152

SYSTEMIC INFLAMMATION IN NEWBORN PIGS WITH MECONIUM ASPIRATION SYNDROME

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Background: Meconium may cause lung injury (meconium aspiration syndrome=MAS). Treatment is symptomatic by ventilatory support or in the worst cases extracorporal membrane oxygenation (ECMO). The pathophysiology is complex including a substantial inflammatory reaction in the lungs, but according to our results this inflammation may be systemic as well. We recently showed for the first time that meconium is a potent activator of complement (Castellheim A. et al. Pediatr. Res. 2004;55:310–318), leading us to hypothesize that complement activation is an essential part of the pathophysiology of MAS.

Methods: MAS was induced by instillation of meconium into the lungs of newborn pigs (n=8). To mimic the asphyxia in clinical MAS, hypoxia was induced by supplying 8% oxygen in nitrogen until base excess reached -20 mmol/l. Anaesthesia was induced by Halothane and maintained intravenously by fentanyl and midazolam. Control animals (n=5) received saline under otherwise identical conditions for 7 hours. Hemo- and lung dynamics were recorded. Systemic complement activation, revealed by the terminal sC5b-9 complex (TCC), and cytokines were measured in plasma samples by enzyme immunoassays. Granulocyte expression of CD18 and CD11b, as well as oxidative burst, were measured by flow cytometry.

Results: Plasma TCC increased rapidly in the MAS animals (0.31±0.34 to 3.10±0.66) (AU7mL) (mean±2SEM), but decreased in the controls (0.55±0.88 to 0.28±0.10) (MAS vs controls: p<0.0005). The TCC concentration correlated closely with oxygenation- and ventilation indices (r=0.48 and 0.57, p=0.001 and <0.0005, respectively), and inversely with compliance (r=-0.63, p<0.0005); all thee reflecting severe deterioration in pulmonary function. Granulocyte oxidative burst declined significantly in the MAS animals compared with the controls (p=0.02) and correlated inversely with TCC (r=-0.37, p=0.02), probably reflecting a paralysis of granulocytes as part of a systemic inflammatory response. Finally, IL-6and IL-8 increased in MAS (IL-6: (26±3 to 188±80)(pg/mL) IL-8 (19±2 to 37±6)(pg/mL) animals compared to the controls (MAS vs controls: IL-6, p=0.002 and IL-8, p=0.001)

Conclusion: We have for the first time demonstrated that complement is rapidly and systemically activated in experimental MAS. We suggest that this activation may induce secondary inflammatory reactions like cytokine production and oxidative burst, which contribute to the pathogenesis of MAS. Anti-complement therapy may be a rational for treatment of this disease.

153

NEONATAL POLYTHYTHAEMIA RESULTING FROM LATE CORD-CLAMPING DOES NOT CAUSE DEVELOPMENTAL OR NEUROLOGIC SEQUELAE

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Objective: To investigate effects of early and late cord-clamping on short- and long-term neurologic and developmental outcome of infants born at full-term. **Design:** A prospective randomised study. **Settings:** The Perinatal Centre of the School of Medicine University of München. **Subjects:** 30 full-term neonates with early (<10 s) and 30 with late (3 min) cord-clamping. **Intervention:** Holding the infant at the level of the introitus vaginae and clamping the cord exactly 3 min after birth, or clamping the cord within 10 s of birth. **Main outcome measures:** Initial haematocrit, blood viscosity, behaviour and neurologic status; developmental and neurologic items.The German version of the Griffiths Scale of Babies Abilities was applied at five and twenty months of corrected post-term age and expressed as developmental quotients.

Results: There were statistically significant differences between the two groups in mean initial haematocrit and blood viscosity, whereas no significant differences were found in short- and long-term neurologic and developmental outcome. When the infants with late cord-clamping were divided into two subgroups with initial haematocrit values <65 (n=17) and >65 (n=13), no significant differences in neurologic and developmental outcome measures were observed between the two subgroups.

Conclusions: We conclude that late cord-clamping results in marked rise of haematocrit and blood viscosity, whereas neurologic and developmental outcome is not affected. Late cord-clamping is thus a safe procedure.

154

EFFECTS OF CLASSICAL, POP AND LULLABY MUSIC ON CEREBRAL CIRCULATION AND OXYGENATION IN PRETERM INFANTS

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Design: Auditory stimulation of preterm infants with music is used in many neonatal intensive care units for stimulation, calming or easing of pain. In accordance with studies in adults, we expected a rise of cerebral blood flow velocity (CBFV) and of the cerebral hemoglobin content during music in preterm infants.

Methods: Fifteen preterm infants with gestational age of 25 to 34 weeks were studied at a postmenstrual age of 33 to 35 weeks. They were exposed to classical piano music ("The Moonlight Sonata" by Beethoven, "Reverie" by Schumann), pop music (Kool and the Gang "Fresh" or Eurythmics "Sweet Dreams") and music from a musical box ("lullaby music") at 75 dB for ten minutes on three consecutive days. CBFV (left and right middle cerebral arteries) was measured using a continuous Doppler method, and cerebral haemoglobin content and oxygen saturation (rSO2) in the fronto-temporal brain region were assessed by near infrared spectroscopy (NIRS).

Results: There were no significant changes in heart rate, right arm SaO2 and CBFV during and after the three types of music when compared with the values before music. Moreover, no signficant differences in BFV between the right and left middle cerebral artery were found before, during and after music. During all three types of music oxygenated haemoglobin (O2Hb) and total haemoglobin (tHb) increased significantly (P<0.05), whereas deoxygenated haemoglobin (HHb) did not change. After pop music, tHb and O2Hb decreased to values that were not significantly different from the values before music. After lullaby music, tHb and O2Hb further increased to values that were significantly higher than those measured during lullaby music. The rSO2 increased by 1.4+/-1.2% during and by 1.7+/-1.2% after lullaby music when compared with the values before music (p<0.05). The changes in tHb, O2Hb and rSO2 showed no relationship to the gestational, postnatal or postmenstrual age.

Conclusions: In contrast to adults, music had no effect on CBFV in preterm infants. The increase in cerebral SO2 suggests that lullaby music has a calming effect in preterm infants.

155

VISUAL ACUITY IS SIMILAR IN VERY LOW BIRTH WEIGHT ADOLESCENTS COMPARED TO SMALL FOR GESTATIONAL AGE AND NORMAL BIRTH WIGHT ADOLESCENTS IN A NORWEGIAN COHORT

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Background: Prematurity has been associated with reduced visual acuity (VA), especially in those with very low birth weight (VLBW). In small for gestational age (SGA) term children, no certain relationship between birth weight (bw) and VA has been found. The aim of this study was to compare the VA of a cohort of two groups of low bw adolescents, with that of a control group with normal bw.

Methods: The distance and near VA of 50 VLBW (mean bw 1129 g), 63 SGA (mean bw 2886g) and 79 control adolescents born at term (mean bw 3682 g) was measured at age 14 in a population based study. Both the adolescents own correction and optimal correction was used and VA was recorded for each eye and binocularly.

Results: With optimal correction, only one (2%) adolescent in the VLBW group had distance visual acuity less than 0,5 compared with no children in SGA and controls (p= 0,25). Mean distance binocular VA with optimal correction was within normal limits for all groups (1,20 for VLBW, 1,27 for SGA and 1,30 for controls), however lower for VLBW vs controls (p<0,01). All distance measurements (monocularly, binocularly, own correction, best correction) showed similar slight differences. Mean binocular near VA was 0,94 in the VLBWgroup, 1,02 for SGA and 1,02 for controls (p=0,15). However mean VA for near, right and left eye measured separately, was slightly lower for VLBW compared to controls (p<0,05)

Conclusion: In this cohort, being born VLBW or SGA did not increase the risk of having distance visual acuity below 0,5. Only one of the 50 VLBW had a distance VA less than 0,5 (0,3). Mean distance and near VA was statistically lower in VLBW compared to controls, however the differences were small and the mean VA was good in all groups. The SGA group did not perform significantly different from the controls.

156

TEENAGE OUTCOME OF BEING BORN AT TERM WITH MODERATE NEONATAL ENCEPHALOPATHY / HYPOXIC ISCHAEMIC ENCEPHALOPATHY

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Background: Population-based, long-term follow-up studies of individuals born at term with moderate neonatal encephalopathy (NE)/hypoxic ischaemic encephalopathy (HIE) are very rare. About 50 % of all such cases are expected to develop unequivocal signs of cerebral palsy (CP). The outcome for those without CP is not well understood.

Aims: Assess cognitive functions and behaviour problems in children with moderate NE/HIE but without CP.

Methods: The study population comprised all 97 468 children born in Sweden in 1985. Of these, 684 were born at term with an Apgar score of <7 at 5 minutes. These children's obstetric and neonatal records were scrutinized and the children were classified according to degree of NE/HIE. Teenagers with moderate NE/HIE without CP were subjected to a clinical assessment including interviews, neuropsychological tests and assessment of data from medical and psychological records. Age at examination was 16–19 years.

Results: 58 children had at least moderate NE/HIE and survived the neonatal period. In this group, 20 had developed CP. Nine of the remaining 38 had parents who declined participation in the study. Of 29 teenagers without CP examined, 21 (75%) had definite cognitive dysfunction. Five had hearing impairments.

Conclusion: Of the total NE/HIE group of 58 teenagers, follow-up data was available in 49 subjects and only 8 of these were without dysfunctions. Of those who were considered to be free from impairments such as CP, our study revealed that 72 % had problems that interfered with their daily life situation. Clinical follow-up including assessments of cognitive functions before school start should be considered for all individuals in this high risk group.

157

RELEASE OF PLACENTAL GROWTH HORMONE (HGH-V) IN THE DUAL IN VITRO PLACENTA PERFUSION MODEL

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Background: hGH-V is a variant of pituitary hGH-N. High maternal hGH-V concentrations are correlated with fetal growth (1). It is not clear, if hGH-V stimulates directly fetal growth as a growth factor, or indirect via modulation of the maternal metabolism. There is a new highly specific assay available to measure hGH-V. The aim of our study was to measure placental release rates of hGH-V into the maternal and fetal circulation.

Methods: Placentas (n=6) were obtained after uncomplicated pregnancies and written informed consent of the mothers at term. Dual in vitro placenta perfusion was performed for 4,5h. Control parameters for placental function were permeabilities of creatinine and antipyrine, as well as glucose consumption and lactate production of the perfused cotyledons. The release rates of Leptin (RIA), hCG (ELISA) and hGH-V (1) into the maternal and fetal circulation were measured.

Results: Placental hGH-V was only released into the maternal circulation of the dual in vitro placenta perfusion model with a release rate of 2,8±2,4 ng/g/min (mean±SD). The release rate for leptin was 239±90 ng/g/min (maternal 98%, fetal 2%) and for hCG 64±37 IU/g/min (99,4% maternal, 0,6% fetal).

Conclusion: We could show first the directional release of placental hGH-V only into the maternal circulation in the dual in vitro perfused placenta. The significant influence of hGH-V on fetal growth is a result of the modulation of the maternal metabolism rather than a direct stimulatory effect on fetal growth. 1Z.Wu et al. J Clin Endocrinol Metab 2003, 88(2): 804–811