Infectious disease

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SEVERE DENGUE HAEMORRHAGIC FEVER IN PEDIATRIC CRITICAL CARE DEPARTMENT DR. KARIADI HOSPITAL, SEMARANG, INDONESIA.

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ABSTRACT

A preliminary study was done in 68 cases with severe Dengue Haemorrhagic Fever (DHF) in the periode of 1st October 1995 untill now. The age was between 1 - 14 years. The diagnosis of DHF was based on the criteria of WHO with positive Dengue Blot Test. Severe DHF consisted of Dengue Shock Syndrome (DSS), DSS with prolonged or reccurent shock, DSS with severe bleeding, DSS with pulmonary edema. The aim of the study is to know of severe DHF and factors which influenced the outcome.

Result of the study: there was a tendency in increasing mortality rate in cases with high serum latic acid level, high anion gap, high arteriolo - alveolair O_2 gradient level and low serum albumin level.

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HEMORRHAGIC SHOCK AND ENCEPHALOPATHY SYNDROME IN THE NEGEV AREA OF ISRAEL: SEVERITY AND INCIDENCE

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Objective and study design: A retrospective study was performed for all patients diagnosed with hemorrhagic shock and encephalopathy syndrome (HSE) during 1984 to 1994. Soroka Medical Center is the only medical facility in the southern Negev region of Israel serving a population of ~400,000 residents, consisting primarily of Jews and Bedouins.

Results: 20 patients (17 Bedouins and 3 Jews) were diagnosed with HSE. Main features on arrival included profound shock and coma with convulsions. Active bleeding and/or disturbing coagulation tests with falling hemoglobin levels and thrombocytopenia was noted in every case. All infants developed diarrhea shortly after arrival. Elevated urea, creatinine and liver enzymes was noted in all cases. Annual incidence for infants <1 year of age was 5:10,000 for Bedouins and 0.6:10,000 for Jews. Patients ranged in age from 6-32 wks and arrived at the hospital late night/early morning (2:00am-11:00am), during winter/early spring (November-April). All were healthy prior to admission, with short prodromal symptoms of upper respiratory tract or gastrointestinal infection noted in 10 cases. Most infants had markedly elevated body temperature on arrival. A history of overwrapping and/or excessive heating was obtained in 4 of 20 infants. Bacteriological and virological cultures were negative in all infants. One infant died and neurological sequelae were observed in all survivors.

Conclusion: The high prevalence of hyperpyrexia during sleep in the presence of negative microbiological results with no evidence of excessive heating, and the high incidence of HSE among a closed, culturally isolated society known to have a high incidence of congenital malformations, may support previous assumptions that HSE results from hyperpyrexia, originating in most cases from a "physiologic" heat induced trigger which starts and peaks during the night in previously healthy infants with susceptible, predisposing genetic underlie.

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ICU MORTALITY IN PAEDIATRIC BACTERIAL MENINGITIS: A DESCRIPTIVE STUDY

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INTRODUCTION Bacterial meningitis is a common cause of admission in the paediatric age group, and one which still carries a high morbidity and mortality. These complications are strongly associated with a delay in antibacterial therapy. A significant proportion of these patients require mechanical ventilation; it is in this particular group of patients that survival is greatly diminished. The identification of risk factors for mechanical ventilation associated with bacterial meningitis may help improving survival by shortening the delay to ICU referral. The Paediatric Risk of Mortality Score (PRISM) is the most widely used scoring system in the paediatric ICU literature; the accuracy of PRISM on predicting outcome in meningitis has been shown to be poor. **AIM** We aimed to describe our population of patients with bacterial meningitis requiring ventilation, and then to identify predictors of survival. **METHODS** This study was conducted at the Baragwanath Hospital in South Africa which is an University-affiliated institution with and average annual paediatric admission of 4500 patients. Baragwanath ICU admits 250 non-neonatal paediatric patients per year. A retrospective chart review from January 1991 to December 1995 of 42 consecutive paediatric ICU admissions with bacterial meningitis was performed. **RESULTS** Approximately 150 cases of bacterial meningitis are admitted to the general paediatric wards every year; this constitutes ± 3% of all admissions. The mortality of these patients is ± 14%. During this time 42 (23M, 19F) patients (7%) were accepted for ICU admission, with a mortality of 42.2%. The median age was 9 months (range 15 days to 17 years). The median delay to hospital admission was 48 hours, and the median delay to ICU admission was a further 4 hours. The median duration of ICU stay was 48 hours (40 for non-survivors, 120 for survivors). The main presenting features were convulsions (34%), altered mental state (40%), fever (50%), respiratory symptoms (24%), headache (18%), and diarrhoea and vomiting (32%). The most common indications for ICU admission were seizures (55%), coma (36%), shock (26%), respiratory failure (29%) and acidosis (21%). In 29% of patients there was a cardiorespiratory arrest prior to admission. The most common organisms in the CSF was pneumococcus (57%), haemophilus influenza (15%) and E coli (12%). The presence of leucopenia (WCC < 5), a low platelet count (<100), acidaemia (pH<7.2), and the need for inotropic support were strongly associated with non-survival. Tachycardia and hypotension were not significantly associated with poor outcome, as has been previously reported. **DISCUSSION** Early diagnosis of meningitis and prompt institution of antibiotic therapy requires a high level of clinical suspicion. Paediatric patients with bacterial meningitis that require mechanical ventilation have a poor prognosis. There is little evidence to suggest that non-survival can be predicted prior to ICU admission, but a rapid deterioration requiring ventilation and inotropic support with evidence of severe sepsis (low platelet count, leucopenia) is almost invariably associated with a fatal outcome. The long term functional outcome of these patients make this disease even more devastating; the role of ICU in the management of these patients has yet to be fully established.

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SEVERE RESPIRATORY SYNCYTICAL VIRUS-ASSOCIATED RESPIRATORY FAILURE: PATTERNS OF LOWER RESPIRATORY TRACT DISEASE IN YOUNG INFANTS

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Approximately 10% of hospitalised infants with respiratory syncytial virus (RSV) infection require mechanical ventilation. Our general practice is not to use specific antiviral therapy. We have undertaken studies of RSV-infected mechanically ventilated patients without underlying congenital heart disease or immunodeficiency.

Study I (n=45): A retrospective review of 45 infants (mean post-conceptual age 48 weeks; median duration of intubation was 8 days (interquartile range 5-11). Blinded review of chest x-rays during the first three days of mechanical ventilation revealed a spectrum of lower respiratory tract findings from marked diffuse consolidation in all zones without hyper-inflation (n=10) to gross hyperinflation without consolidation (n=5), with the remaining patients have an intermediate picture (n=30). Death occurred only in patients who were at the poles of this continuum (4/10 consolidation and 1/5 hyperinflation). Patients at these poles could be differentiated by gender predominance, birth gestation, alveolar-arterial (A-a) oxygen gradient ($p<0.01$), oxygenation index ($p<0.01$), peak inspiratory pressure ($p<0.05$), and intubation days ($p<0.01$).

Study II (n=28): Prospective audit of infants with the aim of verifying the above differentiation. Separating patients based on their early x-rays and A-a gradient we confirmed the above predictable difference in duration of supportive therapy (consolidation *v* intermediate: 6(4-7) *v* 14(12-33) $p<0.01$).

Severe lower respiratory tract RSV-infection in young infants results in different distinctive patterns of disease with characteristic radiological and clinical features, and each has a predictable timecourse. Conflicting reports on special therapy should be interpreted with respect to these observations before making conclusions about the efficacy of any specific treatment.

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NOSOCOMIAL INFECTION AS A MORTALITY RISK FACTOR IN A PAEDIATRIC INTENSIVE CARE UNIT IN A DEVELOPING COUNTRY.

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INTRODUCTION: Globally, nosocomial infection is a major determinant influencing mortality in intensive care units, with an estimated incidence of 20% to 70%. In developing nations, this figure is often significantly higher due to limited resources and noncompliance with infection control procedures.

OBJECTIVES: To identify the incidence of and establish the prognosis for patients diagnosed with nosocomial infection in a paediatric intensive care unit (PICU).

METHODS: The 275 patients admitted to the PICU at Hospital Baca Ortiz, Quito from January 1995 through October 1995 were prospectively studied. Nosocomial sepsis cases were selected according to CDC criteria. Nosocomial pneumonia cases included mechanically ventilated patients following clinical, radiological and bacteriological criteria (positive culture of tracheal aspirate). Nosocomial central venous catheter (CVC) infections were diagnosed by positive cultures obtained from the catheter tip.

RESULTS: Of the 275 patients admitted, 18 (6.5%) developed nosocomial infection documented by positive blood culture. Mean length of stay in the PICU was 27.4 ± 30.6 days for infected patients versus 4.3 ± 4.2 days in uninfected patients (p=0.005). For 12 of the infected patients, the admitting diagnosis was a neurological condition including head trauma (n=2), convulsive disorder (n=2), and Guilliain Barre (n=1). 158 (58%) of the 275 patients underwent mechanical ventilation. Of these, 8 cases (5%) developed nosocomial pneumonia. Average elapsed time between admission to PICU and pneumonia diagnosis was 7.5 days (range 4 to 15 days). Gram negative pathogens, the most commonly identified organisms, were found in 94% of pneumonia cases, and included Pseudomonas aeruginosa (n=4), Klebsiella pneumoniae (n=2), Escherichia coli (n=2), Citrobacter freundi (n=1) and Acinetobacter calcoaceticus (n=1). Fungi were second most common (n=4) and finally gram positive cocci (n=1). Mortality due to nosocomial pneumonia was 40%, and rose to 66% when associated with culture proven bacteraemia. 95 (35%) of the 275 patients had central venous catheters placed. Of these, 76 (80%) developed infections at the catheter tip. In 70% of patients with infected CVC, the only indication for placement was I.V. fluid administration. Most common pathogens isolated from CVCs were gram negative bacteria.

CONCLUSIONS: Our data indicate that nosocomial infection represents an important risk factor influencing outcomes in PICUs in a developing country. Nosocomial infections were most common in patients who underwent mechanical ventilation and CVC placement. More stringent infection control procedures should be initiated, in addition to more clear indications for the need for mechanical ventilation and CVC placement.

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NOSOCOMIAL INFECTIONS IN 18 FRENCH NICU AND PICU : THE « REAPED » NETWORK.

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The French « Reaped » network was created to implement a nosocomial infections (NI) quality care program in NICU and PICU. The first objective was to describe the annual NI incidence rate in each ICU population : all patients stayed more than 48 hours in ICU.

Methods : NI criteria were defined by the Reaped group according to CDC criteria. All data were collected by a medical and nursing team. All infection data were validated by an external investigator.

Results : 4525 patients were admitted over a 14 months period. 68% were newborns. 371 NI were identified among 311 patients. The overall NI incidence rate (IR) was 8.2% and 5.9°/oo person day (from 5.0 to 8.2°/oo according to age, lowest rate for newborns). Septicemia (50% of NI) and pneumonia (41% of NI) were the two main NI. According to age, the septicemia IR varied from 6.8 to 10.9°/oo catheter day (lowest rate for newborns) and the pneumonia IR from 3.9 to 7.4°/oo ventilator day (lowest rate for newborns). There were very few other infections (UTI : 4%, IR : 7.4°/oo catheter day). Gram positive cocci were isolated in 73% of septicemia (70% of them were coagulase negative staphylococcal). Gram negative bacilli were isolated in 53% of pneumonia (40% of them were pseudomonas). 5% of NI were caused by candida, mostly septicemia. The septicemia and pneumonia IR varied according to unit even after adjustment for age.

Discussion : One explanation proposed by the Reaped network is the different uses and maintenance procedures of central line devices in each unit.

Conclusion : Central line related septicemia IR would be considered as a good indicator of quality of care by the Reaped network. Further studies would precise the definition of central line related infection in neonates and describe the different central line uses in each unit.

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CONVENTIONAL VERSUS LIPOSOMAL AMPHOTERICIN B IN CHILDREN.

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Objective: To assess the comparative antifungal efficacy and safety of two amphotericin B formulations in children with invasive mycosis.

Material and methods: The clinical data of 186 children wich suffered from a severe mycosis between Jan.1990-Dec.1994 and wich were treated with amphotericin B in 10 spanish hospitals were collected. Mean age was 6±3.9 years; 157 were male (84%) and 29 female (16%). The most common underlying diseases were leukemia/lymphoma (31%) and congenital heart defects (20%). The major pathogens isolated were candida albicans (61%), other candida (18%) and aspergillus (17%).

Results: Conventional amphotericin (CA) was administered in 118 children (63%) and liposomal amphotericin (LA) in 68 (37%). In the CA group, the starting dose was 0,3±0,1 mg/kg, reaching a maximal dose of 0.9±0.3 mg/kg after 4.7±3 days. Maintenance time was 14±10 days and the cumulative dose: 12±17 mg. In the LA group, the starting dose was 1.1±1 mg/kg, reaching a maximal dose of 2.9±3.4 mg/kg ($p<0.01$) after 5±5 days. Maintenance time was 19±16 days ($p<0.05$) and the cumulative dose 42±37 mg ($p<0.05$). The reasons for LA use were: elective in 66% of cases, previous renal failure in 29%, and CA inefficacy in 4%. Hepatic or renal function impairment was two times more frequent in LA group than in CA group. The antifungal efficacy was 62% for CA and 67% for LA. Therapeutic failure or toxicity induced withdraw of CA in 7% of cases, vs. 1.5% for LA ($p<0,01$). Mortality was not different in both groups (21 vs. 22%). Adverse effects were related to CA in 28 events vs. only one in LA group ($p<0.01$). The commonest side effects in CA patients were fever (18%), chills (10%) and nausea (9%). In CA group, 44 cases (37%) developped analitical anormalities related with amphotericin, vs. 10 cases (15%) in LA patients ($p<0.001$). In the first group, the commonest serum alterations were hypokaliemia (25%), raised creatinine (14%) and bilirrubin (6%). In the second one, hypokaliemia presented in 7% of cases ($p<0.01$), raised bilirrubin in 6% and creatinine in 3% ($p<0.05$).

Conclusions: The antifungal efficacy of LA is at least the same of CA. From the clinical and analitical points of view, LA is much less toxic than CA. LA can be used at a greater dose than CA and is safe in children with renal failure.

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POPULATION PHARMACOKINETICS OF TOBRAMYCIN (TOBRA) IN THE NEWBORN.

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Introduction

The aminoglycoside antibiotics are frequently used in newborns for the treatment of severe infection and sepsis due to Gram-negative microorganisms. The currently recommended dosage schedule for TOBRA (2.5 mg/kg q18h) does not take into account differences in gestational or postnatal age during the first 4 weeks of life. We questioned the validity of these recommendations and studied the population kinetics of tobramycin to establish predictive equations that enables the clinician to select the appropriate initial dosing schedule.

Methods

TOBRA trough ($t=0$) and peak values ($t=1$) were taken on day 2-4 after birth in 460 newborns. TOBRA was administered as a 30-minute intravenous infusion already in an adapted dosage schedule: 3.5 mg/kg q24h in infants with GAs < 28 weeks; 2.5 mg/kg q18h in infants with GAs between 28-36 weeks and 2.5 mg/kg q12h in infants with GAs > 36 wks. TOBRA concentrations were analyzed by TDX-assay.

A one-compartment model was assumed and non-linear mixed effect modelling (using NONMEM) was applied to the data. A trough level < 2 mg/L and a peak level between 6 and 10 mg/L was required.

Results

With the present dosage scheme 40% of the trough levels were too high and almost 60% of the peak levels too low. Calculations showed that the following dosage schedule should result in optimal levels of TOBRA.

preterm infants GAs < 28 wks:	6 mg q48h
preterm infants GAs 28-36 wks:	4.5 mg q36h
preterm infants GAs > 36 wks:	3 mg q24h

Conclusions

1. The currently recommended dosage schedules for TOBRA result in high trough and low peak levels.
2. Prolongation of the dosing interval and increasing the amount of drug per dose according to the above scheme will improve TOBRA level control.