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MATERNAL BLOOD S100B LEVELS IN PREGNANCIES COMPLICATED BY FETAL GROWTH RESTRICTION MAY EARLY PREDICT THE OCCURRENCE OF INTRAVENTRICULAR HEMORRHAGE

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The aim of these present study was to evaluate maternal levels of S100B (a neural protein found in high concentrations in biological fluids after cell injury in the nervous system), in pregnancies complicated by intrauterine growth retardation (IUGR) and to correlate after their measurements with postnatal intraventricular hemorrhage (IVH) occurrence. A case-control study in pregnant women complicated by IUGR(n= 106) of whom a subgroup (n=26) developed postnatal IVH, and a group of normal pregnancies (n=212) matched for gestational age served as control. Ultrasound scanning, Doppler velocimetry patterns (in the utero-placental and in the middle cerebral artery vessels), and maternal blood samples were collected before birth in all women with IUGR. After birth routine laboratory parameters, cerebral ultrasound patterns and neurological examination were recorded in IUGR and control newborns.

Maternal S100B levels were significantly ($P<0.001$) higher in IUGR pregnancies complicated by postnatal IVH, than in those who did not and in controls. At a cut-off of 0.72 mg/L S100B achieved a sensitivity of 99.3% (C.I.95%: from 86.7 to 100) and a specificity of 98.2% (C.I.95%: from 94.3 to 99.8) as a single marker for prediction of IVH (area under the ROC curve: 0.991). The probability of IVH was 8.17% in the whole study population, 93% (C.I.95%: 83.6–100%) when S100B levels were found above the thresholds defined by the ROC curve analysis, and 0% (C.I.95%: 0–2.5%) if they were found unaltered. Maternal S100B assessment may represent an useful tool for the early suspect of postnatal IVH.

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TGF-BETA-1 MEDIATES IL-9/MAST CELLS INTERACTIONS IN A MOUSE MODEL OF PERIVENTRICULAR LEUKOMALACIA

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Periventricular leukomalacia (PVL) is the major cause of cerebral palsy (CP). The mechanisms of this lesion formation is not yet understood but cytokines have been implicated in it. We have developed a mouse model of PVL based on intraneocortical injection of ibotenate, a glutamate analog in a way to study the role of IL-9 (Interleukin 9). Studies had shown that newborns with higher levels of IL-9 were at higher risk to develop CP. In agreement with these data, research using our model has shown that pre-treatment with IL-9 exacerbated brain lesions induced by ibotenate. We have also shown that brain mast cells mediate the toxic effects of IL-9. The goal of this study is to identify the underlying pathophysiological mechanism. Our results showed that neuronal TGF-beta-1 (Tranforming Growth Factor beta 1) plays a key role in the toxic effects of IL-9 : -pre-treatment with TGF-beta-1 produced the same effects as IL-9 on lesions. IL-9 effects were abolished when a specific TGF-beta-1 neutralizing antibody is administered at the same time. -real time PCR, Western blot, and immunohistochemistry showed that pre-treatment with IL-9 increased TGF-beta-1 neocortical expression. In vitro studies demonstrated that neurons were the major contributor in IL-9-induced increase of TGF-beta-1. -in c-Kit mast cell-deficient mice, TGF-beta-1 failed to exacerbate lesions. A specific inhibitor of mast cell degranulation and histamine receptor blockers abrogated TGF-beta-1 effects, suggesting a key role of mast cells and histamine in TGF-beta-1 effects. In vitro studies using a mast cell line showed that TGF-beta-1 increased histamine in the supernatant. In conclusion, these data support the notion that neuronal TGF-beta-1 plays a key role in the IL-9/mast cell interaction, which leads to an exacerbation of neonatal damage through an increased extracellular histamine concentration. The identification of this new pathway might have important implications for understanding CP.

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CARDIAC MRI AT 3.0 TESLA IN PRETERM INFANTS

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Background: Cardiac function is often impaired in preterm infants undergoing intensive care but poorly understood. Cardiac magnetic resonance imaging (CMRI) is the method of choice for assessment of cardiac function in adults, but has not been used previously in the preterm population. CMRI in adults is usally done at 1.5 T, however we hypothesised that in preterm infants it would be possible to take advantage of higher field strengths.

Aims: To assess the feasibility of undertaking CMRI in preterm infants and to develop novel approaches to acquire images at 3.0 T.

Methods: Five preterm babies underwent cardiac MRI. Gestational age was median 33 weeks [range 30 - 35 weeks]. Median birthweight was 1860g [1480 - 2750g]. The median corrected gestational age at time of MRI was 35 weeks [33 - 37 weeks]. Each scan took approximately 45 minutes. Babies were monitored throughout the scan by a trained neonatologist.

Results: Imaging was successful in 3/5 infants, and these images were sufficient to allow detailed assessment of cardiac function. 2 dimensional real time CMRI movies provide precise visualisation of cardiac function.

Conclusion: This preliminary study demonstrates that CMRI can provide detailed assessment of cardiac function in preterm infants, and this can be achieved at 3.0 T.

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SURFACTANT ADMINISTRATION BY ELECTIVE INTUBATION IN NEAR-TERM INFANTS WITH SEVERE RESPIRATORY DISTRESS

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Background: premature infants born near-term may develop severe idiopathic respiratory distress requiring mechanical ventilation (MV). Aim: 1) to ascertain whether, in moderately premature infants with severe respiratory distress, a single dose of surfactant given by rapid intubation and extubation may reduce the entity of the disease and thus avoid MV; 2) to investigate whether infections or pulmonary hypertension may be associated with failure of surfactant treatment. Population: neonates weighing >=1500g at birth (35–37 weeks GA) and presenting with idiopathic respiratory distress requiring an FiO2>=0.70 or an FiO2>=0.6 (Silverman score >=7) to maintain an SaO2 of 90–95%. Infants were treated with oxygen and NCPAP or NSIPPV (Giulia, Ginevri) if necessary. Before surfactant was administered, a bronchoalveolar lavage was obtained for microbiological studies and echocardiography was used to evaluate pulmonary arterial pressures. Results: 18 infants (mean BW 2808g, 2230–3530, 13/18 born by C/S) received surfactant (Curosurf, 100 mg/kg) at an average age of 19h (1–54). The majority of chest radiographs showed retained lung fluid while, in a few cases, granular opacification with air bronchogram or widespread opacification of both lungs was seen. There was a marked and sustained decrease in FiO2 in those infants in whom surfactant treatment succeeded (FiO2 preINSURE: 0.68±0.10; FiO2 postINSURE at 3h 0.30±0.06; at 6h 0.29±0.06; at 12h 0.29±0.07; at 24h 0.26±0.05; ANOVA $p<0.001$). However, 28% of infants showed only a transitory decrease in FiO2 and eventually required MV. Among infants who failed, there were four cases of bacterial infections and one of pulmonary hypertension while no such complications were observed in infants who succeeded.

Conclusions: a single dose of surfactant allows us to reduce the need for MV in most infants with severe respiratory distress at birth, except in cases with infections or pulmonary hypertension.

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EARLY NEWBORN DISCHARGE FOLLOW-UP

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Background: Early postpartum discharge of newborns from hospital is an established routine. However, readmission is reported to occur in various degrees. Karolinska hospital is a III level hospital practicing early discharge, earliest 6 hours but within 72 hours postpartum. Scheduled check-up of the infants takes place at the follow-up clinic, mostly within 3–5 days after delivery and includes also metabolic screening and breast-feeding promotion.

Objective: To describe rates and causes of readmission for early-discharged infants.

Design: Retrospective study of a 18 months-period, Jan 2003 to June 2004 of all newborns born at Karolinska hospital, early discharged and who had to visit the emergency clinic during the first postnatal week.

Results: Total number of deliveries were 7379. 6990 of these were at term gestation (37 weeks). Our data refers to this group of infants. A total number of 5116 / 6990 (73%) infants of mothers with low-risk singleton births were discharged early, 65% within 48 hours. 98 / 5116 (2%) infants early discharged had to visit the paediatric emergency clinic. 69 (1.3%) of these were readmitted to hospital ward for observation / treatment; remaining recieved policlinical advice. Main causes for readmission were: 44 / 69 = jaundice requiring phototherapy and in three cases also exchange transfusion of which two were associated to ABO isoimmune disease, 10 / 69=feeding difficulties, 7 / 69 = respiratory symptoms, 6 / 69 = infection / suspect infection, 2 / 69 = parental anxiety. All infants had a healthy outcome except one who suffered severe brain damage due to an inborn error of metabolism.

Conclusions: We identified the importance of improving our routines connected to the discharge of ABO-incompatible newborns but also in giving parents accurate information on breast feeding and on the physiological changes of newborns (skin color, body weight, alertness). These new routines will be evauated during an oncoming 18 months-period.

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MORPHINE AND MORPHINE-6-GLUCURONIDE SERUM CONCENTRATIONS AND THEIR CORRELATION WITH PAIN RESPONSES

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The aim of the study was to assess morphine and morphine-6-glucuronide (M6G) serum concentrations in preterm neonates requiring mechanical ventilation after continuous morphine infusion during first days of life. We also examined correlation between morphine, its metabolite and pain scores. 14 preterm neonates were randomly assigned. Neonates (mean birth weight 1196g (780 to 1760g), mean gestational age 29 weeks (26 to 33weeks) received morphine for 1 to 5 days (100mcg/kg over 30 minutes followed by 20mcg/kg/h). Blood samples (3–4 samples) were obtained from neonates at 0, 30 minutes, 6 and 24 hours after the start of morphine infusion (at a median postnatal age 4 hours) and 24 hours after discontinuation of infusion. The pain responses were assessed using two scales-Premature Infant Pain Profile (PIPP) and Comfort Scale (CS) at 6 and 24 hours. M6G was found in all samples, even after 30 minutes of morphine infusion. In most samples M6G concentration exceeded morphine concentration. Mean (SD) morphine clearance was 5.5(3.0)ml/min/kg. There was a significant negative correlation between morphine plasma concentration and Comfort Scale scores at 6 hour of the study ($r=-0.72$, $p=0.003$). There was no correlation between M6G and pain scores. Clearance value was similar to values published by other authors. Finding correlation only between morphine concentration and CS at 6th hour of the study confirms sophisticated problem of pain assessment.