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DIAGNOSTIC PREDICTION OF MATERNAL INFLAMMATORY MARKERS FOR NEONATAL SEPSIS

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Background: Elevated concentration of C-reactive protein(CRP) in the maternal blood is associated with the presence of intrauterine infection. Newborns born of mothers with perinatal infection, whether indicated as chorioamnionitis or positive CRP, have been associated with probable sepsis in early neonatal period. We purport this study to evaluate the diagnostic performance of maternal inflammatory markers, CRP and chorioamnionitis for prediction of neonatal sepsis.

Methods: 126 low birth weight newborns(gestation 32±3.2wk, birth weight 1887±623g) and their mothers were recruited. Neonates were divided into sepsis group(65 infants) including both definite(positive blood culture) and probable(negative blood culture but with more than 3 abnormal clinical symptoms) episodes and control(61 infants). Mothers were grouped into histologic chorioamnionitis(n=27), clinical chorioamnionitis(n=18), other infection(n=12), and control(n=69). Mothers were subgrouped into CRP positive(n=32) and CRP negative group(n=94) by CRP 1.86 mg/dL, and calculated relative risk for neonatal sepsis according to maternal condition.

Results: Maternal CRP was significantly higher in neonatal sepsis group than in control (2.18±2.79 vs. 1.09±1.29mg/dl, p=0.0055). Maternal CRP(cutoff value 1.86 mg/dL) had sensitivity 74% and specificity 34% for predicting neonatal sepsis. Maternal CRP positive group had more neonatal sepsis than CRP negative group(69% vs46%, p=0.0245). Relative risk of neonatal sepsis in maternal CRP positive group was 2.61 times(95% CI:1.114–6.106, p=0.027)) as high as CRP negative group. As maternal CRP increases continuously, the risk for neonatal sepsis increases as 1.31 times(95% CI:1.059–1.626, p=0.013). The relative risk of histologic chorioamnionitis was 2.57, clinical chorioamnionitis 1.21, and other infection 2 for neonatal sepsis, but not significant.

Conclusion: The risk of neonatal sepsis significantly increases in the case of positive maternal CRP (more than 1.86 mg/dL). We suggest that maternal CRP should be considered as a risk factor for early neonatal sepsis.

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ABNORMAL PREOPERATIVE EEG'S IN NEWBORN INFANTS WITH CONGENITAL HEART DISEASE

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Introduction: Abnormal preoperative neurological symptoms in infants with congenital heart disease (CHD) may be more common than previously recognised. The aim of the present study was to investigate if EEG correlates with preoperative morbidity. **Method:** We investigated EEG and cranial ultrasound/CT/MRI in 28 newborn infants with CHD. Inclusion criteria were gest. age 36 weeks or more, postnatal age <14 days, no other major malformations, parental consent and no language barrier. Standard EEG's were recorded within 24 hours of arrival and evaluated according to predefined criteria. Seven EEG categories were evaluated: background, assymetry, spikes/sharp waves, seizure activity, sleep-wake cycling, reactivity and a total evaluation of normality/degree of abnormality.

Results: Twenty-eight infants with CHD were included, their median (range) gestational age was 39 (36–41) weeks. The EEG was performed at median 4 (1–14) postnatal days. Twenty-five of the 28 infants received infusion with prostaglandin E_1 (PGE_1). Six infants (21.4%) had suspected or clear clinical seizures, four infants (15.4%) hade abnormal cranial ultrasound/CT/MRI. Six of the infants died, one due to preoperative hypoxic-ischemic brain injury, and the other five later due to heart failure.

Results: The preoperative total EEG evaluation was normal in 12 infants, slightly abnormal in 4, moderately abnormal in 10, and severely abnormal in 2 infants. The EEG background correlated significantly with lowest preoperative pH (p=0.026, r_S= -0.429) and base deficit (p=0.030, r_S= -0.426, and also correlated with the amount of PGE_1 (0.022, r_S =0.438. Presence of seizure activity was negatively associated with lowest preoperative oxygen saturation (p=0.019, r_S =-0.448). Increasing degree of intracranial abnormality correlated with increasingly abnormal EEG background (p=0.005, r_S = 0.532) and sleep-wake cycling in EEG (p=0.023, r_S = -0.452), and the total evaluation of the EEG (p=0.017, r_S = 0.463). Infants with hypoplastic left heart syndrome (HLHS)/single ventricle had significantly more often a moderately or severely abnormal EEG (p=0.044). Mortality was associated with intracranial morphological abnormality (p=0.012) but not abnormal EEG.

Conclusion: Abnormal preoperative neurology and EEG is probably uncommon in infants with CHD. Possible effects on EEG from PGE_1 should be further investigated.

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L-CARNITINE PROTECTS AGAINST GLUTAMATE- AND KAINIC ACID-INDUCED NEUROTOXICITY IN CEREBELLAR GRANULAR CELL CULTURE OF RATS

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Background/objectives: Glutamate mediated intracellular calcium accumulation and free radical generation are tought to be a major mechanism contributing to cell death in hypoxic-ischemic brain injury. For this reason, various glutamate receptor antagonists have been investigated for their therapeutic potential.

Aim: To assess whether L-carnitine, an antioxidant, is able to prevent glutamate- and kainic acid-induced neurotoxicity.

Methods: Glutamate (10–7 M) and one of its receptor agonists, kainic acid (10–4 M) were administered to cerebellar granular cell cultures that prepared from 1-day-old newborn rats. The neuroprotective effect of L-carnitine was examined.

Results: L-carnitine at doses of 10–6, 10–5, 10–4, 10–3 M was applied to culture flasks. L-carnitine at doses of 10–4 M and 10–3 M significantly blocked glutamate-induced neurotoxicity, with the most effective dose being 10–4 M. L-carnitine also blocked kainic acid-induced neurotoxicity only at dose of 10–4 M. 10–4 M L-carnitine, the most effective dose in glutamate- and kainic acid- induced neurotoxicity, decreased glutamate-induced neuronal cell death from 36,14±2,95% to 17,59±2,25%; (p=0,000) and kainic-acid induced neuronal cell death from 21,4±0,41% to 13,4±1,38; (p=0,000).

Conclusions: The present study demonstrates that L-carnitine protects against glutamate- and kainic acid-induced neurotoxicity. This protective effect of L-carnitine may occur via its antioxidant activity because free radical generation is a common result in either glutamate- or kainic acid-induced neurotoxicity. L-carnitine merits further investigation as a treatment modality for perinatal brain injury.

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CEREBRAL HAEMODYNAMICS AND LUNG MECHANICS IN PRETERM INFANTS DURING SYNCHRONIZED INTERMITTENT MANDATORY VENTILATION (SIMV) AND SYNCHRONIZED INTERMITTENT POSITIVE PRESSURE VENTILATION (SIPPV), WITH AND WITHOUT VOLUME GUARANTEED (VG)

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Background: Various techniques of mechanical ventilation can affect cerebral haemodynamics and oxygenation in preterm infants. Few studies have assessed cerebral haemodynamics and oxygenation during different modalities of patient triggered ventilation (PTV) in preterm infants.

Aim: To study cerebral haemodynamics and oxygenation, by Near Infrared Spectroscopy (NIRS) and Echo-Doppler, during SIMV and SIPPV, with and without VG.

Methods: Ten preterms (means±SD: BW=1316±666 g; GA=28.8±4.2 wks) with RDS were studied at 7.7±7.3 days of life, in SIPPV±VG and SIMV±VG, with VG set at 5 ml/kg. Each ventilation modality was used for 30 minutes in a random sequence. Concentration of cerebral oxyhaemoglobin (O2Hb), deoxyhaemoglobin (HHb) and total haemoglobin (tHb) and Tissue Oxygenation Index (TOI) were continuously monitored by NIRS. At the beginning and at the end of each ventilation modality the Resistance Index (RI) in the Anterior Cerebral Artery was assessed by Echo-Doppler. Heart Rate (HR), Respiratory Rate (RR), Inspired Oxygen Concentration (FiO2), transcutaneous oxygen saturation (SaO2) and transcutaneous PCO2 (PtcCO2) were continuously monitored. Mean Airway Pressure (MAP), Mean Arterial Blood Pressure (MABP), Tidal Volume (Vt), and Compliance of the respiratory system (Crs) were measured at 5 minutes intervals. The results were expressed as means ± SD. Differences between the 4 ventilation modalities were considered statistically significant for $p < 0.05$ by the Student's t test for paired values.

Results: O2Hb, HHb, tHb and IR were stable and similar in the 4 ventilation modalities; oscillations never exceeded 5% of baseline values. TOI was always > 60%. No differences were found in RR, Vt, HR, SaO2 and PtcCO2. Crs was below normal values in all modalities (SIMV=0.5±0.1; SIMV+VG=0.6±0.2; SIPPV=0.4±0.1; SIPPV+VG=0.5±0.1 ml/cmH2O/kg) and was slightly higher in SIMV than in SIPPV (p<0.02).

Conclusions: These preliminary data suggest that acute changes in cerebral haemodynamics and oxygenation and in lung mechanics are minimal during PTV with low VG, irrespective of the type of ventilation used (SIMV or SIPPV ± VG).

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LOW MANNOSE BINDING LECTIN (MBL) SERUM LEVELS AND HOSPITAL ACQUIRED INFECTIONS (HAI) IN NEONATES IN A NEONATAL INTENSIVE CARE UNIT (NICU)

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Background: MBL is a serum lectin, synthesised by the liver, that is part of the innate immune system; it behaves as an acute phase reactant and plays an auxiliary rather than a critical role in host defence. Individuals with MBL deficiency may experience an increased number of infections, particularly in the course of immunodeficiency (e.g. chemotherapy). A MBL concentration of 0.5 mcg/ml has been suggested as a cut-off level for MBL deficiency. Serum MBL levels in term neonates are similar to those in adults, but values in preterms are approximately 50% lower. HAI are an important cause of neonatal morbidity and mortality. Known risk factors account only in part of the (inter)individual variability of the frequency and severity of neonatal infections. Part of this variability could be related to individual differences in the maturation of the innate immune system.

Aim: To investigate the relationship between MBL serum levels and incidence and severity of HAI in newborn infants admitted to a NICU.

Methods: We studied retrospectively 190 neonates (133 preterm and 57 at term) consecutively admitted to a NICU. MBL serum levels were measured by a specific immunoassay (Antibody Shop, Copenhagen, Denmark) in all infants on admission; 68 infants subsequently developed a HAI, defined according to the CDC definitions.

Results: Median MBL serum levels on admission were 1.2 mcg/ml (IQR 0.2–2.9) in the whole sample, 0.9 mcg/ml (IQR 0.2 – 2.2) in preterm and 1.7 mcg/ml (IQR 0.3 – 3.9) in term infants (p<0.05). Median level on admission in infants who subsequently developed one or more HAI (0.5 mcg/ml; IQR 0.1 – 1.7), was significantly lower (p<0.001) than in those who did not develop HAI (1.5 mcg/ml; IQR 0.4 – 3.6;). Among infants with HAI, median MBL levels on admission were significantly lower in those who had two or more episodes of HAI than in those with only one episode (0.1 mcg/ml IQR 0.05–0.5 vs 0.8 mcg/ml IQR 0.1–1.9; p<0.01), and in infants who developed HAI within 10 days following admission compared to those who developed HAI later on (0.2 mcg/ml IQR 0.05–1.2 vs 1.2.mcg/ml IQR 0.2–2.1; p<0.05). Among infants with HAI, MBL levels on admission were not significantly different in survivors and non survivors .

Conclusion: Early MBL serum levels are low in neonates who subsequently develop HAI. Low MBL levels at birth are likely to represent a predisposing factor for infections in newborn infants.

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MATURATION OF LUNG FUNCTION DURING THE FIRST TWO YEARS OF LIFE IN INFANTS WITH CONGENITAL DIAPHRAGMATIC HERNIA (CDH) TREATED WITH A GENTLE VENTILATION AND DELAYED SURGERY STRATEGY

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Background: CDH is still characterized by high morbidity and mortality, mostly due to lung hypoplasia. Recently, gentle ventilation and delayed surgery have been suggested to improve mortality and long-term pulmonary sequelae. The assessment of lung volumes, particularly functional residual capacity (FRC), is crucial for understanding lung development during the first year of life. The sulphur hexafluoride (SF6) wash-in / wash-out technique together with an ultrasonic flow meter, can measure both FRC and lung clearance index (LCI), a very sensitive and stable index of ventilation homogeneity.

Aim: To evaluate changes in lung function during the first two years of life in infants with CDH requiring mechanical ventilation and surgically corrected in the neonatal period.

Methods: Ten CDH infants (means±SD: BW=3082±570 g and GA=39.1±1.7 wks, M/F=8/2, Left/Right CDH 8/2) surgically corrected in the neonatal period were studied twice during the first two years of life, with at least six months interval between measurements. Tidal Volume (Vt), Respiratory Rate (RR) and time to peak expiratory flow/expiratory time ratio (tPTEF/Te, an index of lower airways patency) were measured with an ultrasonic flow meter; Compliance (Crs) and Resistance (Rrs) of the respiratory system were studied with the single occlusion technique; FRC and LCI were assessed with the multiple breath SF6 wash-in/wash-out technique. The differences between the first and second measurement were considered statistically significant for $p < 0.05$ by the Student's t-test for paired values.

Results: All 10 infants were studied at 5.0±2.7 (T1) and 12.8±4.2 (T2) months of age. At T1: Vt (7.9±2.1 ml/kg), RR (47.8±14.0 b/m'), Crs (2.1±0.4 ml/cmH2O/kg) were within normal limits; tPTEF/Te (0.18±0.05) and FRC (19.2±4.2 ml/kg) were slightly lower, while Rrs (52.2 ± 19.2 cmH2O/l/s) and LCI (10.8±2.5; normal values <7.1) were higher than normal. At T2: Vt (9.7±1.8 ml/kg) and RR (32.5±6.4 b/m') improved significantly (p<0.05 and p<0.01), while Crs (2.2±0.6 ml/cmH2O/kg), Rrs (53.0±25.8 cmH2O/l/s), tPTEF/Te (0.17±0.05), FRC (21.6±3.4 ml/kg) and LCI (11.2±2.5) did not change appreciably when compared with T1.

Conclusions: Lung function in infants with severe CDH is characterized by a persistent impairment of lung volumes and ventilation inhomogeneity, despite an improvement in Vt and RR and normal values of Crs, during the first two years of life. These results can explain in part the higher respiratory morbidity in these patients.

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