Pulmonary

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EARLY VERSUS LATE DEXAMETHASONE TREATMENT IN PREMATURE INFANTS WITH HIGH RISK FOR CHRONIC LUNG DISEASE

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In this controlled, prospective study 30 ventilated premature infants with a birth weight ≤ 1250 g were randomized to receive treatment with dexamethasone (DEX) either on day 7 of life or on day 14 of life. DEX was given over 16 days tapering from 0.5 mg/kg/day to 0.1 mg/kg/day.

The infants treated with DEX on day 7 of life could be weaned earlier from the ventilator - in median after 14 days (range 10 - 34) versus 24 days (range 8 - 44) in the late treatment group ($p = 0.01$). The need for supplemental oxygen was shorter in the early treatment group - in median 24 days (range 10 - 50) versus 40 days (range 10 - 70) ($p = 0.2$, ns). The incidence of chronic lung disease was lower in the early treatment group - 6 of 14 infants (42.9%) versus 10 of 16 patients (62.5%) (ns).

To evaluate the long-term efficacy of early DEX treatment we performed a respiratory function test in the age of 3 - 6 months using an infant whole body-plethysmograph. The intrathoracic gas volume (ITGV), the airway resistance (R_{aw}) and the airway conductance (G_{aw}) were measured and no significant differences could be detected between the groups.

The frequency of adverse effects due to DEX therapy was found to be without significant differences between the early and the late treatment group.

We conclude that early DEX treatment had short-term improvements in pulmonary outcome in our study population, long-term efficacy however, remained unproven.

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OXIDATIVE STRESS AND ANTIOXIDANTS IN CHRONIC LUNG DISEASE OF PREMATURITY

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Several factors contribute to the development of chronic lung disease (CLD) in premature infants including structural immaturity of the lung, mechanical ventilation, and oxidative stress. Reactive oxygen species are formed during normal cellular metabolism but they are generated in higher concentrations during inflammation or inhalation of high oxygen concentrations.

To study the relationship between increased oxidative stress, antioxidants and the development of CLD we examined 102 ventilated premature infants with birth weights below 1500g. 32 infants developed severe chronic lung disease of prematurity (CLD), defined by radiological signs of CLD and an increased oxygen requirement at a postconceptional age of 36 weeks, and 29 infants had moderate CLD with an increased oxygen requirement on day 28 but not at an age of 36 weeks. Ventilator settings (FiO_2 , peak inspiratory and mean airway pressure) and the incidence of early-onset-sepsis were significantly higher in the severe CLD group than in infants with moderate CLD or without CLD ($n=41$) during the first week of life. Plasma concentrations of the two antioxidative substances bilirubin and uric acid (UA) were comparable in all groups during the first days of life. However, on day seven bilirubin and UA were significantly decreased in the plasma of infants with severe and moderate CLD compared to the non CLD group ($p<0.001$). There was no difference between both CLD groups.

In serially obtained tracheal aspirate fluids (TAF) malondialdehyde (MDA) was measured by HPLC as an indicator of lipid peroxidation reflecting oxygen injury of the lung. UA was found in higher concentrations in TAF than bilirubin. UA has been proven to be a potent antioxidant, capable to react especially with hydroxyl radicals and hydrochlorous acid, which play an important role in the induction of lipid peroxidation. Infants with severe CLD had significantly higher MDA/UA ratios in TAF from day 5 to 14 compared to the non-CLD group ($p<0.01$). MDA/UA ratios in TAF of infants with moderate CLD were significantly higher from day 7 on but still lower than in the severe CLD group. In addition, the ratio oxidized / reduced glutathione was significantly increased in TAF of infants with CLD compared to infants without CLD between day 5 and 14.

The data support the hypothesis that an imbalance of oxidative stress and antioxidant defense contributes to the onset of CLD at the end of the first week of life.

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TITLE: ROCURONIUM USE IN CRITICALLY ILL CHILDREN

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Introduction. Rocuronium bromide (Roc), a neuromuscular blocking agent with an onset time close to that of succinylcholine^{1,2}, has been studied in American Society of Anesthesiologists' Physical Status (ASA) I or II pediatric patients under non-critical elective conditions. There is a paucity of studies looking at the pharmacodynamics of Roc under emergent conditions, involving pediatric patients who are ASA III or IV, without the use of adjuvant inhaled anesthetics³.

Methods. With approval of our Committee on Clinical Investigations (IRB), Roc 1.2 mg/kg was administered to 15 ASA III/IV pediatric intensive care patients (age 40 days to 23 months; M:F=8:7) on intravenous sedation. The time to reach 25% and 10% of baseline tetanic stimulus response was recorded using a Relaxograph NMT-100 nerve stimulator/recorder (Datex, Helsinki). Depth of clinical relaxation at the 25% level was recorded.

Results. The time from rapid bolus to 25% was 25.4 ± 12.6 sec with a range of 10-50 sec; and to 10% was 30.1 ± 17.6 sec, with a range of 10-69 sec. At the 25% level, excellent clinical relaxation was seen.

Conclusion. In critically ill children, use of Roc at 1.2 mg/kg produces rapid onset of neuromuscular blockade and excellent clinical relaxation, such that Roc should be considered for rapid sequence intubation.

References.

1. *Int Anesth Clin.* 1995;33(1):39-60.
2. *Anesthesiology.* 1994;81(5):1110-1115.
3. *Anesthesiology.* 1991;75(3A):A787.

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COMPUTED TOMOGRAPHY OF THE CHEST IN MECHANICALLY VENTILATED CHILDREN

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Computed tomography of the chest (CT) in mechanically ventilated adults can detect intrathoracic pathology not appreciated on chest radiographs (CXR) and influence intensive care management. No such data exists for ventilated children.

AIMS: 1) To assess if CT provides additional information over CXR regarding extent and nature of intrathoracic disease in ventilated children. 2) To determine whether such information alters clinical management.

INCLUSION CRITERIA : 10 ventilated children with CXR changes inconsistent with their respiratory status underwent CT if either a) $PaO_2:FiO_2$ ratio <30 and/or mean $Paw > 15$ cm H_2O or b) there was an unexplained increase in ventilatory requirement.

METHODS : High resolution CT was performed in 3 patients and spiral CT in 7 patients. To ensure minimal transport related morbidity, patients were transferred to the CT scanner by a specialised mobile intensive care team.

RESULTS: In 2/10 patients CT demonstrated greater extent of disease than appreciated on CXR but did not significantly alter clinical management. In 7/10 patients CT provided additional information regarding the nature of disease present. In 2/7 children this involved a further diagnosis and in 5/7 children the exclusion of a suspected pathology.

New information led to a positive therapeutic intervention in 2 children, prevented inappropriate manoeuvres in 3, and had no significant effect on acute management in 2 children.

CONCLUSIONS: Initial data suggests that in a selected group of mechanically ventilated children chest CT can add to the sensitivity and specificity of intrathoracic diagnosis provided by the chest radiograph and directly influence acute management. Case selection criteria and choice of the most appropriate protocol requires further study.

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PRESSURE CONTROL VENTILATION INCREASES DYNAMIC COMPLIANCE AND DECREASES PEAK INSPIRATORY PRESSURE IN INFANTS AND CHILDREN Ira M. Cheifetz, MD; Jon N. Meliones, MD; Barbara G. Wilson, RRT; Frank H. Kern, MD; William J. Greeley, MD. Duke University Medical Center, Division of Pediatric Critical Care Medicine, Box 3046, Durham, NC 27710 USA

Introduction: Pressure control ventilation (PCV) utilizes a decelerating flow pattern which may improve gas distribution and lead to alveolar recruitment. In contrast, volume control ventilation (VCV) employs a constant flow. In children, the effects of PCV as compared to VCV are unclear. The purpose of this study was to determine how these two modes compare in terms of dynamic compliance (C_{dyn}), peak inspiratory pressure (PIP), and mean airway pressure (Paw) at equivalent minute ventilation.

Methods: Sixteen infants and pediatric patients ranging in age from 1 day to 13 years were studied. Diagnoses included ARDS (6), postoperative cardiac surgery (7), head trauma (1), and restrictive lung disease (2). Patients were randomized to PCV (9) or VCV (7). Initial measurements of gas exchange (ABG's) and respiratory mechanics (Ventrak, Novamatrix Medical Systems) were obtained after a 20 minute stabilization period. Respiratory mechanics included PIP, PEEP, Paw, delivered tidal volume, and C_{dyn} (ΔVolume/ΔPressure). The patients were then crossed over to the alternate mode of ventilation holding delivered tidal volume, PEEP, inspiratory time, minute ventilation, and FiO₂ constant. Data were collected after 20 minutes. In each mode the absence of intrinsic PEEP was confirmed. To assure that the measurements were not affected by changes in clinical status, the patients were returned to the initial mode of ventilation and measurements repeated (Final). Patients were ventilated with a Siemens 900C or SV300.

Results: Data were analyzed using 2-way analysis of variance with repeated measures. (mean ± sem; * = p < 0.05 vs. VCV)

	VCV	PCV	Initial	Final
C _{dyn}	3.5±0.7	4.3±0.8 *	3.7±0.6	3.9±0.7
PIP	32±1.0	30±1.0 *	31±1.0	31±1.0
Paw	9.2±0.6	10.9±0.7 *	9.7±0.7	10.0±0.8
PaO ₂	97±14	92±10	87±9	97±14

Discussion: At the same minute ventilation, the decelerating flow pattern of PCV resulted in a 23% increase in C_{dyn} and an 18% increase in Paw while decreasing PIP by 6%. The lack of a significant change in oxygenation may be a result of the limited time in each ventilator mode as well as the inclusion of patients with both normal and abnormal lungs. There was no significant difference in initial and final measurements indicating patient stability.

The beneficial effects of increasing C_{dyn} and Paw while decreasing PIP indicate that PCV may be a preferable mode of ventilation in patients with lung injury. Further randomized studies examining the effect of PCV on respiratory outcome measures in pediatrics are indicated.

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NASAL HIGH FREQUENCY OSCILLATION AND NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE FOR RESPIRATORY INSUFFICIENCY IN NEWBORN INFANTS Eric G. Brouwer, Mark A. van der Hoeven, Danilo W. Gavilanes, Pieter L. Degraeuwe, Wiel J. Maertzdorf, Carlos E. Blanco, Department of Neonatology, University Hospital Maastricht, The Netherlands

OBJECTIVE: to evaluate the effect of nasal high frequency oscillation (nHFO) during nasal continuous positive airway pressure (nCPAP) in newborn infants with moderate respiratory insufficiency we performed a non controlled observational study.

PATIENTS AND METHODS: 10 patients (gestational age 25-37 weeks, birth weight 570-3100 gram, age 4 hrs - 21 days) were treated with nHFO. We used an Infant Star ventilator, initial setting mean airway pressure 4-8 cm H₂O and amplitude ΔP 35-45 mm H₂O. A tube with an inner diameter 2.5-3.0 mm was placed nasally at a depth of 3 cm. Indications for nHFO were clinical signs of respiratory distress, increasing oxygen need and/or CO₂ retention during prior nCPAP.

RESULTS: In 9 patients we observed a decline in pCO₂ within 2.5 hours (Wilcoxon, p=0.013; figure). There was no effect on oxygen need, heart rate or blood pressure.

CONCLUSION: nHFO reduces pCO₂ in selected newborn infants with moderate respiratory insufficiency. A randomized study should be done to determine the exact value of nHFO.

034

CONTINUOUS NEGATIVE EXTRATHORACIC PRESSURE (CNEP) FOR POSTOPERATIVE MANAGEMENT OF CONGENITAL DIAPHRAGMATIC HERNIA (CDH).

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Prolonged positive pressure ventilation following repair of CDH is associated with a high prevalence of iatrogenic lung injury. In our unit during 1981-1990 3/4 late deaths after repair of CDH were due to chronic lung disease.

Since 1990 babies requiring assisted ventilation for more than 7 days following surgery were transferred to a CNEP chamber to limit lung injury. CNEP of -6cm of H₂O was combined with positive pressure ventilation via an endotracheal tube during the transition phase. Immediate reduction of peak inspiratory and positive end pressures were possible and following extubation respiratory support was maintained by CNEP with appropriate inspired oxygen.

Overall outcome:

	1981-1990 n=68	1990-1995 n=40
Deaths before surgery (%)	11 (16.2)	3 (7.5)
Postoperative Deaths (%)	12/57 (21)	1/37 (2.7)*
Postoperative Survival (%)	45/57 (78.9)	36/37 (97.3)
Overall Survival (%)	45/68 (66.2)	36/40 (90.0)

Ventilatory support after Surgery:

	1981-1990 n=57		1990-1995 n=37	
Ventilation	< 7 days	> 7 days	< 7 days	> 7 days
Died (%)	8 (14)	4 (7)	0	1* (2.7)
Survived (%)	35 (61)	10 (17.5)	20 (54)	16 (43)
CNEP	0	0	0	11/16

* Referred for ECMO

During 1990-1995 11/16 who were ventilated for more than 7 days received CNEP and there were no deaths and no chronic lung disease in that group.

CNEP assisted ventilation may be an important management option for babies who require prolonged respiratory support to avoid the adverse effects of chronic positive pressure ventilation.

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Perfluorocarbon Associated Gas Exchange (PAGE) - Middle European Experience in Human Babies

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Introduction So far 2 modes of liquid ventilation (LV) have been used in experimental animals and, exceptionally, in humans: 1. **total liquid ventilation** (TLV)-functional residual capacity (FRC) is filled by perfluorocarbons (PFC), and slow tidal volume (T_v) breathing is performed by PFC. 2. **partial liquid ventilation** (PAGE) - only FRC is filled by PFC. Gas T_v is delivered by conventional mechanical ventilation (CMV), high frequency jet ventilation (HFJV) or high frequency oscillation (HFO). The aim of our study is to present our limited experience with PAGE in newborns and infants.

Methods PAGE was used in two groups of infants: 1. in 2 infants with brain death before disconnection from CMV, because recipients for organ transplantation were not available. These infants have relatively normal lungs (FiO₂ less than 0.4). Infants stayed on PAGE for 1 hour, during that period no ventilator manipulations were made. After PAGE, infant were switched to CMV for next 6 hours. 2. very critically diseased infants with ARDS (RDS) - 2 on ECMO more than 5 days, 1 before cannulation for ECMO, 4 on HFO because of intractable respiratory failure. Preoxygenated RM 101 (Mitenti, Italy) was used in the doses up to 40 ml/kg intratracheally. Blood gases and parameters of pulmonary mechanics were followed (dynamic compliance - C_{dyn}, airway resistance - Raw, Bicore monitor). PAGE was combined with NO inhalation (5-80 p.p.m. in 2 infants). In both groups ad hoc an approval from a local ethical commission and informed parental consent were obtained.

Results In the first group with relatively normal lung parameters of oxygenation drops after PFC instillation intratracheally and stayed depressed for 4-6 hours. Slight pCO₂ retention occurred in both cases during PAGE. C_{dyn} increased almost double during PAGE period, Raw drops transiently after PFC instillation but in 10 minutes they were identical like in prePAGE period. Parameters of oxygenation (PaO₂/FiO₂) after 4-6 hours after PAGE improved and were better than in prePAGE period. After that time infants were disconnected and died. In the second group no improvement of oxygenation was seen in one ECMO baby, in spite of transient improvement of C_{dyn}. In the second ECMO baby, oxygenation improved and flow of pump could be decreased by more than 20%. None of these babies, however, survived, improvement was only transient in spite of repeated doses of PFC. In these babies serious problems were to maintain the adequate FRC by liquid, because of severe air leak. In 5 babies on HFO/HFJV with severe ARDS/RDS the improvement of oxygenation were seen in all the cases immediately after PFC instillation for the period of 4-6 hours. After that period, PFC dose had to be repeated. Two babies of this group survived.

Conclusion. PAGE is going steadily from labs to clinical practice. It is simple, could be performed anywhere, cheaper than TLV. However, because Liquivent - Perflubron (Alliance Pharmaceutical) is not available in Europe, RM 101 of 82 (Mitenti, Italy) is the only solution, which could be currently used here. Before the widespread use of PAGE in clinics, liquid network among most NICUs and PICUs must be built up, the criteria for PAGE must be defined and ethical-legal problems resolved as well. After resolution of these particular problems PAGE can be life saving procedure for very special part of critically ill newborns and infants.

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THE USE OF BI-LEVEL POSITIVE AIRWAY PRESSURE (BIPAP) IN END-STAGE CYSTIC FIBROSIS PATIENTS AWAITING LUNG TRANSPLANTATION.

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Introduction: Cystic fibrosis (CF) patients awaiting lung transplantation present a therapeutic dilemma when severe respiratory decompensation occurs. Endotracheal intubation and mechanical ventilation is known to have no long term benefits and is associated with high morbidity and mortality. Noninvasive respiratory support appears to be a beneficial alternative.

Methods: We instituted BIPAP (Respironics, Inc., Murrayville, PA) in 9 end-stage CF patients who were admitted to the Pediatric ICU with severe respiratory decompensation. All patients were awaiting lung transplantation. After a control period, BIPAP was applied via a tight fitting nasal or facial mask, using the spontaneous breathing mode. Expiratory pressures were set at 4-8 cm H₂O. Inspiratory pressures were started at 8 cm H₂O and increased in 2 cm H₂O increments until the patient's respiratory comfort was achieved and substantiated by non-invasive monitoring. Patients were instructed to use BIPAP during night sleep and whenever subjectively required. Data are reported as mean $\pm$ S.D.

Results: All 9 patients utilized nocturnal BIPAP for 6-10 hours/day during a follow-up period of 2-19 months. Compared to their pre-BIPAP status, the patients' oxygen requirement and respiratory rate both decreased significantly ($p < 0.05$), and their arterial oxygen saturation increased significantly ($p < 0.05$) with the use of BIPAP [see figure]. All patients tolerated BIPAP without any reported discomfort. 3 patients ultimately underwent successful lung transplantation after having utilized nocturnal BIPAP for 4, 6, and 16 months.

Conclusion: BIPAP therapy improves the respiratory status of decompensating end-stage CF patients. It is well tolerated for long term use at home, and provides an extended period of respiratory comfort and stability for CF patients awaiting lung transplantation.

*Piper AJ, et al: Chest 1992; 102(3):846-850.