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PREDICTORS OF EARLY HOSPITAL READMISSION IN CHILDREN WITH ASTHMA

P OZUAH¹, M REZNIK¹ ¹ALBERT EINSTEIN COLLEGE OF MEDICINE / CHILDREN'S HOSPITAL AT MONTEFIORE (USA)

Objective: To identify predictors of early readmission in children with asthma.

Design/Methods: A case-control study of a cohort of children hospitalized for asthma. Cases were children with asthma readmitted with the same diagnosis within 30 days of the index admission. For each case, we identified up to two controls which were children hospitalized for asthma but not readmitted within 30 days. Cases and controls were matched for age, gender, ethnicity, season and year of index admission. Data were abstracted from the medical records. Bivariate analyses (clogit, GEE statistics) were performed. Conditional logistic regression analysis determined the relative contribution of independent variables.

Results: 458 subjects were analyzed (161 cases, 297 matched controls). Cases and controls were successfully matched (mean age for cases 6.4 years (SD 5.3) vs 6.4 years (SD 5.1) for controls; for both groups 64% were male, 61% Hispanic and 36% African American). Cases had a greater mean number of lifetime admissions for asthma (8.2 vs 3.3, $p < .0001$), were more likely to have received a pulmonary consultation prior to the index admission (OR 2.49, 95% CI 1.45–4.29) and to have a history of asthma ICU admission (OR 2.20, 95% CI 1.31–3.70). Using conditional logistic regression, history of multiple lifetime admissions was found to be an independent predictor of readmission. Exposure to environmental triggers was not associated with readmission. No significant difference was found between the groups on mean oxygen saturation at index admission or discharge, need for oxygen supplementation during the index admission, and presence of wheezing at discharge.

Conclusions: Our findings suggest that early readmission occurs among a subset of children with greater disease severity. History of multiple admissions, receipt of pulmonary consultation and prior ICU admission may identify children who are more likely to be readmitted and thus, guide inpatient and outpatient asthma management.

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PRENATAL EXPOSURE TO DEXAMETHASONE PERMANENTLY ALTERS THE EXPRESSION OF 11BETA HSD1, MINERALCORTICOID AND 5HT1B RECEPTOR IN RAT HIPPOCAMPUS

KC PAGE¹ ¹BUCKNELL UNIVERSITY (USA)

Changes in gene expression in the brain, pituitary, and adrenal have been reported in a number of prenatal stress studies. However, it is not clear whether the high maternal glucocorticoid (GC) level is directly responsible for these perturbations. We exposed rat dams to DEX during gestation days 14–19 and found a significant decrease in birth weight and adult weight of the male offspring. In addition, this treatment elicited a significant increase in serum ACTH and CORT. In contrast, circulating levels of serotonin were significantly lower in the DEX-exposed adult males. Using real time RT-PCR we measured a significant decrease in the hippocampal mineralcorticoid receptor (MR) and serotonin receptor, 5-HT1B. In contrast, the mRNA levels measured for hippocampal 5-HT1A, 5-HT2A, and glucocorticoid receptor (GR) were not significantly different from the control animals. Interestingly, males exposed to DEX in utero exhibited a significant increase in hippocampal 11 beta hydroxysteroid dehydrogenase 1 (11beta HSD1). Unlike the placental 11beta HSD2 isozyme which inactivates endogenous CORT, hippocampal 11beta HSD1 regenerates active corticosterone from inert 11dehydrocorticosterone. It is becoming increasingly apparent that glucocorticoid actions are not only mediated via intracellular GR and MR, but by the presence of 11beta HSD1 and its capacity for regulating intracellular concentration of active GC. HPA axis hyperactivity may result, in part, from a reduced hippocampal tonic inhibition. It is possible that the significant changes in hippocampal corticosteroid receptor and 11beta HSD I gene expression contribute to this loss of inhibition. Moreover, since 5HT receptors in the rat hippocampus are normally under tonic inhibition by corticosteroid, the elevation of both circulating and intracellular CORT would suppress the serotonergic system in this region. These data demonstrate that exposure to DEX in utero has persistent effects on the adult brain thus supporting the prenatal origin of adult dysfunction hypothesis.

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CORRELATION BETWEEN CYTOKINES, BDP AND MODALITY OF VENTILATION IN PRETERM NEWBORNS: IMPROVEMENT WITH MELATONIN

E GITTO¹, RJ REITER¹, C BUGGE¹, I BARBIERI¹, R PANTANO ¹DPT. OF MEDICAL PEDIATRICS, NEONATAL INTENSIVE CARE UNIT, UNIVERSITY OF MESSINA (ITALY)

Background: Ventilator-associated lung injury traditionally has been believed to result from the use of high pressures and multiple ventilation strategies have been tried to reduce injury and improve outcomes. Inflammatory cytokines are present in the lungs of newborns with BPD, oxidant injury may be another serious cause of lung injury and melatonin is known act as radical scavenger.

Aims: The aim of current study was to evaluate lung inflammatory response in preterm infants with respiratory distress syndrome (RDS), mechanically ventilated with and without VG, as measured by proinflammatory cytokines (IL-6, IL-8, and TNF α) in tracheobronchial aspirate and by clinical outcome in a group of 55 newborns treated with melatonin, and 55 newborns without melatonin treatment

Results: Considering ventilator parameters and clinical outcome of the studied population, the two groups (treated and untreated) differed statistically significantly in maximal O₂ concentration used, PIP (peak inspiratory pressure), PEEP (end expiratory pressure) as well as in the ventilatory modes used and in the oxygenation index (Median airway pressure x O₂ concentration / PaO₂). Higher values were in untreated group. In both groups (treated and untreated) the values were higher in patients ventilated in the A/C mode and were lower in HFV patients and in PSV with VG. IL-6 at time 0 presents values similar in treated and untreated infants and equivalent in the six groups of ventilation modes; at 24 hr and at 71 hr IL-6 is higher all groups without a correlation with ventilation mode or treatment. At 7 days, IL-6 levels are significantly reduced in treated-newborns relative to those that received diluent and those ventilated in PSV and in GV had lower levels of IL-6. IL-8 values at 0 hr did not differ in the groups; at 24 hr there was a significant rise in the six groups; at 72 hr the melatonin treated newborns had a significant reduction in IL-8 serum levels that remain also at 7 days. TNF α levels did not differ at 0 time. At 24 hr there were no differences from the basal values in melatonin or untreated newborns. At 72 hr the melatonin-groups showed a statistical significant reduction compared to those in the diluent treated newborns which increased at 7 days, when higher TNF α levels were seen in untreated in relation to the group and to the ventilation mode. There were no differences in serum levels of any cytokines prior to the onset of treatment.

Conclusion: Compared with the melatonin treated RDS newborns, the concentrations of inflammatory cytokines were significantly higher in the newborns given only the diluent. The current study suggests that reducing volutrauma will also reduce biotrauma as expressed by a reduction of inflammatory cytokines and an improved outcome; clearly, melatonin treatment provides benefits in this regard.

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NEAR-INFRARED REFLECTANCE ANALYSIS (NIRA) FOR THE EVALUATION OF NITROGEN AND FAT EXCRETION IN STOOLS OF PRETERM AND TERM NEWBORNS

V PAOLETTI, L CORVAGLIA, G.P. SALVIOLI, G FALDELLA¹ ¹ISTITUTO CLINICO DI PEDIATRIA PREVENTIVA E NEONATOLOGIA NEAR-INFRARED REFLECTANCE ANALYSIS (NIRA) FOR THE EVALUATION OF NITROGEN AND FAT EXCRETION IN STOOLS OF PRETERM AND TERM NEWBORNS CLINICAL INSTITUTE OF PREVENTIVE PEDIATRICS AND NEONATOLOGY, BOLOGNA UNIVERSITY, (ITALY)

To fulfill the high nutritional needs of preterms, preterm formulas are very rich in proteins and energy. Data on fat and protein absorption in premature babies are limited. We compared fat and nitrogen excretion of (P) preterm infants' stools with those of term newborns (T). We studied 20 P (GA 26–34 weeks), 9 SGA (small for gestational age) and 11 AGA (adequate for gestational age) and 23 AGA T. All P were fed with 150/160 ml/kg/day preterm formula. T were breast fed. Nitrogen and fat excretion was measured by Near-Infrared Reflectance Analysis (NIRA), a method based on the relationship between the reflectance intensity spectrum of the fecal sample at specific wave lengths and nitrogen and fat content. Results are g/100g of stools. NIRA was performed in all infants at day +12 and in P also at day +60. At +12d, fat excretion was significantly higher in SGA P (18.2) vs AGA P (12.3) ($p = 0.015$) and vs T (12.6; $p = 0.004$). At +60d, fat excretion did not show any significant difference (AGA P 15.4 vs SGA P10.6). At +12d, nitrogen excretion was higher in SGA P (1.95 vs AGA P 1.26; $p = 0.046$) and at +60d (2 vs AGA P 1.3; $p = 0.015$). SGA preterm infants have long lasting nitrogen malabsorption. As many studies have found that SGA P have best growth and development when fed on high protein formula, the relative nitrogen malabsorption may explain the higher nutritional needs of SGA P.

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THE ROLE OF 7-NITROINDAZOLE IN PROLONGED SEIZURES INDUCED BY KAINIC ACID IN YOUNG RATS, SUBMITTED TO HYPOXIA DURING THE PERINATAL PERIOD.

I PAPADOPOULOU¹, G KARKAVELAS², E SPANDOU¹, C SIMEONIDOU¹, I LIANGOURIS¹, N GRIGORIADIS³, O GUIBA-TZIAMPIRI¹ ¹DEPARTMENT OF PHYSIOLOGY, ARISTOTLE UNIVERSITY OF THESSALONIKI, ²DEPARTMENT OF PATHOLOGY, ARISTOTLE UNIVERSITY OF THESSALONIKI, ³DEPARTMENT OF NEUROLOGY, ARISTOTLE UNIVERSITY OF THESSALONIKI (GREECE)

Background: Perinatal hypoxia is one of the most common causes of neonatal seizures. Nitric oxide (NO) has been involved in the pathophysiology of seizures. Furthermore, NO as well as nuclear factor- κ B (NF- κ B) have been implicated in the oxidative stress-induced neurodegeneration, associated with hypoxia and/or kainic acid (KA). Objective: The aim of the present study is to examine the role of 7-Nitroindazole (7NI) on hypoxic (H) and KA-induced seizures during early life. The expression of NF- κ B has been also examined.

Methods: Wistar rats (P10–11) were divided into 4 groups: A (H), B (H/KA), C (H/KA and 7NI) and D (control, vehicle). Hypoxia was induced by decreasing O₂ concentration from 7% to 4% within 15 minutes. At P21–22, rats of groups B and C were administered with KA (10mg/kg i.p.). Animals of group C were pre-treated with 7NI (50mg/kg i.p.). Histological assessment was performed at P24 with hematoxylin-eosin staining and cell counts in the hippocampal area. NF- κ B expression was examined by immunohistochemistry.

Results: Histologic evaluation revealed significantly decreased cell loss in 7NI treated group, compared with group B (10.1% $\pm$ 3.5 and 25.1% $\pm$ 10.5 respectively $p < 0.05$). In control group NF- κ B immunostaining was slight and restricted to the cytoplasm. In H/KA group over-expression of NF- κ B was clearly observed at 4 hr, following KA administration, reduced in 24 hrs and almost totally abolished in 48 hrs. NF- κ B immunoreactivity was localized mainly in the cytoplasm of neuronal, glial and endothelial cells. Dense nuclear immunostaining of NF- κ B was observed in damaged neurons and reactive astrocytes of hippocampal area. There was no obvious difference in NF- κ B staining between H/KA group and animals pre-treated with 7NI.

Conclusion: According to our results administration of 7NI, a selective inhibitor of nNOS, clearly diminished seizures-induced damage in the hippocampus, which might indicate a possible role of NO in the pathophysiology of prolonged seizures during infancy. Additionally, alteration of NF- κ B expression points to a potential implication of NF- κ B in mechanisms of seizures that may be correlated with NO.

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ANTENATAL BETAMETHASONE (ANB) MAY PREVENT SEVERE RETINOPATHY OF PREMATURITY (ROP) IN VERY LOW BIRTH WEIGHT (VLBW) INFANTS

C PAPAGAROUFALIS, G POLLALIS, M XANTHOU ¹AGHIA SOPHIA CHILDREN'S HOSPITAL, ²AGHIA SOPHIA CHILDREN'S HOSPITAL, ³AGHIA SOPHIA CHILDREN'S HOSPITAL (GREECE)

Background: Previous studies have shown that prenatal steroids may indirectly reduce the incidence of severe ROP, by decreasing the incidence of RDS and oxygen use.

Aim: To determine whether ANB may directly affect the incidence of severe ROP in VLBW infants

Methods: Prospective perinatal data were collected in 106 VLBW neonates with a gestational age of <30 weeks who had RDS, required mechanical ventilation and received exogenous surfactant. All infants underwent serial eye examinations by the same pediatric ophthalmologist who was not aware whether the infants had received or not ANB. Pearson Chi-Square and Logistic Regression Analysis were used to evaluate the relationship between ANB exposure (one or more doses) and threshold ROP, as well as the relationship between other perinatal variables and threshold ROP.

Results: Threshold ROP was developed in only 5 (8%) out of the 65 infants who received one or more doses of ANB compared to 12 (29%) out of the 41 controls ($p < .005$). Multivariate logistic regression analysis showed that ANB was independently associated with a decreased incidence of threshold ROP (RR=0.28, 95% CI=0.14–0.79), while birth weight <1000g (RR=4.9, 95% CI=1.8–28.4), gestational age <27 weeks (RR=4.7, 95% CI=2.1–24.8), mechanical ventilation >7 days (RR=4.1, 95% CI=1.8–30.6) and bronchopulmonary dysplasia (RR=3.5, 95% CI=1.2–28.7) were independently associated with an increased incidence of threshold ROP.

Conclusions: ANB may directly reduce the incidence of severe ROP in VLBW infants, probably by enhancing fetal antioxidant activity and/or by preventing early retinal ischemia through stabilization of arterial blood pressure.