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MATERNO-FETAL TRANSFER OF 125-I-LEPTIN IN THE DUAL IN VITRO PERFUSED PLACENTA PERFUSION MODEL AND INCREASED LEPTIN MRNA-EXPRESSION IN ADIPOSE TISSUE OF PREGNANT WOMEN

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Background: Leptin is a growth factor for the fetus. The sources for maternal and fetal leptin plasma levels are the adipose tissue and the placenta. Placental leptin release elevates maternal leptin levels only about 15%. We hypothesize that activated adipose tissue is an additional source for the high leptin levels in pregnancy. However it is further not clear if maternal leptin reaches the fetal circulation and supports fetal growth by that way. Aim of the study: (1) Do maternal leptin arrive the fetal circulation and (2) is maternal adipose tissue leptin production activated during pregnancy ?

Methods: Placentas and adipose tissue was obtained after written informed consent of the patients. (1) Dual in vitro perfusion of isolated cotyledons (n=7) for 3h. Addition of 125-I-leptin and unlabeled leptin (1+3, 22 ng/ml total leptin) to the maternal circulation. Control of vitality and integrity by measurement of glucose consumption, lactate production, creatinine- and antipyrin transfer. (2) Sampling of subcutaneous maternal adipose tissue during cesarean sections (n=10, no gestational pathology) and during other gynecological surgery (n=10, age matched, no malignancies). Measurement of leptin mRNA using Taqman real time PCR.

Results: (1) Materno-fetal transfer rate of the labeled leptin was 4,5 ± 1,4% of the initial concentration. Permeability of 125-I-leptin accounted for 0,04 ± 0,02 ml min-1 g-1, and was 1,3 ± 0,1 ml min-1 g-1 normalized to creatinine transfer. Existence of free 125-iodine was excluded by comparison of dialysated and undialysated fetal perfusion medium. (2) Leptin mRNA was significant higher in adipose tissue of pregnant women than in the control group (1,0 ± 0,5 v. 0,5 ± 0,4 rel. Units; p<0,05)

Conclusion: (1) We could show first, that leptin from the maternal circulation passes the placenta and enters the fetal blood. There seems to be an active transplacental transport from the maternal to the fetal circulation, due to molecular weight and calculated permeability. (2) Maternal adipose tissue leptin production is activated during pregnancy. A basic leptin supply in the beginning of fetal development seems to be guaranteed by the placenta and maternal adipose tissue and was supplemented by the own leptin production of the fetus during further maturation and growth.

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EFFICACY OF HIGH-FREQUENCY OSCILLATORY VENTILATION FOR TREATMENT OF SEVERE RESPIRATORY FAILURE IN NEONATES

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Objective: Neonatal infants with severe respiratory failure have no response to conventional mechanical ventilation (CMV). Our goal was to evaluate the efficacy of high-frequency oscillatory ventilation (HFOV) for treatment of these infants.

Methods: From December 1998 to December 2003, 66 infants with respiratory failure and not responsive to CMV were treated with HFOV. The primary efficacy variables were improvement in oxygenation, lung function, complications and survival. Gestational age of the studied infants was 38°À5 wk and birth weight 2.9°À0.6 kg, and first treated with CMV at 20.9°À4.6 h of postnatal life, and shifted to HFOV at 62.8°À12.4 h.

Results: After 3 h of HFOV, PaO2/FiO2 and a/A were significantly improved from 50.6°À4.5 to 88.5°À9.8 and 0.08°À0.02 to 0.15°À0.08, respectively. Oxygenation index (OI) and PaCO2 were rapidly decreased from 30°À9 to 17°À5 and 56.6°À8.9 to 43.4°À9.4, respectively (p<0.01). These parameters were further improved at 9, 12, 24 and 48 h of HFOV. After 12 h of HFOV, the tidal volumes and dynamic compliance of 46 infants were significantly improved from 3.1°À0.9 to 4.2°À1.8 and from 0.89°À0.8 to 1.36°À1.44, respectively, and were further improved at 24 and 48 h of HFOV (p<0.05). The survival of all the patients was 81%. The high survivals were found in the patients with meconium aspiration syndrome (17/18), pulmonary interstitial emphysema with air leak (9/9), and respiratory distress syndrome (RDS) whose birth weight >1500g (20/23). Complications were found in those infants with birth weight <1500g, including 6 with ventricular hemorrhage, 3 with pulmonary interstitial emphysema and 1 with hypotension.

Conclusion: Our data suggested that improved HFOV effects in neonates with respiratory failure deserve further investigation on whether if it should be used alternative of CMV.

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CEREBRAL PALSY IN VERY PRETERM BIRTHS : PREVALENCE, SUBTYPE AND RELATIONS WITH NEONATAL CEREBRAL INJURIES AT TWO YEARS - EPIPAGE STUDY

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Background: The objectives of our study were to estimate the prevalence of cerebral palsy and sensorineural impairments in very preterm infants born between 22 and 32 weeks of gestation at two years of age and to study its variations according to gestational age and brain lesions in the neonatal period. The subtype and the level of severity of cerebral palsy are also studied.

Methods: All births occurring from 22 to 32 weeks of gestation in all maternity wards of nine French regions in 1997 were included in the EPIPAGE cohort study. Neurodevelopmental status, including cerebral palsy, blindness and deafness, diagnosed at two years of age, were available for 1950 children (83% of the population enrolled in the follow-up). Impairments have been identified from the medical examination at two years of age.

Results: The incidence of cerebral palsy was 8% [95% Confidence Interval CI : 7%–10%] in very preterm infants; 44% of the children had diplegia, 28% had tetraplegia, 9% had hemiplegia, 10% had monoplegia and 7% ataxia or dyskinesia. Two percent of the children have not been classified. Of all children with cerebral palsy, half did not walk at two years. The incidence of cerebral palsy decreased from 21% at 24–26 weeks, 12% at 27–28 weeks, 8% at 29–30 weeks to 5% at 31–32 weeks. The cerebral palsy rate was higher in boys (9%) than in girls (7%) (p=0.10) and was higher in twins (18%) than in singletons (14%) before 29 weeks. After 29 weeks, rates were the same (6%). Neonatal cerebral injuries were strongly associated with cerebral palsy : 74% of children with bilateral cystic leukomalacia and 60% of children with grade IV intraventricular hemorrhage had cerebral palsy. Only 4% of children without brain lesions had cerebral palsy. The overall rates of blindness and deafness were 0.5% [IC : 0.2%–0.9%] and 0.8% [IC : 0.4%–1.2%] respectively.

Conclusion: Our study evaluated the neurological outcome of a large cohort of very preterm infants, which is of particular interest given the recent advances in perinatal care and the question of the quality of survival.

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FATAL HYPERTENSIVE CRISIS AS PRESENTATION OF COMPLEX I DEFICIENCY

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Background: In a family with three male siblings two died at the age of two and three years, respectively. Both affected brothers had deficits of their motor functions and coordination as well as nystagmus. Their now five year-old male sibling is clinically unaffected. **Case presentation:** The older sibling suddenly died at two years of age. Eating a piece of cake he suddenly developed erythema and collapsed immediately. Resuscitation efforts were unsuccessful. Our present patient presented in a similar fashion at three years of age. During a car ride his face suddenly reddened, he sweated, his hands became cold and he almost immediately lost consciousness. His blood pressure was 150/90 mmHg. He had strong capillary pulses despite the cold periphery and a body temperature of 34.5 °C. Pulmonary edema and severe left heart failure with massive dilatation of the left ventricle were confirmed by radiological imaging and cardiac ultrasound. High dose catecholamine support soon had to be initiated because of severe hypotension. With improving condition the structure of the left ventricle became normal. Blood pressure was difficult to control with systolic pressures rising to more than 200 mmHg despite treatment. Weaning from ventilation was never possible, the patient ultimately died.

Results: In our present patient, hypertension did not have an anatomical correlate, renal arterial stenosis and pheochromocytoma were excluded. Cerebral MRI before deterioration was inconspicuous. Fundoscopic examination after deterioration showed severe optic nerve atrophy bilaterally. Biochemical examination of muscle tissue revealed a reduced ATP production rate combined with a strongly reduced enzymatic activity of complex I. The complex I deficiency was also expressed in fibroblasts. The clinically unaffected remaining brother has moderately reduced activity of the complex I enzyme in muscle tissue.

Conclusion: Two brothers acutely deteriorated with sudden flushing and collapse, the outcome was fatal in both cases. Both had slight motoric retardation and nystagmus. The younger brother, in whom resuscitation efforts initially were successful, showed widely uncontrollable hypertension. To our knowledge this is the first description of a complex I deficiency presenting with fatal hypertensive crisis.

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MICROBIOLOGICAL ANALYSIS OF EXPRESSED BREAST MILK AND STOOL SPECIMENS OF PRETERM INFANTS IN A NEONATAL INTENSIVE CARE UNIT

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Background: In France, systematic microbial screening of all expressed breast milk is recommended if given to the newborn more than 12 hours later. Breast milk samples are discarded if the total bacterial count is over 1000000 /ml. This recommandation makes it difficult to encourage breastfeeding in neonatal units. The aim of the study was to determinate the impact of commensal and pathogenic bacteria present in expressed breast milk on fecal assessment of premature infants.

Methods: Prospective, nonrandomized observational study, in a level 3 NICU including 15 preterm infants with median gestational age 33 weeks (31.3 to 35.5 weeks) and median birthweight 1860 g (1240g to 2210g) fed exclusively or partially with the mother's own breast milk. All breast milk samples were screened for bacteria before feeding the infants (196 samples from 15 mothers). Fecal samples of the newborns were weekly sampled for bacterial count. Gastrointestinal and infectious problems were tracked.

Results: No gastrointestinal or infectious problems occurred during the hospital stay. Staphylococcus epidermidis was isolated in at least 2 breast milk samples from all mothers and was detected in stool specimens between day 3 and 10 of 9/15 preterm infants. After 10 days of life, Staphylococcus epidermidis disappeared from stool samples in 7/9 preterm infants (one preterm infant was followed up only to 6 days of life; one infant still presented Staphylococcus epidermidis in stool samples after day 18). When Gram-negative organisms were detected in breast milk (9/15), they were also present and persisted in the stool samples.

Conclusion: All breast milk samples were contaminated. No gastrointestinal or infectious problem was recorded. In case of breast milk contamination with Staphylococcus epidermidis, stool analysis could show transient contamination with the same bacteria which disappeared generally after 10 days of life. The efficacy of the microbiological standards for expressed breast milk recommended in NCIU in France may be questionable.

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IMPLEMENTATION OF CPAP FOR THE EARLY STABILIZATION OF VLBW INFANTS

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Background: The introduction of continuous positive airway pressure (CPAP) in neonatal units offers a new strategy in the early stabilization and management of the newborn, especially in very-low-birth-weight (VLBW) infants.

Aims: To compare the number of VLBW infants intubated within the first 36 hours of life when CPAP was introduced for early stabilization, with another group of VLBW infants managed without the use of early CPAP. To compare in both groups of VLBW infants the frequency of pneumothorax, bronchopulmonary dysplasia (BPD), mortality, severe brain injury, length of stay and days of intubation.

Methods: Study of evaluation with comparison before-after of VLBW infants born in a tertiary care hospital during two periods: Group 1: 78 VLBW infants born during 2001 and Group 2: 80 VLBW infants born from June 2003 to February 2004. In the group 1, conventional management was performed (intubation and administration of surfactant in the delivery room in <28wks or <1000g with respiratory distress syndrome). In the group 2, CPAP was introduced for early stabilization.

Results: In the group 1 mean weight was 1059±309 g and in the group 2 was 1127±295 g (p= 0.15). The mean gestational age was 29±3.3 weeks in the group 1 and 29±2.8 weeks in the group 2 (p=1). There were no significant differences in intrauterine growth restrictions, CRIB and use of antenatal steroids. In the group 1 CPAP was used for early stabilization in 8,9% and in the group 2 in 48,7% (p<0,0001). Intubated in the delivery room, 54% in group 1 versus 31% in the group 2 (p=0,004). Intubated in the first 36 hours 73% versus 49% respectively (RR=1,5(1,15–1,95). Mean days of intubation were 4±11 in the group 1 and 2.7±5,8 in the group 2 (p=0,15). The mortality rate was the same (15%) in both groups. BPD at 36 weeks was 19% in the group 1 and 14.5% in the group 2 (RR=1,34 (0,63–2,84)). Mean days on oxygen were 34±47 and 21±25 respectively (p=0,04). Pneumothorax was similar in both groups (RR=1,03 (0,21–4,95)). Severe brain injury was similar in both groups: intraventricular haemorrhage III RR=1,03 (0,15–7,10) and cystic brain lesions RR=1,03 (0,22–4,92). The mean length of stay was 68±37 days in the group 1 and 58±25 in the group 2 (p=0,08).

Conclusion: The use of CPAP for early stabilization of VLBW infants seems to be a reasonable alternative as any adverse effects has been observed, although we have not long term follow up outcomes.