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TREATMENT OF DUCTUS ARTERIOSUS IN VERY LOW BIRTH WEIGHT INFANTS: IBUPROFEN VERSUS INDOMETHACIN

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Background/aims: Since December 2002 we use ibuprofen to treat PDA. Success rates, however, were lower than expected. We therefore compared efficacy and side effects of ibuprofen in very low birth weight infants to a historical control group treated with indomethacin.

Methods: Charts of all infants < 1500g admitted from 1.1.2000 to 1.3.2005 were reviewed. Infants mechanically ventilated on day 3 of life, with echocardiographically confirmed PDA received indomethacin (3 x 0.2 mg/kg in 12 hours intervals; time period 1: before 1.12.2002) or ibuprofen (10; 5; 5 mg/kg in 24 hours intervals; time period 2. after 1.12.2002), respectively.

Results: Fifty-three (25%) of 214 infants born in time period 1 were treated with indomethacin. Median birth weight 830 g (380 - 1460), gestational age 26 wks (22 - 31). Fifty-six (36%) of 155 infants were treated with ibuprofen. Median birth weight 895 g (355 - 1430), gestational age 26 wks (23 - 30). Closure rates with first treatment cycle were 60% (indomethacin) and 34% (ibuprofen) (p=0.005). Surgical ligation was performed in 7% of infants during time period 1 versus 14% in time period 2 (p=0.02). Temporary oliguria/anuria occurred in 19% of infants in the indomethacin and in 11% in the ibuprofen treatment group. Focal intestinal perforation or NEC with perforation occurred during time period 1 in 4/53 infants treated with indomethacin and in 7/139 infants not treated, in time period 2 in 2/56 infants treated with ibuprofen and in no infant without treatment.

Conclusion: Ibuprofen was less effective than indomethacin in closing the PDA in very low birth weight infants in our centre. Need for surgical ligation was twice as high following ibuprofen treatment. The difference to results of other centres may be explained by extreme prematurity of our population.

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PULMONARY FUNCTION AT ONE YEAR OF AGE IN PREMATURE INFANTS WITH BRONCHOPULMONARY DYSPLASIA

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Background: Bronchopulmonary dysplasia (BPD) was recently classified as mild, moderate or severe in step with oxygen (O2) or positive pressure (PP) requirement at 36 wks post conceptional age (PCA).

Objective: To assess pulmonary function at one year of age of premature infants born before 32 wks PCA in step with initial BPD severity. Patients and methods: 25 infants (mean GA±SD = 27.6±1.9 wks; birthweight = 851±174g) with BPD (i.e., O2 requirement for more than 28 days) were classified as mild BPD if weaned of O2 and PP at 36 wks PCA (group1; n=8) and moderate to severe if not (group2, n=16). At 14.3±3.5 months of age (i.e.; 11.7±3.6 months corrected age) functional residual capacity (FRC) was assessed with the nitrogen washout method and the partial forced expiratory flow (Vmax FRC) with the jacket method. Values were expressed as percentage of predicted normal values.

Results: Vmax FRC and FRC of the population studied were 42.6±26.5% and 77.4±14.9% of predicted normal values, respectively. 4 infants (16.7%) had pure restrictive disease (i.e.; FRC < 80% of predicted values), 8 (33,3%) had pure obstructive disease (i.e.; Vmax FRC < 80% of predicted values) and 11 (45%) had both diseases. There was no statistical correlation between any measurements of pulmonary function and birthweight, GA, duration of mechanical ventilation nor duration of oxygen therapy. There was no significant difference in pulmonary function at 1 year of age between the 2 groups.

Conclusion: Infants with a history of BDP exhibited very frequent severe pulmonary function abnormalities at one year of age characterized by airflow obstruction, restrictive disease or both. These abnormalities were no predicted by initial BPD severity.

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CORD BLOOD ADIPONECTIN, HIGH MOLECULAR WEIGHT FORM OF ADIPONECTIN AND LEPTIN IN FULL- TERM NEONATES ARE POSITIVELY CORRELATED WITH ANTHROPOMETRIC PARA

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OBJECTIVE The aim of this study was to examine cord blood adiponectin, high molecular weight form of adiponectin (HMW) and leptin concentrations in full-term neonates, and their correlations with anthropometric parameters at birth.

DESIGN Venous cord blood samples were obtained from 135 full-term healthy newborns (57 males and 78 females, gestational age 37.0–41.6 weeks, birth weight 2,261–4,164 g, birth length 43–55 cm, birth head circumference 29–36.5 cm).

MEASUREMENTS The adiponectin and leptin concentrations were determined by enzyme-linked immunosorbent (ELISA) assays using commercially available kits. The HMW concentration was determined by ELISA originally developed by Nakano Y.

RESULTS The adiponectin, HMW and leptin concentrations in cord blood were 30.4 ± 10.4 μg/ml, 29.7 +/- 11.6 μg/ml, and 5.8 +/- 4.2 ng/ml, respectively. The percentage of HMW in the adiponectin concentrations was 99 +/- 30%. The concentrations of leptin in female infants were significantly higher than those in male infants ($p < 0.05$), but there was no significant gender differences in adiponectin and HMW concentrations among newborns. Plasma adiponectin, HMW and leptin levels had significantly positive relationships with birth weight, birth length, birth head circumference and birth weight/birth length ratio. Plasma leptin concentrations were also positively correlated with placental weight ($r = 0.342$, $p < 0.001$). Plasma adiponectin and HMW concentrations were correlated with leptin concentrations ($r = 0.286$, $p < 0.01$, $r = 0.304$, $p < 0.001$, respectively).

CONCLUSIONS These results indicate that the adiponectin concentration in newborn infants mainly exists in a HMW form, and the concentrations of plasma adiponectin, HMW and leptin may reflect fetal growth.

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CEREBRAL ENERGY DEPLETION DURING HYPOXIA-ISCHAEMIA, THERAPEUTIC WINDOW, AND REGIONAL SEVERITY OF SECONDARY ENERGY FAILURE IN NEWBORN PIGLETS

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Background: Following transient hypoxia-ischaemia (HI) a latent phase or therapeutic window exists when intervention, such as hypothermia, may ameliorate the secondary energy failure (SEF), which is associated with neuronal death. In clinical practice, there is an unavoidable lag between the recognition of HI and the opportunity to initiate neuroprotective interventions; the precise duration of the therapeutic window is unknown.

Aims: To assess the relationships between the severity of transient HI, the duration of the latent phase and the regional SEF quantified by the brain-water apparent diffusion coefficient (ADC).

Methods: Eighteen newborn piglets were subjected to transient HI (bilateral carotid occlusion and FiO2 12–16%) for up to 45min giving a range of insult severity within the bore of a 7 Tesla magnetic resonance (MR) scanner. During HI phosphorus MR spectroscopy was used to assess insult severity, which was quantified by the duration and magnitude of depletion of nucleotide triphosphate (NTP) relative to the exchangeable high-energy phosphate pool (EPP). Grey matter ADC was serially measured to provide an index of the severity of SEF. The 99% confidence interval (CI) for NTP/EPP prior to HI was defined. The duration of the latent phase was the period following HI between NTP/EPP recovering to within CI and NTP/EPP falling below CI again indicating the development of SEF.

Results: The latent phase duration correlated negatively with insult severity ($r=-0.625$, $p<0.05$). During SEF cortical ADC correlated linearly with the duration of the latent phase ($r=0.852$, $p<0.01$ at 12 hours and $r=0.89$, $p<0.05$ at 24 hours).

Conclusion: The more severe the acute HI insult, the shorter the latent phase. A shorter latent phase led to a greater extent of subsequent brain SEF. Newborn infants who have suffered severe HI may be less likely to respond to neuroprotective treatments because of the shorter therapeutic window.

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COOLING FOR NEWBORNS WITH HYPOXIC ISCHAEMIC ENCEPHALOPATHY

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Background: Experimental studies suggest that hypothermia following peripartum hypoxia-ischaemia in newborn infants may reduce neurological sequelae.

Aims: To determine whether therapeutic hypothermia in encephalopathic asphyxiated newborn infants reduces mortality and neurodevelopmental disability, without clinically important side effects.

Methods: Randomised controlled trials (RCTs) evaluating therapeutic hypothermia in newborns with hypoxic ischaemic encephalopathy (HIE) were identified using the standard search strategy of the Neonatal Review Group of the Cochrane Library. The primary outcome was death or long-term major neurodevelopmental disability. Other outcomes included adverse effects of cooling. Three reviewers independently selected, assessed the quality of and extracted data. Meta-analyses were performed using relative risk and risk difference for dichotomous data, and weighted mean difference for continuous data with 95% confidence intervals.

Results: Four RCTs were included in this review, comprising 349 term infants with HIE. Two studies (Gunn 1998, Gluckman 2005) achieved excellent follow-up rates at 18 months of age; one (Eicher 2005) had incomplete follow-up at 12 months (81.5%) and one (Shankaran 2002) has not reported long-term outcomes. The pooled analysis of the 2 higher quality studies showed no significant effect of therapeutic hypothermia on the combined outcome of death or major neurodevelopmental disability in survivors followed (RR 0.89 [95% CI 0.69, 1.05]). Inclusion of the poorer quality study (Eicher 2005) resulted in a significant reduction in death or major disability in infants allocated to therapeutic hypothermia (RR 0.80 [95% CI 0.66, 0.96]). No adverse effects of hypothermia on short term outcomes were detected.

Conclusions: Four RCTs showed no evidence of harm from therapeutic hypothermia. Evidence of efficacy remains inconclusive. Therapeutic hypothermia for infants with HIE should continue to be evaluated in well designed RCTs. This abstract is a preliminary version of the update to be included in the Cochrane Library Issue 4 2005.

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IMPROVING RESULTS WITH PERCUTANEOUS FETAL ENDOSCOPIC TRACHEAL OCCLUSION (FETO) FOR SEVERE LEFT CONGENITAL DIAPHRAGMATIC HERNIA.

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Isolated congenital diaphragmatic hernia (CDH) with intrathoracic liver and lung-head-ratio <1 (LHR) is associated with high neonatal mortality due to pulmonary hypoplasia and hypertension. We described a percutaneous technique for FETO with a balloon and report on the evolution of results in a consecutive series of 20 patients. Within two years time-period, FETO was done between 26–28 weeks in 20 fetuses with LCDH, meeting the criteria above. Under feto-maternal analgesia and immobilization, endoluminal balloon (GVB16, Cathnet) occlusion between carina and vocal cords was performed, using a 3.0 mm sheath and a 1.2mm fetoscope (11505, Storz). Under general, epidural or local anesthesia (resp. n=5;13;2) the balloon could always be successfully positioned and no maternal complications occurred. Mean operation time was 18 min and GA at delivery 33.4 weeks. PPROM occurred in 20% at <28 resp. 30% at <32 wks. Airways were restored either perinatally (n=9) or prenatally (n=11). Neonatal (7d) survival resp. at discharge were 70%(14/20) and 60%(12/20). Late (>7 d) losses were due to pulmonary hypoplasia in one, but in a second baby care was withdrawn for a prenatally missed chromosomal anomaly, however with adequate ventilatory function. During that period 17 contemporary controls of LCDH were evaluated, with an antenatal loss rate of 29% (5/17 TOP) and survival at discharge of 8 % (1/12). There seems to be a trend for decreasing operation time, PPROM rates, lesser risk for preterm delivery and potentially better results with prenatal versus perinatal balloon retrieval (44 vs.73 %). FETO is reproducible, minimally invasive to the mother, but carries a risk for PPROM. With increasing experience, incidence of PPROM and preterm delivery drop. Airways can be restored prior to birth, allowing vaginal delivery and further management at the referring center. FETO improved prognosis in highly selected cases with LCDH as compared to contemporary controls.