The AFH-Ab titer does not necessarily correlate with disease activity and other factors must be triggering relapse. Identifying these factors is essential to deciding the best therapy.

P373 - RENAL GRAFT EVOLUTION IN TRANSPLANTATION SIMULTANEOUS LIVER AND KIDNEY TRANSPLANTATION

LAURA ESPINOSA[1], CARMEN GARCÍA MESEGUER[1], ANGEL ALONSO[1], CARLOTA FERNÁNDEZ CAMBLOR[1], MARTA MELGOSA[1], ENRIQUE JAUREGUIZAR[2], Mª JOSE MARTINEZ URRUTIA[2], MERCEDES NAVARRO[1]
[1]PEDIATRIC NEPHROLOGY. HOSPITAL UNIVERSITARIO LA PAZ. MADRID
[2]PEDIATRIC UROLOGY. HOSPITAL UNIVERSITARIO LA PAZ. MADRID

Introduction: Evolution of renal function in simultaneous liver-kidney transplantation (SLKT) in children.
Material and methods: Since 1997, 10 SLKT have been performed in our institution. Patients` mean age was 10.5± 3.7 years; 6 received dialysis 22.6±25.9 months. Etiology was: type 1 hyperoxaluria (4 p), atypical hemolytic uremic syndrome with factor B deficiency (1 p), recessive polycystic disease (4p) and dysplasia with Byler disease (1p). One patient had received a previous kidney transplant.
Results: Average cold ischaemia time was 11.04±3.4 hours. Induction employed CsA / TAC, MMF and PRED, supplemented with anti-CD25 antibody in 8. Nine had immediate diuresis and none required renal replacement techniques. Median minimum Cr was 0.72±0.28 mg / dl at 9.5± 4.2 days. One patient required liver retransplantation on day seven due to hepatic artery thrombosis. After 5.5± 3.4 years follow-up kidney and patient survival is 83.3 % by Kaplan-Meyer analysis. One patient died during liver retransplantation surgery 5.5 years after the earlier simultaneous transplant. Only one case had acute renal rejection in the first month post-transplantation (without anti CD25 Ab). Another 2 patients have required treatment for liver rejection. Weight has increased by 0.07±0.1 SD and height by 0.76±0.31 SD of the standard values. At the end of follow-up, 7 cases show a GFR>80 ml/min/1.73 m2 (2 with proteinuria and 2 with hypertension treatment) and 2 present CKD stage 2.
Conclusions: Simultaneous liver-kidney transplantation shows good short and long term results, with few complications. The donor shortage creates a long waiting list time, especially for cases with normal liver function. The existence of immediate diuresis allows us to avoid dialysis in cases with hyperoxaluria. The renal graft in a hepatorenal transplantation has a low incidence of acute rejection episodes and good evolution of glomerular filtration.

P374 - The comprehensive treatment for acute humoral rejection after renal transplantation for 14 years old boy

DIANA DOBILIENE, BIRUTE PUNDZIENE
CLINIC OF CHILDREN´S DISEASES HOSPITAL OF LITHUANIAN UNIVERSITY OF HEALTH SCIENCES KAUNO KLINIKOS

Introduction: Renal peritubular capillary deposition of C4d is a marker of antibody mediated allograft rejection, that condition often necessitates an intensive therapeutic rescue regimen and is associated with poor graft survival.
Material and methods: Clinical and histopathological features, treatment and outcome of children with acute humoral allograft rejection was retrospectively reviewed.
Results: A 14 years old boy. Now he is 2 years after cadaveric renal transplantation due to membranoproliferative glomerulonephritis. He received immunosuppressive treatment with prednisolone 4 mg/d, azathioprine 50 mg/d and cyclosporine 175 mg/d. He always has chronic renal insufficiency I°, (GFR=61,5 ml/min/1,73 m²), the titres of donor's specific antibodies became positive (0-5-30 %) and C4 was less than normal. Renal function was stable, there was no clinical sings of the renal rejection. We performed renal biopsy. The answer was chronic allograft nephropathy with acute antibody madiated humoral rejection and C4d deposition in the 90 % peritubular capillary space. We had prescribed oral prednisolone 1 mg/kg/d (44 mg/d) for one month and prolonged the same immunosuppressive treatment. After that renal biopsy was repeated. It was cofirmed that humoral rejection had been progressing with leucocytes infiltration in the peritubular space. After repeated renal biopsy he was treated with 5 plasmaferesis every second day, 6 IgG infusions 400 mg/kg/d every second day and 2 Rituximab infusions 50 mg/kg once a month. After this treatment, we repeated renal biopsy and the humoral rejection disappeared, only small tubular atrophy had left. The boy is at home now, his renal function is stable, the titres of donor's specific antibodies are negative and C4 is normal.
Conclusions: Comprehensive treatment for acute humoral rejection was successful in our case.

P375 - CAN STRATIFICATION OF RISK FACTORS FOR MONONUCLEOSIS PREDICT POST-TRANSPLANT LYMPHOPROLIFERATIVE DISEASE IN PAEDIATRIC RENAL TRANSPLANT RECIPIENTS?

VALERIE SAID CONTI[1], JUDITH BREUER[2], COLETTE SMITH[2], JANANNI VIGNESWARAN[3], RUKSHANA SHROFF[4]
[1]*MATER DEI HOSPITAL, MALTA*
[2]*UNIVERSITY COLLEGE, LONDON, UK*
[3]*ST GEORGE'S UNIVERSITY, LONDON, UK*
[4]*GREAT ORMOND STREET HOSPITAL, LONDON, UK*

Introduction: Since symptomatic seroconversion to EBV has been linked to increased risk for lymphoma, we characterised the features associated with acute EBV infection.
Material and methods: 48 children who received a renal transplant between January 2009 and December 2010 were included retrospectively. Clinical findings and EBV viral loads (VL; DNA PCR in copies/ml whole blood, lower assay limit of detection of 100) at each clinic visit/admission were noted. This cohort was compared to a second cohort of 8 children with histologically diagnosed PTLD, transplanted between 2002 to date.
Results: 39/48 (81 %) children experienced viraemia >100 and 30/48 (63 %) children had mononucleosis-type

symptoms at some point post-transplantation, (median (range) peak VL of 15,890 (1953–11,300,000)). 13/16 (81.3 %) EBV seronegative children at baseline developed symptoms vs 9/14 (64.3 %) EBV seropositives (p=0.42). In a total of 1707 clinic visits/admissions, 72 (4.2 %) were symptomatic. The median VL in the 1635 non-symptomatic visits was 381 compared to 72402 at the 72 symptomatic visits (p=0.0004). No children developed PTLD during the study period. Current VL was highly predictive of symptoms (p<0.0001); the risk of symptoms doubled in children whose VL was 10,001-100,000 as compared to 1000–10,000. A VL of>10,000 with a VL of >100 in the previous two weeks further doubled the risk of symptoms. All 8 children who developed PTLD had prior mononucleosis-like symptoms on several occasions (median 6). While all 8 had detectable viraemia, with a median peak VL of 3,900,000, peak VLs ranged from 17,795-19,000,000.

Conclusions: Children who develop PTLD have a history of symptomatic EBV infection, although not all experience high VL levels. While higher VLs are associated with symptoms, a VL >10,000 together with rise of 0.5 logs or more in the previous 2 weeks was the best predictor for risk of symptomatic EBV and may provide a useful indicator of when to reduce immunosuppression.

P376 - Rationale and design of a study evaluating the efficacy and safety of early conversion of calcineurin inhibitor to everolimus in paediatric renal transplant recipients

LUCA DELLO STROLOGO[1], BURKHARD TÖNSHOFF[2], LARS PAPE[3], ROBERT ETTENGER[4], PATRICK NIAUDET[5], EL-DJOUHER MARTZLOFF[6], MARCELA VERGARA[7], ALISON BALFOUR[6], CATHERINE CORNU-ARTIS[6]

[1]*RESPONSABILE UOS CLINICA DEL TRAPIANTO RENALE, ITALY*

[2]*UNIVERSITÄTSKLINIKUM HEIDELBERG, GERMANY*

[3]*MEDIZINISCHE HOCHSCHULE HANNOVER, GERMANY*

[4]*UCLA CENTER FOR THE HEALTH SCIENCES, UNITED STATES*

[5]*SERVICE DE NÉPHROLOGIE PÉDIATRIQUE, FRANCE*

[6]*NOVARTIS PHARMA AG, SWITZERLAND*

[7]*NOVARTIS PHARMACEUTICALS CORPORATION, UNITED STATES*

Introduction: Current immunosuppressive regimens in paediatric renal transplant recipients (pRTxR) are associated with steroid attributed growth impairment, glucose intolerance, bone diseases, and calcineurin inhibitor (CNI) ascribed renal dysfunction and post-transplant diabetes mellitus. The introduction of an everolimus (EVR) based regimen may improve this situation by allowing tacrolimus (TAC) reduction and steroid elimination.

Material and methods: This is a 12-month (M), multicentre, open-label, parallel group study with a follow-up to M36 post-transplantation designed to assess the efficacy and safety of early switch to EVR with reduced TAC (EVR+rTAC) and steroid withdrawal at M6 in pRTxR (≥1 and <18 years). After 4–6 weeks treatment with TAC (C0 8-12 ng/mL)/mycophenolate mofetil/steroids, pRTxR (eGFR >50 ml/min/1.73 m^2) will be randomised (1:1) to continue this regimen (TAC-C; C0 7-10 ng/mL, starting at M4 C0 5-8 ng/mL) or start EVR+rTAC (EVR C0 3-8 ng/mL; TAC C0 4-6 ng/mL, starting at M4 C0 2-4 ng/mL) and steroid withdrawal at M6. After M12 each centre may adjust TAC target levels as per local practice. The co-primary objectives are to estimate the rate of composite efficacy failure (biopsy-proven acute rejection [BPAR], graft loss or death) and renal function (eGFR by abbreviated Schwartz formula) at M12. Key secondary endpoints include components of composite efficacy failure, incidence of antibody mediated rejection, evolution of renal allograft function over time, incidence of proteinuria, incidence/progression of interstitial fibrosis/tubular atrophy, assessment of growth and development, and overall safety [AEs, SAEs especially viral reactivation and primary infections (CMV, EBV, BKV)].

Results: Patient recruitment started in March 2012. Approximately 106 pRTxR will be enrolled across 25 sites in 10 countries in 2012 and 2013 with M12 results expected in 2014.

Conclusions: This study will determine the benefits of early switch to an EVR-based protocol in pRTxR with a specific focus on efficacy, renal function, diabetes, growth and development along with a long term follow-up to M36 post-RTx.

P377 - IONIZING RADIATION EXPOSURE IN PEDIATRIC SOLID ORGAN TRANPLANTATION

LIESBETH VAN DAMME, JEAN HERMAN, HILDE BOSMANS, NOEL KNOPS

UNIVERSITY HOSPITAL LEUVEN

Introduction: High exposure to ionizing radiation is associated with an increased long-term risk for malignancies. This risk is dependant on the cumulative dose, exposed tissue, age and the length of follow up. Medical imaging procedures constitute the most important source in the industrialized world. Children with a solid organ transplant are exposed to a high number of imaging procedures. In addition their cancer risk is increased due to immunosuppression. Nonetheless data on radiation exposure in children are scarce and nonexistent in this particular high-risk group. Objective: to assess the total amount of radiation exposure due to medical imaging in children with an organ transplant.

Material and methods: Retrospective study in a single center with an active program for pediatric kidney, liver and intestinal transplantation. We selected patients in current follow up, aged 0–18 years. Data on recipient age, type, and frequency of radiological and nuclear investigations using ionizing radiation were collected from the electronic patient files. Internal and external reference values for radiation exposure per procedure were used to calculate the cumulative effective dosis (CED).
Results: We included 57 children: 34 kidney, 18 liver, 1 intestinal, 1 liver-intestinal-pancreas and 3 combined kidney-liver transplant recipients. The median number of radiologic examinations: 85/patient (range 10–457). 159 CT /PET CT scans were performed. 14 % of the children were exposed to a mean CED of ≥50 mSv. We found no differences in exposure between liver and kidney recipients. Patients with (suspected) PTLD had an increased exposure.
Conclusions: Children with a solid organ transplantation are being exposed to a high number of medical investigations with ionizing radiation. 14 % have experienced a CED of ≥50mSV associated with an increased long-term risk for malignancies, in addition to their already increased risk. Professionals involved in the care for these children should be aware of their CED and seek means to minimize exposure.

P378 - Health-related quality of life of pediatric renal transplant recipients and their parents: the role of clinical, socioeconomic and psychological factors and continuous counselling.

BAHAR BÜYÜKKARAGÖZ[1], NECLA BUYAN[1], NAHIDE DOGRUCAN[2], BÜLENT ÇELIK[3]
[1]*GAZI UNIVERSITY DEPARTMENT OF PEDIATRIC NEPHROLOGY*
[2]*GAZI UNIVERSITY HOSPITAL*
[3]*GAZI UNIVERSITY FACULTY OF HEALTH SCIENCES*

Introduction: The aim of this prospective study to investigate the clinical, socioeconomic and psychological factors and their potential role in the health-related quality of life (HRQOL) of pediatric renal transplant recipients and their parents.
Material and methods: Twelve patients aged between 8–16 years (mean 14.9±2.9 years) and one of their parents were enrolled. The clinical and demographic data were noted. Beck depression inventory (BDI), Rosenberg self-esteem scale (RSES), Piers-Harris children's self-concept scale (PHSCS) and KINDL questionnaires for children and BDI, RSES, parent-proxy version of KINDL and short-form 36 for parents were applied initially (step 1) to determine HRQOL. After a continuous counselling program for both the patients and their parents, the same tests were repeated one year later (step 2).
Results: Mean duration of time after renal transplantation was 3.2±2.3 years. Mean number of medications were 6.8±1.7 and 4.8±2.2, consecutively ($p<0.05$). In 50 % of the families monthly income was <350 USD. In children, RSES scores were decreased ($p>0.05$) and PHSCS scores were increased ($p>0.05$) in step 2. In the parents RSES scores were decreased ($p<0.05$) and BDI scores were increased ($p>0.05$). The BDI scores were higher in the parents compared to the children in both periods ($p<0.05$ and $p<0.01$, respectively). The patients with co-existing urological problems (16.7 %) had lower PHSCS scores only in the beginning ($p<0.05$). Additionally there was a negative correlation between the creatinine levels of the patients and PHSCS scores only in the beginning ($r=-0.668$, $p<0.05$). Also the BDI scores were higher in the parents with lower monthly income in Step 1 ($p<0.05$).
Conclusions: Renal transplant team should be aware of that not only continuous education but also continuous psychosocial counselling for renal transplant recipients and their parents are crucial to improve their HRQOL in the post-transplant period.

P379 - Successful en bloc donation after circulatory death renal transplant into a paediatric recipient

HELEN JONES[1], MARTIN DRAGE[2], STEPHEN MARKS[1]
[1]*GREAT ORMOND STREET HOSPITAL NHS FOUNDATION TRUST*
[2]*GUY'S AND ST THOMAS' NHS FOUNDATION TRUST*

Introduction: We report a case and seven month follow-up data of a fifteen year-old female who presented with end stage renal disease secondary to renal dysplasia two years previously and received a paediatric en bloc donation after circulatory death (DCD) renal transplant.
Material and methods: A retrospective case review, including clinical assessment, results and renal growth by serial ultrasound measurement.
Results: The recipient (weight 55 kg, CMV and EBV positive) received an en bloc DCD renal transplant (HLA mismatch 1,1,1) from a 23-month old who had died as a result of intra-cerebral haemorrhage. The kidneys were transplanted en bloc and anastomosed onto the recipient's common iliac artery and vein, and the ureters connected to the bladder with ureteric stents left in-situ. Subcutaneous heparin was given for two weeks without surgical complications or delayed graft function. Initial immunosuppression of prednisolone, azathioprine and tacrolimus was changed with fast wean of prednisolone due to NODAT at day 11 and conversion of tacrolimus to ciclosporin. She developed Grade 1b acute T-cell mediated rejection at week 6 with increase in plasma creatinine from 100 μmol/l to 178 μmol/

l, which was successfully treated with methylprednisolone and conversion of azathioprine to mycophenolate mofetil. However, she developed further renal allograft dysfunction at two months without significant rejection on biopsy and ciclosporin was converted back to tacrolimus due to side effects. She is normotensive without proteinuria and has good renal allograft function with eGFR of 83mls/min/1.73 m2. She has no viral complications and serial ultrasounds have shown progressive renal growth; the superiorly and inferiorly positioned kidneys increasing in length from 73 to 93 mm and 74 mm to 103 mm respectively over seven months without evidence of focal scarring in either kidney on DMSA.

Conclusions: We report the successful outcome of en bloc DCD renal transplant despite developing NODAT and acute rejection with good linear growth resulting in improving eGFR post-transplantation.

P380 - HYPOMAGNESAEMIA IN PEDIATRIC RENAL TRANSPLANT RECIPIENTS

ARIFE USLU GÖKCEOĞLU[1], ELIF ÇOMAK[1], ÇAĞLA SERPIL DOĞAN[1], HALIDE AKBAŞ[2], MUSTAFA KOYUN[1], SEMA AKMAN[1]

[1]*AKDENIZ UNIVERSITY MEDICAL FACULTY, DEPARTMENT OF PEDIATRICS, DIVISION OF PEDIATRIC NEPHROLOGY*

[2]*AKDENIZ UNIVERSITY MEDICAL FACULTY, DEPARTMENT OF BIOCHEMISTRY*

Introduction: In pediatric renal transplant recipients, the data about the frequency of hypomagnesaemia was scarce.

Material and methods: Serum magnesium levels and urinary magnesium excretion was investigated in 49 pediatric renal transplant recipients and 19 healthy controls. Hypomagnesaemia was regarded as a serum magnesium level below 1.70 mg/dl. Fractional magnesium excretion was calculated as FEMg=(urine magnesium x plasma creatinine/urine creatinine x plasma magnesium) x 100; a level above 5 % was regarded as high.

Results: A total of 49 pediatric renal transplant recipients (27 boys) with a mean age of 13.1±4.1 years were included in the study. The mean duration between renal transplantation and the study time was 18±12 months. Mean estimated glomerular filtration rate (eGFR) was 69±22 ml/dak/1.73 m². Mean serum magnesium levels of the patients were lower than that of the control group (1.77±0.23 and 1.93±0.09 mg/dl, p=0.004).Twenty-three patients (46 %) had hypomagnesaemia. None of the patients with hypomagnesaemia had any symptom. There was a statistically significant positive correlation between serum magnesium and both serum creatinine and cystatin C and a negative correlation with eGFR (r=0.433, p=0.002; r=0.440, p=0.002; r=−0.372, p=0.008). Mean serum magnesium levels and also hypomagnesaemia rates of patients receiving tacrolimus and cyclosporine were similar (1.76±0.26 vs 1.79±0.12 mg/dl and 50 % vs 38 %, p=0.47). Mean FEMg of patients was higher than that of the controls (6.02±3.87 % vs 2.54±1.37 %, p=0.002). Seventeen of all patients (34 %) had hypermagnesuria. Mean FEMg of patients receiving tacrolimus and cyclosprine were similar (6.01±4.22 % vs 6.06±2.86 %, p=0.61). There was an inverse correlation between serum tacrolimus –but not cyclosporine- and magnesium levels (r=−0.609, p=0.000).

Conclusions: Hypomagnesaemia is a frequent finding in pediatric renal transplant recipients because of increased excretion of magnesium, so these patients should be screened by serum magnesium levels periodically.

P381 - Conversion to sirolimus in pediatric renal transplant recipients

BORA GÜLHAN[1], REZAN TOPALOGLU[1], YELDA BILGINER[1], ASLI TAYFUR-CELEBI[1], CIGDEM YILDIZ[1], FATIH OZALTIN[1], ALI DÜZOVA[1], SEZA OZEN[1], F.TUNCAY AKI[2], NESRIN BESBAS[1]

[1]*HACETTEPE UNIVERSITY FACULTY OF MEDICINE DEPT OF PEDIATRIC NEPHROLOGY*

[2]*HACETTEPE UNIVERSITY FACULTY OF MEDICINE DEPT OF UROLOGY*

Introduction: Sirolimus is an immunosuppressive agent that offers potentially significant benefits for pediatric transplant patients. In this study, we investigated the effects and efficacy of sirolimus in pediatric renal transplant recipients.

Material and methods: We performed a retrospective analysis of 15 renal transplant recipients who underwent sirolimus/everolimus conversion.

Results: Between years 2002–2012, 96 patients were transplanted and sirolimus/everolimus was not used as a baseline immunosuppressive therapy. During follow-up, 13 patients (2 girls, 11 males) were converted to sirolimus and 2 patients were converted to everolimus (2 males). Four patients were transplanted from deceased donors and the rest from living related donors. The median age of these patients was 16.5 year (range 5.3-26). The mean age of transplantation was 10.3±3.9 year (range 3.16-16.5). These 15 patients were converted to sirolimus/everolimus at 24.5±19.1 months after transplantation for biopsy-proven chronic allograft nephropathy (CAN) (n=6), BK-virus associated nephropathy (BKVAN) (n=2), progressive decline of renal function (n=3), gingival hypertrophy/tremor (n=2), post-transplant lymphoproliferative disease (PTLD) (n=1), cyclosporine nephrotoxicity (n=1). Median follow-up after switch was 17 months (range 1–69 months). Three patients with declining renal function and 5 out of 6 patients with

CAN had stabilized creatinine after sirolimus/everolimus. Patients with BKVAN (n=2) had functioning grafts after sirolimus. Patient with PTLD had diminished cervical lymph node sizes and complete remission occured after sirolimus. There was no graft loss during observation period. Most common side effects of sirolimus were hyperlipidemia (n=7), development of proteinuria (n=3), increase in proteinuria (n=2) and they were controlled with antilipidemic drugs and angiotensin converting enzyme inhibitors.

Conclusions: In conclusion, conversion to sirolimus/everolimus is an effective option for selected patients with tolerable side effects.

P382 - Long-term outcomes of rituximab for antibody mediated rejection in paediatric renal transplant recipients

JON JIN KIM, HELEN E JONES, STEPHEN D MARKS
GREAT ORMOND STREET HOSPITAL FOR CHILDREN NHS FOUNDATION TRUST

Introduction: Antibody mediated rejection (ABMR) is a significant cause of renal allograft dysfunction. We examined the clinical response to intravenous rituximab, a B-cell depleting agent as the current optimal treatment is unknown.

Material and methods: Retrospective cohort series of ABMR cases treated with rituximab. ABMR was defined as allograft dysfunction with evidence of antibody mediated disease. Histology was classified based on Banff criteria. Results are presented as median (interquartile range).

Results: Seven children received eight courses of rituximab 7.1 (1.2, 8.2) years post transplant. All episodes were positive for de novo donor-specific antibodies (3/8 Class I, 2/8 Class II, 3/8 both). Pre-treatment biopsies showed acute ABMR in two cases and chronic active ABMR in the remaining six. There was concomitant T-cell rejection in three cases. C4d was positive in six biopsies and CD20 aggregates were detected in three biopsies. There was an improvement in the rate of change in GFR from −2.81 (−16.60, -1.79) mls/min/1.73 m2 per month to 1.34 (−1.32, 2.71) mls/min/1.73 m2 per month after rituximab (p=0.008). However, there was no difference in estimated GFR pre-rituximab, 1 month and 3 months post-rituximab: 24.6 (13.2, 14.4), 31.5 (19.8, 51.6) and 35.3 (15.9, 44.7) mls/min/1.73 m2 respectively (p=0.8). Patients also received concomitant treatment with high dose methylprednisolone (three) and increase in baseline immunosuppression (four). One patient with acute ABMR and thrombotic micro-angiopathy two weeks post-transplant had plasma exchange and intra-venous immunoglobulin. At last follow-up 3.0 (2.0, 4.5) years post rituximab, three children had stable renal allograft function and four children had Stage V chronic kidney disease (of whom three were requiring chronic dialysis).

Conclusions: The outcomes for children with ABMR were variable, although rituximab decreased the rate of GFR deterioration. Prospective randomised controlled studies of current therapies and newer treatments are required to effectively treat ABMR.

P383 - TRANSITION OF CARE FROM PAEDIATRIC TO ADULT NEPHROLOGY FOR RENAL TRANSPLANT RECIPIENTS: MORE THAN JOINT CLINICS

LARISSA KERECUK[1], CLARE EDWARDS[1], GRAHAM LIPKIN[2], MARK THOMPSON[2], DAVID MILFORD[1], EMMA LAWSON[2], MAXINE PENDLEY[1]
[1]*BIRMINGHAM CHILDREN'S HOSPITAL*
[2]*UNIVERSITY HOSPITAL BIRMINGHAM*

Introduction: Transition of care from paediatrics to adult nephrology care is a critical period associated with higher rates of renal transplant graft loss from non-compliance for many reasons: small numbers of adolescents and young adults in adult renal units with loss of peer support; lack of confidence as a result of loss of medical and nursing staff continuity; need to adapt to new system of medical supervision; loss of a 'child and adolescent friendly' environment and expectation of decreased parental input. The original system was one of transfer (an event) rather than transition (a process) and consisted of a letter summarising the past 10 – 18 years of renal care in the paediatric unit to an adult consultant in one of 7 renal units in the West Midlands. This system was inappropriate for many paediatric patients who often have several co-morbidities, learning difficulties and psychological issues.

Material and methods: A transition pathway was implemented in 2006 after agreement from regional nephrologists to transfer paediatric transplant patients to a Young Persons clinic: a single adult nephrology consultant and transplant nurse running clinics jointly with a paediatric nephrology consultant and paediatric transplant nurse. Clinics run every 2 months and patients are seen in this clinic until they are ready to engage fully with adult services. The process of transition commences at 13 years of age) and involves topics such as understanding the diagnosis, medication, self-care. Integral to the transition process was: 1. Youth Worker appointed to support patients undergoing transition especially with special needs 2. Tours of the adult unit for patients and carers before they start attending the Young Persons clinics

Results: The further developments that have enhanced the transition process more recently include: -Workshops covering adherence, sexual health, career, peer support for

parents/carers & patients -Day trips for young adults e.g. to Alton Towers, bowling to encourage the development of peer support -Residential activity weekends to build up confidence and peer support -Appointment of a Psychologist

Conclusions: The transfer process from the paediatric to the adult renal unit for renal transplant patients has evolved to one in which there is a prior phase of transition that may last 3–5 years and patients and carers have reported greater satisfaction with this change. Feedback from the Day Trips has been 10 out 10 from the young adults. A formal audit of graft function is about to be commence. Challenges still exist especially for patients with comorbitidies and special needs. This process is focused on transplant patients and unfortunately there are currently no resources to include renal young adults with other renal conditions e.g. CKD stages 2 – 4, nephrotic syndrome with require ongoing renal care in an adult unit.

P384 - Tubular phosphate and calcium handling in cyclosporine and tacrolimus-based immunosuppression in pediatric renal transplant recipients

ELIF COMAK[1], ARIFE USLU GÖKCEOGLU[1], CAGLA SERPIL DOGAN[1], MUSTAFA KOYUN[1], HALIDE AKBAS[2], SEMA AKMAN[1]

[1]*AKDENIZ UNIVERSITY MEDICAL FACULTY DEPARTMENTS OF PEDIATRIC NEPHROLOGY*

[2]*AKDENIZ UNIVERSITY MEDICAL FACULTY DEPARTMENTS OF BIOCHEMISTRY*

Introduction: Post-transplant proximal tubular dysfunction is a common disorder after kidney transplantation due to the wide usage of calcineurin inhibitors. Aims: To assess whether cyclosporine- and tacrolimus-based immunosuppression impairs tubular reabsorption of phosphate and calcium in pediatric renal transplant recipients.

Material and methods: In children who had undergone renal transplantation between January 2008 and December 2010 at our hospital with stable graft function were included in the study. Their BUN, serum creatinine, cystatin C, phosphorus (P), calcium (Ca), tacrolimus or cyclosporine levels and urine creatinine (cre), calcium (Ca), phosphorus (P) levels were analyzed. Urinary Ca/creatinine ratio and (%) tubular reabsorption of phosphate (TPR) were calculated. Tubular reabsorption of phosphate was calculated using the formula as TPR (%)=1- (urine P x plasma creatinine/plasma P x urine creatinine) x 100; a level below 85 % was regarded as low. Patients were divided into two groups according to their immunosuppressive modality as group I including children using cyclosporine, MMF/MYF, and prednisone, and group II tacrolimus, MMF/MYF, and prednisone.

Results: The study included 60 children, 33 males (55 %), with a mean age 13.2±4.0 years and a mean follow-up period of 15.0±7.3 months. Mean estimated glomerular filtration rate was 73.5±17.6 ml/min/1.73 m2. 11 and 49 children were in groups I and II, respectively. No significant difference was found between the groups in serum Ca and P levels (10.0±0.3 vs 9.9±0.4, p=0.431 and 5.4±0.5 vs 5.0 ±0.8, p=0.276), as well as urinary Ca/cre ratio and TPR (0.06±0.06 vs 0.059±0.05, p=0.91 and 90.8±3.5 vs 91.3 ±4.5 %, p=0.53). In all patients, TPR was low in 6 patients (10 %), all of whom were receiving tacrolimus.

Conclusions: In this cross-sectional study, we did not find any difference in renal tubular phosphate reabsorption and calcium excretion between patients using tacrolimus and cyclosporine.

P385 - BONE MINERAL DENSITY AND VITAMIN D STATUS OF PEDIATRIC RENAL TRANSPLANT RECIPIENTS

ELIF COMAK[1], CAGLA SERPIL DOGAN[1], ARIFE USLU GOKCEOGLU[1], HALIDE AKBAS[2], FUNDA AYDIN[3], MUSTAFA KOYUN[1], SEMA AKMAN[1]

[1]*AKDENIZ UNIVERSITY MEDICAL FACULTY DEPARTMENTS OF PEDIATRIC NEPHROLOGY, ANTALYA, TURKEY*

[2]*AKDENIZ UNIVERSITY MEDICAL FACULTY DEPARTMENTS OF BIOCHEMISTRY, ANTALYA, TURKEY*

[3]*AKDENIZ UNIVERSITY MEDICAL FACULTY DEPARTMENTS OF NUCLEAR MEDICINE, ANTALYA, TURKEY*

Introduction: The aim of this study was to evaluate the bone mineral density and vitamin D status in pediatric renal transplant patients.

Material and methods: Pediatric renal transplant recipients who had an outpatient visit between March and June 2011 were evaluated. Serum creatinine, calcium, phosphorus, alkaline phosphatase (ALP), parathyroid hormone (PTH), 25 hydroxyvitamin D[25(OH)D] and 1,25-dihydroxyvitamin D [1,25(OH)2D] levels were analyzed; also bone mineral density was measured by DEXA technique at femoral neck and lumbar spine regions; a Z-score<−2 is considered as osteoporosis.

Results: A total of 53 patients, 24 (45.3 %) girls, with a mean age of 13.2±3.9 years (3 – 18 years) and a median follow-up period of 15 months were included in the study. 11 (20 %) of the transplants were pre-emptive, while the remaining 42 were performed after a median of 11 months (11–96) of hemo- or peritoneal dialysis. Mean estimated glomerular filtration rate was 73.7±18.3 ml/min/1.73 m2. Three patients (5.7 %) were using vitamin D supplement at the time of the study. Mean serum 25(OH)D and 1,25(OH) 2D levels were 13.5±7.4 ng/ml and 38.3±11.6 pg/ml,

respectively. Only 9 patients (17 %) have adequate vitamin D levels(25(OH)D>20 ng/ml), whereas only 3 patients (5.6 %) have inadequate 1,25(OH)2D levels (<20 pg/ml).Bone mineral density Z-scores were −1.46±0.91 and −1.63±1.28 at femoral neck and lumbar spine.Osteoporosis was detected in 16 patients (30.2 %).There was a positive correlation between Z-score and 25(OH)D (r=0.297, p=0.031). Serum ALP and PTH levels were high in 6 (11.3 %) and 27 patients (50.9 %), respectively. Hypercalcemia and hyperphosphatemia was found in 13 (24.5 %) and 44 patients (83 %), respectively. There was a negative correlation between Z-score and PTH (r=−0.343, p=0.012), and a positive correlation between Z-score and phosphorus (r=0.313, p=0.023).

Conclusions: Both bone mineral metabolism disorders and -as a risk factor- low (25(OH)D vitamin levels with normal 1,25(OH)2D levels is common in pediatric renal transplant recipients.

P386 - Failure of bortezomib in acute antibody-mediated rejection after a pediatric renal transplantation

RYCKEWAERT AMéLIE[2], ALLAIN-LAUNAY EMMA[1], BLANCHO GILLES[1], CESBRON ANNE[3], MOREAU ANNE[1], ROUSSEY KESLER GWENAELLE[1]
[1]*HOSPITAL CENTER AND UNIVERSITY OF NANTES*
[2]*HOSPITAL CENTER AND UNIVERSITY OF RENNES*
[3]*HLA LABORATORY, ETABLISSEMENT FRANÇAIS DE SANG, NANTES*

Introduction: Bortezomib has appeared as a potential active treatment for acute antibody-mediated rejection (AMR) and for desensitization protocols for few years.

Material and methods: A 16-year-old patient received preemptively a two HLA antigen-mismatched deceased donor kidney transplant. He had no prior HLA immunization. He received an immunosuppression (IS) protocol included induction (basiliximab and one corticosteroids (CS) injection), tacrolimus (FK) and mycophenolate mofetil (MMF). Eighteen months after transplantation, the patient presented an acute degradation of renal function, with undetectable level of FK. The graft biopsy demonstrated a mixed acute cellular rejection (ACR) and an acute AMR with large C4d deposition. The patient had high levels of two de novo Donor Specific antibodies (DSA). Increased MMF and FK dosing, CS pulses, IntraVenous ImmunoGlobulin (IVIG) and PlasmaPheresis (PP) were then initiated. Hemodialysis was started. Bortezomib therapy (1.3 mg/m² in 4 doses at day 1, 4, 8 and 11) was added 3 days later.

Results: The allograft biopsy revealed a grade IIA ACR without C4d staining; the anti-A2 DSA decreased by 80 % but the anti-DQ2 DSA remained elevated. A second course of bortezomib associated with PP and IVIG was then purchased. Ten days after, graft function did not improve and the biopsy demonstrated a grade IA ACR, and a progression of the fibrosis (> 30-40 % area). The rejection was thus unrelenting and the patient carried on dialysis. Of note, bortezomib had been well tolerated.

Conclusions: This is the first reported case, to our knowledge, of a treatment with bortezomib in a pediatric renal transplantation. However it does not seem to be effective in the treatment of a late acute AMR, even when associated with PP and IVIG. This AMR was diagnosed with a very poor graft function, that seems to be predictive of failure of bortezomib

P387 - Evaluation of Bone Metabolism in Children After Renal Transplantation

BAHAR BÜYÜKKARAGÖZ, SEVCAN A. BAKKALOGLU, YASAR KANDUR, MELTEM AKCABOY, EMEL ISIYEL, ENVER HASANOGLU, NECLA BUYAN
GAZI UNIVERSITY DEPARTMENT OF PEDIATRIC NEPHROLOGY

Introduction: The aim of this study is to evaluate the bone mineral density (BMD) and relevant bone biomarkers; to investigate the effects of immunosuppressives on bone metabolism after renal transplantation (RTx).

Material and methods: 33 children aged 16.7±3.7 years who had RTx at least six months before the onset of study and healthy age-/sex-matched controls (n=32) were enrolled. The BMD and cumulative corticosteroid (CS) doses at RTx, at sixth month, first year and then annually up to the time of study and mean duration of calcineurin inhibitor treatment were noted. At the time of study, osteoprotegerin (OPG), receptor activator of nuclear factor kappa B-ligand (RANK-L), fibroblast growth factor-23 (FGF-23), parathormone (PTH), 25-hydroxy-(OH) vitamin D and 1,25-dihydroxy-(OH)2 vitamin D levels and BMD values were measured.

Results: The mean follow-up time after RTx was 45.9±30.9 months. No difference was detected between the pre-RTx BMD and BMD at the time of study, while both values were lower than controls (p<0.001). The worst BMD scores were obtained in sixth month of RTx (−2.3±0.9) and the best in fourth year (−1.4±1.0). No fractures were observed. Osteoporosis frequency increased from 19 % at RTx to 36 % at the time of the study. There was no difference in PTH or 1,25-(OH)2 vitamin D levels between patients and controls, while 25-(OH) vitamin D and OPG were higher in patients (p <0.001) as was FGF-23 (p=0.054). BMD scores were negatively correlated with OPG and cumulative CS

doses at the time of study (r=−0.439, p<0.05 and r=−0.563, p<0.05, respectively). Regression analysis revealed OPG as the only predictor of BMD (β: -0.78, 95%CI: -0.004 - -0.013, p<0.001).

Conclusions: The increase in OPG, a significant predictor of BMD, could either be secondary to graft dysfunction or as a compensation to the decreased BMD. CS doses should be minimized to avoid their untoward effects on bone metabolism.

P388 - Evaluation of Growth in Children Following Renal Transplantation

BAHAR BÜYÜKKARAGÖZ, SEVCAN A. BAKKALOGLU, YASAR KANDUR, MELTEM AKCABOY, EMEL ISIYEL, ENVER HASANOGLU, NECLA BUYAN
GAZI UNIVERSITY DEPARTMENT OF PEDIATRIC NEPHROLOGY

Introduction: One of the major goals of pediatric renal transplantation (RTx) is to maintain optimal growth. In this study, growth and the factors impacting on linear growth in children with RTx were evaluated.

Material and methods: Children and adolescents (n=33, 12 girls/21 boys) aged 16.7±3.7 (5–21) years who had RTx at least six months before the onset of the study and 32 age-/sex-matched controls were enrolled. The antropometric measurements were recorded at the time of the RTx (step 1), at six months and then one year apart and at the time of the study (step 2). Cumulative corticosteroid (CS) doses were calculated at these time periods.

Results: The mean follow-up time after RTx is 45.9± 30.9 months. The height was<−2SDS in 50 % and 24 % of the patients in step 1 and step 2, respectively. There was a significant difference in height SDS between the patients in step 1 and 2 (p<0.001). In step 2, the height SDS turned to be positive in 12 % of the patients. The mean body mass index (BMI) of the patients was lower in step 1 than step 2 (p<0.001). The height of the patients were found to be shorter than the controls (p<0.01), whereas there was no difference in respect to BMI between the two groups (p>0.05) in step 2. During the follow-up period, the rate of height gain was minimum in sixth month (2.6±2.3 cm) and maximum in the second year (5.4±3.7 cm) post-RTx. There was a strong negative correlation between height SDS of the patients and the cumulative CS doses used in all post-RTx periods (r=−0.529, p<0.01).

Conclusions: It is clear that RTx is beneficial for the height and weight gain of the patients. CS doses should be minimized in order to lessen their negative effects on linear growth.

P389 - MANAGEMENT POLICIES FOR CHILDREN WITH RENAL TRANSPLANTATION IN THE NETHERLANDS, BELGIUM AND GERMANY – REPORT FROM THE RICH-Q STUDY.

MAIKE VAN HUIS[1], NIKKI J. SCHOENMAKER[1], JOHANNA H. VAN DER LEE[2], ANTONIA H.M. BOUTS[1], LAURE COLLARD[3], RITA VAN DAMME-LOMBAERTS[4], NATHALIE GODEFROID[5], KOENRAAD VAN HOECK[6], BERND HOPPE[7], LINDA KOSTER-KAMPHUIS[8], MARC R. LILIEN[9], ANN RAES[10], NADEJDA RANGUELOV[11], JAAP W. GROOTHOFF[1], KARLIEN CRANSBERG[12]
[1]*EMMA CHILDREN'S HOSPITAL ACADEMIC MEDICAL CENTRE AMSTERDAM, THE NETHERLANDS*
[2]*DEPARTMENT OF PAEDIATRIC CLINICAL EPIDEMIOLOGY EMMA CHILDREN'S HOSPITAL AMC AMSTERDAM, THE NETHERLANDS*
[3]*CENTRE HOSPITALIER UNIVERSITAIRE DE LIEGE, BELGIUM*
[4]*UNIVERSITY HOSPITAL LEUVEN, BELGIUM*
[5]*UC LOUVAIN, BRUSSELS, BELGIUM*
[6]*UNIVERSITY HOSPITAL ANTWERP, BELGIUM*
[7]*UNIVERSITY HOSPITAL COLOGNE, GERMANY*
[8]*RADBOUD UNIVERSITY NIJMEGEN MEDICAL CENTRE, THE NETHERLANDS*
[9]*WILHELMINA CHILDREN'S HOSPITAL UNIVERSITY MEDICAL CENTRE UTRECHT, THE NETHERLANDS*
[10]*UNIVERSITY HOSPITAL GENT, BELGIUM*
[11]*HOSPITAL UNIVERSITAIRE DES ENFANTS REINE FABIOLA BRUSSELS, BELGIUM*
[12]*SOPHIA CHILDREN'S HOSPITAL ERASMUS MEDICAL CENTRE ROTTERDAM, THE NETHERLANDS*

Introduction: The effective management of paediatric renal transplantation (Tx) is essential for long-term graft function. The low prevalence of childhood End-Stage Renal Disease and the small centre sizes have been a barrier for clinical studies and for the development of evidence based guidelines for Tx in children. The aim of this study was to quantify variation in treatment policies regarding renal Tx in children.

Material and methods: All 11 centres in the Netherlands and Belgium and one in Germany participated. Data on treatment policies were gathered by questionnaires; actually provided care was registered prospectively from 2007 to 2011.

Results: We found relevant differences between centres in Tx treatment policies on various topics. Maximum accepted donor age varied between 50 and 75 years and between 45 and 65 years for living and deceased donors, respectively. Minimum accepted recipient weight varied between 8 and 12 kilograms. Non Related Living Donor renal transplantation is provided in 6 centres, ABO-incompatible

transplantation in 7 centres and non heart-beating transplantation in 3 out of 11 centres. Furthermore, minimum accepted HLA-match varied between the centres. In Belgium, relatively more deceased donor Tx are performed (75 % vs. 47 %, respectively in Belgium and the Netherlands), possibly due to a more liberal organ donation legislation in Belgium. Waiting time for the first Tx did not differ between Belgium and the Netherlands. Median [IQR] waiting time in Belgium was 18 [9,8-30] months, in the Netherlands 17,5 [9,8-36] months.

Conclusions: Within 3 European countries, Tx policies differ. There is insufficient evidence to show an association with patient outcome, although this is expected. Differences in policies may be explained by a lack of evidence based paediatric guidelines. This emphasizes the need for a national and international collaboration of paediatric nephrology centres.

P390 - Vitamin D deficiency in children after renal transplantation – prevalence and association with growth and blood pressure

TOMAS SEEMAN[1], JIRI DUSEK[2], NADEZDA SIMANKOVA[1], JAROSLAV SPATENKA[3], KAREL VONDRAK[2], JAKUB ZIEG[2]

[1]*DPT. OF PEDIATRICS AND TRANSPLANTATION CENTER, UNIVERSITY HOSPITAL MOTOL, PRAGUE, CZECH REPUBLIC*

[2]*DPT. OF PEDIATRICS*

[3]*TRANSPLANTATION CENTER*

Introduction: Vitamin D deficiency is common in adults after renal transplantation (RTx). Only few studies investigated vitamin D status in transplanted children. They have suggested that vitamin D deficiency is common also in transplanted children and that it is associated with short stature and may influence clinic blood pressure (BP) control. No data are known on the association of vitamin D and ambulatory BP. The aim of our study was to investigate the prevalence of vitamin D deficiency in children after RTx and its associations with growth and BP.

Material and methods: Vitamin D (25-hydroxyvitamin D, 25-OH-D), parathormon (PTHi), body height, blood pressure (clinic and 24 hr ambulatory BP), graft function (Schwartz) were investigated in all transplanted children in our center.

Results: 32 children were investigated (18 girls, mean age 12.8 years, time after RTx 4.9 years, body height −1.39 SDS), two children were treated with vitamin D, 29 children with antihypertensive drugs and no child with growth hormone. The mean 25-OH-D level was 56.6 nmol/l. Vitamin D insufficiency (25-OH-D <75 and>25 nmol/l) was detected in 27 children (84 %) and vitamin D deficiency (<25 nmol/l) in 2 children (6 %). Only 5 children (16 %) had normal 25-OH-D level (including both children with vitamin D therapy). Twelve children (38 %) had elevated PTHi, 10 of them had vitamin D insufficiency. No child had hypocalcaemia, one child had hyperphosphataemia. There was no statistically significant correlation between 25-OH-D levels and PTHi, body height, clinic or ambulatory BP, graft function or time after RTx.

Conclusions: Children after RTx suffer very often from vitamin D insufficiency. It is frequently associated with hyperparathyreoidism. Insufficient levels of vitamin D are not associated with short stature, clinic or ambulatory blood pressure. Vitamin D levels should be monitored regularly in all children after RTx. Supported by grant IGA NT11457-5.

P391 - PHARMACOKINETICS OF MYCOPHENOLIC ACID IN PEDIATRIC RENAL TRANSPLANT RECIPIENTS RECEIVING ORALMYCOPHENOLATE MOFETIL

ELISABETH A M CORNELISSEN[1], MICHIEL SCHREUDER[1], BART JACOBS[2], ROB AARNOUTSE[2], ROGER BRUGGEMANN[2]

[1]*PED. NEPHROLOGY, RADBOUD UNIVERSITY NIJMEGEN MEDICAL CENTRE, NETHERLANDS*

[2]*PHARMACY, RADBOUD UNIVERSITY NIJMEGEN MEDICAL CENTRE, NETHERLANDS*

Introduction: Mycophenolate mofetil (MMF), a pro-drug of mycophenolic acid (MPA), is used for the prevention of renal transplant (RT) rejection in pediatric patients (600 mg/m2 orally twice daily (BID)). In our population, MMF is administrated as part of a regimen of basiliximab, cyclosporine and prednisolone. The optimal area under the plasma-concentration curve of a 12 hour dosing interval (AUC0-12) of MPA is considered to be 30–60 mg*h/L as 79 % of acute rejections within 3 months after transplantation are associated with MPA AUC0-12 of <30 mg*h/L) [Kiberd et al. AJT 2004]. An AUC0-12 of>60 is associated with increased chance of toxicity. Based on the predictive association between exposure and outcome, Therapeutic Drug Monitoring (TDM) of MPA is warranted. The aim of this study was to clarify the MPA pharmacokinetics (PK) of the local pediatric population and quantify the attainment of target concentrations.

Material and methods: Pediatric renal transplant recipients were retrospectively selected. MPA AUC0-12 PK profiles (minimum 6 time points) were, according to routine practice, obtained from Jan 2008-Aug 2011. Standard two-stage PK analyses were done using WinNonLin (Pharsight Inc, v5.2). The effect of age, gender, body weight, height, BMI, BSA, MMF dose, cyclosporine co-medication, kidney

function, albumin levels and time after transplantation on MPA were determined using SPSS.

Results: 36 Patients (18 male; mean age: 12.5 years; mean weight: 41.4 kg; mean height: 1.46 m) were selected. The cohort was divided in two subgroups based on the time after transplantation: subgroup (SG) early (n=26) and SG late (n=10) of which the MPA AUC0-12 were measured at 11 days (range: 10–18 days) and >500 days post transplantation, respectively. Median (IQR) MPA AUC0-12 was 24.7 mg*h/L (19.6-34.9) for SG early (73 % <30 mg*h/L), receiving a median (range) dose of 574.3 mg/m2 BID (244.1-686.2). A median (IQR) Cmax of 9.05 mg/L (6.49-11.84) and Cmin of 0.54 mg/L (0.20-0.85) were measured in SG early. No correlation between selected factors and MPA AUC0-12 were detected. There was a correlation between Cmax and MPA AUC0-12 (R2=0.673; p<0.01). Cmin did not correlate with AUC0-12. Median (IQR) MPA AUC0-12 for SG late was 68.0 (48.8-81.0) mg*h/L, which correlated (R2=0.613; p<0.01) to MMF dose (all>30 mg*h/L and 60 %>60 mg*h/L). Median (range) MMF dose in SG late was 470.8 mg/m2 BID (349.9-722.0). Median (IQR) Cmax and Cmin were 13.95 mg/L (11.30-17.05) and 2.25 mg/L (1.45-4.18) respectively.

Conclusions: In 73 % MPA SG early AUC0-12 values were below the target range shortly after transplantation, which could not be predicted on basis of other variables. A higher empiric starting dose of MMF should be considered (ie 750 mg/m2) and routine TDM of MPA is recommended as follow up. MPA AUC0-12>500 days post transplantation are adequate or even above the recommended range. Increased renal clearance could explain the higher AUC despite lower dose. Although based on a limited sample size, Cmax instead of Cmin may be preferred as best predictor for AUC0-12 in this cohort.

P392 - Association between Vitamin D Deficiency and Graft Function, Proteinuria, Fibrosis And Tubular Damage Marker In Pediatric Renal Transplant Recipients

ELIF COMAK[1], ARIFE USLU GOKCEOGLU[1], CAGLA SERPIL DOGAN[1], HALIDE AKBAS[2], MUSTAFA KOYUN[1], SEMA AKMAN[1]

[1]*AKDENIZ UNIVERSITY MEDICAL FACULTY DEPARTMENTS OF PEDIATRIC NEPHROLOGY, ANTALYA, TURKEY*

[2]*AKDENIZ UNIVERSITY MEDICAL FACULTY DEPARTMENTS OF BIOCHEMISTRY, ANTALYA, TURKEY*

Introduction: Some studies showed that vitamin D has a role in the maintenance of normal kidney structure and function, yet longer-term studies have failed to confirm these findings. Aim: To assess whether low serum vitamin D concentrations are related to graft function, proteinuria, fibrosis and tubular damage markers

Material and methods: The children with renal transplant recipients who had an outpatient visit between March and June 2011 were evaluated. Their serum BUN, creatinine, CystatinC, 25 hydroxyvitamin D[25(OH)D]and urine fibrosis and tubular damage markers were analyzed.Patients divided two groups according to their 25(OH)D levels: group I 25(OH)D<15 ng/ml, group II 25(OH)D>15 ng/ml.

Results: The study included 60 children, 27 females (45 %), with a mean age 13.24±4.01 years and mean follow-up period 15.06±7.37 months. 48 (80 %) of the transplants were from a living donor and 13 (21.7 %) transplants were pre-emptive, while the remaining 47 followed a median of 10 months on dialysis. The mean estimated glomerular filtration rate was 73.56±17.61 ml/min/1.73 m2. The mean serum 25(OH)D and 1,25(OH)2D levels of all patients were 13.78±6.12 ng/ml and 38.85±10.48 pg/ml respectively. 25 (OH)D levels were lower than 15 ng/ml at 34 children (56.7 %), and higher than 15 ng/ml at 26 children (43.3 %). eGFR and tubular reabsorption of phosphate was higher in group II than group I(p=0.001, p=0.001).Cystatin C and uric acid was lower in group II than group (p=0.01, p=0.023). And also there was significant association between 25(OH)D and eGFR and CystatinC (r=−0.43, p=0.001 and r=−0.27, p=0.03 respectively). There weren't any significant differences between two groups serum creatinine, PTH and urine protein-creatinine ratio, urinary connective tissue growth factor, bone morphogenetic protein-7,neutrophil gelatinase-associated lipocalin kidney injury molecule 1,urinary Transforming Growth Factor ß-Induced Gene-h3,interleukin 18 levels.

Conclusions: These finding suggest that low levels of 25 (OH)D in pediatric renal transplant recipients can be associated with bad graft function and disability without high creatinine level.

P393 - Early protocol biopsies in pediatric renal transplantation: a monocentric study

BRUEL ALEXANDRA, ALLAIN LAUNAY EMMA, RENAUDIN KARINE, ROUSSEY KESLER GWENAELLE

NANTES UNIVERSITY HOSPITAL

Introduction: Graft protocol biopsies (GPB) are usually performed in pediatric renal transplantation (RT), and revealed subclinical acute rejection (SBAR) in 10 to 30 % of the recipients.

Material and methods: Children less than 18 years who received a RT between 01/04/2009 and 31/12/2011 were included. Immunosuppression (IS) consisted in an induction therapy, tacrolimus (FK) and mycophenolate mofetil

(MMF) for all. Corticosteroids (CS) were administered in children under 5-year-old and in second RT. GPB were performed between 3 to 6 months. Creatinine clearance was calculated according to Schwartz formula.

Results: Twenty seven children were included. Median recipient and donor age were respectively 9 and 16 years. Most of the transplantations were from a deceased donor (82 %), 28 % of the recipients had HLA immunization. Thirteen children (48 %) were CS-free. During the first 6 months, GPB were performed in 25 cases, 6 others biopsies were performed for reason (all were normal). GPB biopsies revealed in one case an important inflammatory interstitial infiltrate considered as a SBAR (treated with CS pulses) and one borderline acute rejection (treated with increase IS). Three others GPB presented interstitial fibrosis and tubular atrophy (IF/TA) grade 1. C4d staining was negative for all. Among these 5 abnormal GBP, 3 children out of 5 were CS free. Donor age seemed to have no impact on IF/AT in our cohort. The median creatinine clearance was 70, 66 and 78 ml/min/1.73 m² at respectively 7 days, 3 months and 1 year after transplantation. Significant proteinuria was observed only in the patient with borderline rejection.

Conclusions: SBAR was infrequent in our cohort, despite that half of the recipients were CS free. IS including induction therapy, FK and MMF seemed to prevent clinical and SBAR in pediatric RT, and was associated with correct renal function at 1 year. These results have to be confirmed in larger cohorts.

P394 - Fludrocortisone as a new tool for managing tubulopathies after renal transplantation?

AMELIE FERDINAND, JUSTINE BACCHETTA, ANNE LAURE SELLIER-LECLERC, AURELIA BERTHOLET-THOMAS, PIERRE COCHAT, BRUNO RANCHIN
HOSPICES CIVILS DE LYON, UNIVERSITé LYON1

Introduction: The management of proximal tubulopathies after renal transplantation (Tx) may require high oral doses of sodium and bicarbonate, to optimize growth and bone quality thus decreasing the quality of life and the global therapeutic compliance. In adults, a few reports have highlighted the potential interest of fludrocortisones (fludro) for the management of severe tubulopathies.

Material and methods: We retrospectively reviewed the medical charts of all the children treated with fludro for a severe tubulopathy after renal Tx in our centre. Results are presented as mean±SD or median [range] in case of skewed distribution. Paired t-tests were used to compare parameters before and at the time of the maximal dose of fludro.

Results: Seven children begun fludro 9.2 [4.8-91.8] months after Tx at a median age of 9.7 [3.6-16.8] years and a median body weight of 25 [13–64] kg; all but one were receiving tacrolimus at the time of fludro initiation. One patient stopped the treatment in the first 15 days due to gastric pain and was therefore excluded from further analysis. The maximum daily dose of fludro was 4.2 [1.4-7.8] μg/kg The daily doses of sodium bicarbonate and sodium chloride before fludro were 10 [5–17] g and 11.5 [0–20] g, respectively, whereas; they were 0.5 [0–18] and 2 [0–12], respectively, at the time of maximal fludro dose (both $p < 0.05$). Serum potassium was significantly decreased (4.4± 0.4 vs. 3.5±0.8 mmol/L, P=0,025) under fludro, but there were no changes for sodium, bicarbonate and creatinine. Fludro was secondary withdrawn in four patients due to the onset of arterial hypertension (n=1), severe hypokalemia following acute infectious enteritis (n=1), and parents' decision (n=2). Among these 4 patients, the dose of both sodium bicarbonate and chloride was re-increased after withdrawal in one, the doses where not changed during and after fludro in two, and supplementation was stopped under treatment with no need for restarting it after fludro stop in one

Conclusions: If high doses of sodium and/or bicarbonate are required after renal Tx despite a regular evaluation of their necessity the use of fludro may be of interest but side effects may occur, and these preliminary findings need to be confirmed in prospective and larger clinical trials.

P395 - A potential for individualized dosing of prednisolone in pediatric renal transplant recipients

RAGNHILD KRISTINE HEIER SKAUBY[1], ANNA KRISTINA BJERRE[2], INGJERD SAEVES[3], STEIN BERGAN[3]
[1]*DEPT OF MEDICAL BIOCHEMISTRY, OSLO UNIVERSITY HOSPITAL, NORWAY*
[2]*DEPT OF PEDIATRICS, OSLO UNIVERSITY HOSPITAL, NORWAY*
[3]*DEPT OF PHARMACOLOGY, OSLO UNIVERSITY HOSPITAL, NORWAY*

Introduction: Children are extra vulnerable to glucocorticoid related complications, therefore the present study was initiated with the purpose to identify pharmacokinetic parameters that may be used for dose individualization. Prednisolone is a standard component of immunosuppressive protocols in renal transplantation. Although frequent adverse events like diabetes, bone loss and cardiovascular effects are attributed to this drug, the dosing is not individually tailored. Patients receiving high dose prednisolone on indications like renal transplantation and acute lymphoblastic leukemia ALL, altogether 28, are included in this prospective non-interventional study to gain statistical power,

but only the renal transplant recipients are analyzed in the present substudy.

Material and methods: Blood samples were collected before transplantation and during selected dose intervals (0, 1, 2, 4, 6 and 12 hrs postdose; less frequent in the smallest children) at 1, 2, 3, 4 weeks, 3 and 12 months postTx. Prednisolone and cortisol, their inactive keto forms plus methylprednisolone were assayed using a validated LC-MS/MS method, and the pharmacokinetic profiles (area under the plasma concentration vs time curves, AUC) were analyzed. Correlations with clinical indicators like bone mineral density changes (DEXA scans) and new onset diabetes after transplantation (NODAT) were investigated.

Results: The analysis so far (n=5 patients, age 1–15 yrs) indicates a tendency towards a higher ratio of prednisolone AUC/prednisone AUC during the first 4 weeks (median 15.0 vs 7.6; n.s.) in patients experiencing significant bone loss and NODAT.

Conclusions: The preliminary results need confirmation, and if this tendency persists overall or in the transplant or ALL group when all patients are followed up, the prednisolone/prednisone ratio will be further tested as a potential parameter for individualized dosing with the aim to reduce the adverse events while maintaining the clinical effect.

P396 - En-bloc pediatric kidney transplantation together with a partial bladder segment: a case report.

CANER ALPARSLAN[1], ONDER YAVASCAN[1], NEJAT AKSU[1], MURAT SAIT DOGAN[2], CEM TUGMEN[2], EYUP KEBABCI[2], CEZMI KARACA[2]
[1]*TEPECIK TRAINING AND RESEARCH HOSPITAL, PEDIATRIC NEPHROLOGY, IZMIR, TURKEY*
[2]*TEPECIK TRAINING AND RESEARCH HOSPITAL, DEPARTMENT OF TRANSPLANTATION, IZMIR, TURKEY*

Introduction: There is a continuing debate about the techniques of kidney transplantation from small donors because of the high vascular thromboses and ureteric leak rates. Transplantation of en-bloc pediatric kidneys with a partial bladder segment has potential benefits over established techniques.

Material and methods: We transplanted cadaveric en-bloc kidneys together with a partial bladder segment from a 1.5-year-old donor to a 12-year-old boy with end-stage renal disease due to vesicoureteral reflux (VUR) of a solitary kidney.

Results: En-bloc kidneys were transplanted together with both ureters and a partial bladder segment. Using donor bladder segment, we augmented the recipient bladder. Thereby, potential complications of bilateral ureteroneocystostomies of small ureters were avoided. During the following 30 months, the clinical course was normal and there was no evidence of VUR.

Conclusions: In conclusion, the technique of using en-bloc pediatric kidneys together with a partial bladder segment is feasible and safe as well as an efficient procedure to preserve the natural anti-reflux mechanism in childhood.

P397 - Graft Survival in Pediatric Renal Transplanlantation: A 15-year experience in a single center.

CANER ALPARSLAN[1], ALKAN BAL[1], ENGIN KOSE[1], ONDER YAVASCAN[1], NEJAT AKSU[1], ISMAIL GENCER[2], CEM TUGMEN[2], MURAT SAIT DOGAN[2], EYUP KEBABCI[2], CEZMI KARACA[2]
[1]*TEPECIK RESEARCH AND TRAINING HOSPITAL, PEDIATRIC NEPHROLOGY, IZMIR, TURKEY*
[2]*TEPECIK RESEARCH AND TRAINING HOSPITAL, DEPARTMENT OF TRANSPLANTATION, IZMIR, TURKEY*

Introduction: Renal transplantation is the best renal replacement modality for end stage renal disease especially in pediatric population. In this retrospective study, we analyzed the results of pediatric renal transplant children treated in our center between 1995 and 2010 and searched the graft survivals and related factors.

Material and methods: This study concluded 61 children. All transplanted patients were followed up in our nephrology unit. Statistical evaluation was made by using chi-square and student's t –tests. Kaplan-Meier test determined the survival.

Results: A total 61 children (35 girls, 26 boys; mean age 14±3) received organs either from 35 living donors or 26 cadeveric donors. Preemptive renal transplantation was performed in 8 patients (27.2 %). Mean follow-up period was 64.33±51.44 months (range : 12 to 188 months). Acute rejection was determined in 23 patients. Overall, 1- and 5-year graft survivals and patient survivals were 91.4 % and 78 % and 95.1 % and 90.2 %, respectively. Donor age (>40 years), acute rejection and delayed graft fuction were associated factors for the graft survival (p=0.001). Recipient characteristics, underlying diseases, immunosupression regimen, type of induction threapy, being related donor or cadaveric kidney and donor gender did not influenced the graft survival (p>0.05).

Conclusions: In conclusion, renal transplantation is the best method for treatment in children with end stage renal disease. Younger donor age as well as prevention of acute rejection and delayed graft function would improve graft survival in pediatric renal transplantation.

P398 - calcimimetic therapy for persistent hyperparathyroidism after renal transplantation in a 7-year-old boy

CLAIRE DOSSIER, MARIE-ALICE MACHER, GEORGES DESCHENES, ANNE MAISIN
DEPARTMENT OF PEDIATRIC NEPHROLOGY, ROBERT DEBRE HOSPITAL, PARIS FRANCE

Introduction: Persistent hyperparathyroidism after renal transplantation is a rare condition in children. In adult patients, it negatively affects graft function, bone metabolism and cardiovascular system. Cinacalcet, a calcimimetic drug, has been reported efficient in controlling hyperparathyroidism in adult transplant, as well as adult and paediatric dialysed patients. We report on the first paediatric transplant patient treated with cinacalcet.
Material and methods: Case report
Results: A 7-year-old boy underwent renal transplantation after binephrectomy for bilateral nephroblastoma. He had been on haemodialysis for 3.7 years, and developed refractory hyperparathyroidism with bilateral parathyroid hyperplasia and severe hypercalcemia three months before transplantation. After transplantation, calcemia, calciuria and PTH levels remained dramatically high. Phosphate supplementation, intraveinous calcitonine and pamidronic acid failed to reduce calcemia and calciuria. Four months after transplantation, serum calcium was still 3 mmol/l, ionized calcium 1.52 mmol/l, and PTH value 382 ng/l. Thereafter, as an alternative to parathyroidectomy, cinacalcet was initiated by day 125, at 15 mg/day (0.7 mg/kg/d) and raised up to 60 mg/day within 2 months. We observed normalization of calcium level, but no benefit on hyperparathyroidism. Cinacalcet was then raised up to 90 mg/d, and little dose of vitamin D analog introduced, with subsequent effective control on hyperparathyroidism. At 2 years of follow-up, with an ongoing cinacalcet (60 mg/d) and clodronic acid (200 mg/d) treatment, calcemia remains normal, PTH level is 69 ng/l and parathyroid glands are no more detectable. Moreover, renal function remained stable, and no allograft rejection or adverse effect were observed.
Conclusions: Cinacalcet was safe and effective in normalizing calcemia in a 7-year-old renal transplant boy with parathyroid hyperplasia. Addition of vitamin D analog was though no more contraindicated and effective in correcting hyperparathyroidism. Cinacalcet should be considered as a treatment option in children with persistent hyperparathyroidism after renal transplantation.

P399 - Disseminated Fungal Infection by Aureobasidium pullulans in a renal transplant recipient

HULYA NALCACIOGLU[1], Y. KAMIL YAKUPOGLU[2], GURKAN GENC[1], NURSEN BELET[3], GULNAR SENSOY[3], ASUMAN BIRINCI[4], OZAN OZKAYA[1]
[1]*ONDOKUZ MAYIS UNIVERSITY FACULTY OF MEDICINE, DEPARTMENT OF PEDIATRIC NEPHROLOGY*
[2]*ONDOKUZ MAYIS UNIVERSITY FACULTY OF MEDICINE, DEPARTMENT OF UROLOGY*
[3]*ONDOKUZ MAYIS UNIVERSITY FACULTY OF MEDICINE, DEPARTMENT OF PEDIATRIC INFECTIOUS DISEASES*
[4]*ONDOKUZ MAYIS UNIVERSITY FACULTY OF MEDICINE, DEPARTMENT OF MICROBIOLOGY*

Introduction: With potent immunosuppressive therapies, renal transplant patients are more prone to a variety of infections with atypical pathogens and presentations.
Material and methods: We report a rare case of disseminated fungal infection due to Aureobasidium pullulans in a renal transplant patient.
Results: A 16-year-old female patient received a cadaveric renal transplant. She was discharged on tacrolimus based triple immunosuppressive therapy with good graft function. On posttransplant 6th month she was admitted with a draining subcuticular abscess on the incision site. Ultrasound showed signs of cellulitis with diffuse oedema and fluid collections which required surgical drainage. After obtaining cultures from blood and wound, broad spectrum antibiotics including cefoperazon-sulbactam, teicoplanin and antifungal therapy with fluconazole were initiated with simultaneous reduction in the immunsuppresive therapy. Cultures revealed multicellular filamentous hyphal structures classified as Aureobasidium pullulans. Due to lack of response and recurring subcuticular abscesses after 2 weeks, fluconazole was substituted with liposomal amphotericin B for 5 weeks and then to voriconazole. However 6 days later, voriconazole had to be switched to caspofungin because of complaints of blurred vision, which was considered as a side effect of voriconazole. Despite therapy, she started to experience increasing dyspnea with cough and diffuse nodular pneumonic infiltrates were noticed on chest X-ray and thoracic computarized tomography. All immunsupresive treatment except prednizolon 10 mg/d was withdrawn for 7 months. Voriconazole was started again due to detection of Aureobasidium pullulans in sputum. The lesions completely healed without signs of recurrence after 5 months. The patients is now well with a creatinine level of 0.7 mg/dl.
Conclusions: Although Aureobasidium pullulans is a saprophytic fungal pathogen, it should be kept in mind as an aetiological agents of opportunistic infections in renal transplant patients. Timely interventions including surgical drainage, antifungal treatment with reduction/cessation of immunosuppresives are associated with good outcomes.

P400 - Prevalence of hyperlipidemia in pediatric renal transplant recipients

IPEK KAPLAN BULUT, NIDA DINCEL, SEVGI MIR
EGE UNIVERSITY MEDICAL FACULTY, DEPARTMENT OF PEDIATRIC NEPHROLOGY

Introduction: Hyperlipidemia is a significant metabolic disorder that is common after solid organ transplantation and ıt is a risk factor for atherosclerosis. Studies associated with dyslipidemia were done commonly in adult patients and involved short-term follow-up results. But, a few papers were performed about dyslipidemia on long-term follow-up

in renal transplant recipients. The aim of the present study was to determine lipid abnormalities, to detect prevalence of dyslipidemia, and to describe profile of lipid in pediatric renal transplant recipients.

Material and methods: This study was done performed in children who underwent renal transplant recipients on Ege University. The inclusion criteria were: age from 3 years to 17 years, follow-up time at least 1 year after RTx. Blood samples for lipid were taken after a 12-hour overnight fast. Hypercholesterolemia was defined as total cholesterol≥ 200 mg/dL or low-density lipoprotein (LDC)≥100 mg/dL, and hypertriglyceridemia as triglycerides≥150 mg/dL. Values<40 mg/dL for male and 50 mg/dL for female was defined low high-density lipoprotein (HDL).

Results: There were 53 (50.5 %) male patients and 52 (49.5 %) female patients.Fifty-six (53.3 %) patients received a kidney from a cadaver donor and 49 (46.7 %) patients received a kidney from a living donor. The prevalence higher total cholesterol level at 1, 3, 5, and 10 years were 36.4 %, 38.4 %, 43 %, and 21.7 %, respectively. The prevalence higher LDL level at 1, 3, 5, and 10 years were 33 %, 37.4 %, 40.2 %, and 30.4 %, respectively. The prevalence higher TG level at 1, 3, 5, and 10 years were 31.3 %, 34 %, 37.5 %, and 34.7 %, respectively.

Conclusions: In conclusion, we observed a high prevalence of hyperlipidemia in pediatric renal transplant recipients. Lipid levels should be monitoring needed on follow-up. Longitudinal prospective studies are needed associated with prevalence of hyperlipidemia in pediatric renal transplant recipients.

P401 - Cooperative and interdisciplinary research platform for paediatric renal transplantation in Europe: the web-based CERTAIN Registry

LUKASZ PLOTNICKI[1], BRITTA HÖCKER[1], KAI KRUPKA[1], CHRISTIAN D. KOHL[2], AXEL RAHMEL[3], LARS PAPE[4], PETER HOYER[5], STEPHEN D MARKS[6], NICK WEBB[7], OGUZ SÖYLEMEZOGLU[8], REZAN TOPALOGLU[9], SZABó ATTILA[10], TOMAS SEEMAN[11], E. A. MARLIES CORNELISSEN[12], NOEL KNOPS[13], RYSZARD GRENDA[14], BURKHARD TÖNSHOFF[1]

[1]*UNIVERSITY CHILDREN'S HOSPITAL HEIDELBERG*
[2]*COORDINATION CENTRE FOR CLINICAL TRIALS, UNIVERSITY OF HEIDELBERG*
[3]*EUROTRANSPLANT FOUNDATION, LEIDEN*
[4]*CENTRE FOR PAEDIATRICS AND ADOLESCENT MEDICINE OF HANNOVER MEDICAL SCHOOL, HANOVER*
[5]*UNIVERSITY CHILDREN'S HOSPITAL, ESSEN*
[6]*GREAT ORMOND STREET HOSPITAL FOR CHILDREN, LONDON*
[7]*ROYAL MANCHESTER CHILDREN'S HOSPITAL, MANCHESTER*
[8]*GAZI UNIVERSITY, ANKARA*
[9]*HACETTEPE UNIVERSITY, ANKARA*
[10]*UNIVERSITY CHILDREN'S HOSPITAL, BUDAPEST*
[11]*UNIVERSITY CHILDREN'S HOSPITAL, PRAGUE*
[12]*RADBOUD UMC, NIJMEGEN*
[13]*UNIVERSITY CHILDREN'S HOSPITAL, LEUVEN*
[14]*CHILDREN'S MEMORIAL HEALTH INSTITUTE, WARSAW*

Introduction: The outcome of paediatric renal transplantation has improved significantly during the last decade. However, several unmet clinical needs such as graft failure mainly caused by chronic rejection, long-term toxicity of immunosuppressive therapy, absence of tolerance-inducing protocols, secondary cardiovascular co-morbidity, post-transplant lymphoproliferative disease, suboptimal longitudinal growth, quality of life, adherence and structured transition programmes to adult care require intense interdisciplinary clinical research. Therefore, we recently founded the Cooperative European Paediatric Renal TransplAnt INitiative (CERTAIN; www.certain-registry.eu) as a research platform built upon a novel, web-based registry: the CERTAIN Registry.

Material and methods: The registry collects essential information on kidney transplantation-related and paediatric-specific topics. Its post-transplant outcome dataset is compatible with the European Framework for Evaluation of Organ Transplants (EFRETOS) project.

Results: The CERTAIN web application does not require any local software installation and can be used as (i) a registry capturing a minimum or extended dataset, (ii) a centre- and/or country-specific transplantation database, and as (iii) an electronic patient chart. In each scenario, data can be exported directly from the CERTAIN web application into an SPSS- or SAS-compatible data format for scientific analyses. The aspects of data ownership, evaluation and publications are regulated by the registry's rules of procedure. Automatic software-validation and a two-step manual data review process ensure data quality. To minimise redundant data entry, the registry establishes data exchange with systems such as Eurotransplant, the Collaborative Transplant Study (CTS) and the registry of the European Society of Paediatric Nephrology (ESPN/ERA-EDTA registry). The system fulfils all regulatory and ethical requirements regarding patients' data privacy and security, incorporating the concepts of the German Technology, Methods and Infrastructure for Networked Medical Research (TMF: www.tmf-ev.de) organisation.

Conclusions: Utilising modern information technology, the recently established multinational CERTAIN Registry fills a gap for European collaborative research and quality assurance in paediatric renal transplantation.

P402 - A Plasmocitoma like PTLD Epstein-Barr virus (EBV) negative after kidney transplantation

IRENE ALBERICI, FRANCESCA MENCARELLI, FRAIA MELCHIONDA, MARTINO MARSCIANI, GIOVANNI MONTINI, ANDREA PESSION
S.ORSOLA-MALPIGHI HOSPITAL - DEP. PEDIATRICS

Introduction: Post-transplant lymphoproliferative disease (PTLD) is a major graft and life-threatening complication of pediatric renal transplantation (RT). It is usually an uncontrolled B lymphocyte proliferation, within the context of post-transplant immunosoppression and is frequently driven by EBV infection. PTLD typically appears within a short post-transplant period: 47 % of cases occur within 6 months and 90 % within 5 years. Plasmoblastic lymphoma are anecdotal.
Material and methods: We report the case of a 19-year-old boy with primary diagnosis of ARPKD, who developed ESRD and started dialysis when he was 7. He successfully underwent RT from a cadaveric donor at the age of 8 years. He subsequently developed hepatic fibrosis and portal hypertension, which required annual MRIs, Doppler ultrasound and endoscoscopic evaluation. He received immunosoppression with calcineurin inhibitor (FK506) and mycophenolate mofetil (MMF), as steroids were stopped 2 years after transplantation. Despite kidney donor was EBV positive, our patient never showed a rise of EBV viral load.
Results: He came to our attention for an acute abdominal pain at the age of 19 years. US and CT imaging showed abdominal enlarged lymphnodes packages and suspected ileal intussusception, which required partial ileal resection for an important endoluminal lesion. The hystological picture showed a plasmocytoma-like PTLD. EBV and CD20 negative. Bone marrow biopsy was normal. Treatment of PTLD was done by reduction of immunosoppresion, discontinuing MMF and lowering the target level of FK506; oral steroids were started. PET-CT and MRI, performed 10 and 30 days later, were normal.
Conclusions: We described this case because there are some atypical features: 1. the histological picture is exceptional: a plasmablastic lymphoma not EBV related and 2. the latency (11 years) from the transplant to the PTLD appearance is rather long. Remission was obtained only reducing immunosoppression, after surgery of the abdominal mass.

P403 - Mycophenolate mofetil intolerance in paediatric renal transplant patients

HARSHINI DHARMAWARDANE, MOHAN SHENOY, NICHOLAS J A WEBB
ROYAL MANCHESTER CHILDREN'S HOSPITAL, MANCHESTER, UK

Introduction: Mycophenolate mofetil (MMF) is increasingly becoming a part of most immunosuppressive protocols, especially as part of a steroid sparing regime. However, the use of this agent has been reported to be associated with a number of adverse events.
Material and methods: We retrospectively analyzed the clinical records of 24 children who were commenced on MMF as part of initial immunosuppression (TWIST protocol) and also of 11 children who were switched to MMF as rescue therapy.
Results: Twenty four children with a median age of 16y (range 5 to 18) were administered MMF for a mean duration of 15±7 months. The mean dose of MMF was 289±72 mg/m2/dose. There were 11 episodes of acute rejection (AR) in 8 patients (33 %), including 7 episodes in the first 3 months. The mean eGFR at 1 year was 84 ml/min/1.73 m2. Twelve (34 %) developed gastrointestinal symptoms, including 8 who experienced weight loss (mean 9.7 %). The mean weight z scores at transplant, 6 months and at 1 year following the transplant was −1.13, -0.97, -0.73 respectively. 62 % of the children were anaemic at 1 year and 29 % also developed leucopaenia/neutropaenia. EBV and CMV viraemia were detected in 23 % and 17 % respectively. MMF had to be discontinued in 20 % due to GI symptoms, neutropaenia or recurrent infection after a period of 2–24 months. A further 31 % required dose reduction due to significant weight loss, neutropaenia or recurrent infection. In the MMF rescue group 3 developed weight loss necessitating withdrawal of the drug.
Conclusions: MMF therapy was associated with significant side-effects, necessitating drug discontinuation or dose reduction in nearly half the patients. In our experience, the TWIST protocol was associated with increased incidence of AR when compared to the original study.