HIE. Our results confirm the potential utility of miRNA biomarkers in the early diagnosis of HIE.

PS-152 ACTIVIN-A: A BIOMARKER OF SEVERE ENCEPHALOPATHY

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Background Hypoxicischaemic encephalopathy (HIE) remains one of the leading causes of neonatal morbidity and mortality. Therapeutic hypothermia may improve the outcome of infants with moderate/severe encephalopathy but only if initiated within six hours of the initial insult. The aim of our study was to determine if umbilical cord blood (UCB) levels of Activin-A, a glycoprotein previously implicated in neuronal brain injury, could identify infants with moderate/severe encephalopathy at birth.
Methods Full term infants with perinatal asphyxia (PA) were identified by a cord pH < 7.1 and/or five minute Apgar score ≤ 6 and/or requirement for intubation/CPR at birth. Following diagnosis at delivery, UCB was drawn, processed and bio-banked. HIE grade was confirmed with early continuous EEG monitoring and modified Sarnat score. Activin-A analysis was carried out using ELISA (R&D Systems).
Results In total 156 infants (controls = 78, cases = 78) were included in the study. Cases included 56 infants with PA (non-HIE) and 24 infants with HIE (mild = 14, moderate = 6, severe = 4). Following analysis, a significant increase in Activin-A expression was observed between the control and severe HIE groups, and between the perinatal asphyxia and severe HIE groups (median (SD) = 487.48 (470.21) vs 911.54(594.1) p = 0.032 and 487.95 (384.1) vs 911.54 (594.1), p = 0.035, respectively). No significant difference was seen between PA and mild or moderate HIE. Using a cut-off value of 724.5 pg/ml we report Activin-A has a 100% negative predicitive value, with a sensitivity and specificity of 100% and 70% respectively.
Conclusion Our study supports the use of Activin-A as a biomarker of severe encephalopathy.

PS-153 REFERENCE VALUES OF MALONDIALDEHYDE IN BLOOD AND URINE OF THE HEALTHY TERM NEWBORN IN THE PERINATAL PERIOD

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Introduction A certain amount of oxidative stress has a role in the normal progression of embryonic and fetal growth, as well as during labour. In contrast, increased OS has been involved in the causation or worsening of several gestational, fetal and neonatal diseases. Cell lipid peroxidation by free radicals causes membrane lipid disruption and is potentially harmful. Malondialdehyde (MDA) is one of the end products of lipid peroxidation, which can be interpreted as a marker of the extent of damage to cells and the anti-oxidative system capacity.
Objective As part of a study on oxidative stress on the term newborn, we aimed to determine the baseline levels of MDA in blood and urine of healthy term newborns.
Patients and methods All newborns above 35 gestational weeks born in our institution from October 2012 – March 2013 were eligible for study. Newborns with potential risk factors for increased oxidative stress were excluded for this analysis. Blood samples at birth (cord arterial and venous blood) and at 48 h postnatal life (heel puncture) were collected. Urine from the first and second day was collected.
Results 204 newborns (90 females and 114 males) met the inclusion criteria. Reference MDA levels were as follows (μM, mean ± SD): cord vein 3.37 ± 1.16; cord artery 3.33 ± 0.94. At 48 h postnatal life, 3.29 ± 0.91. Urinary levels were as follows: first day urine 1.24 ± 0.87; second day urine 1.48 ± 0.99. There were no statistical differences between males and females.
Conclusions These are data from a large group of newborns, aiming to give an accurate description of the baseline levels of malondialdehyde in our population, which could be useful when it comes to making therapeutic decisions in the future.

PS-154 HAS THERAPEUTIC HYPOTHERMIA (TH) CHANGED THE PROGNOSTIC VALUE OF CLINICAL EVALUATION OF NEONATAL HYPOXIC-ISCHAEMIC ENCEPHALOPATHY (HIE)? A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background Clinical grading of HIE correlates with outcome. TH improves survival and neurodevelopment in HIE. Aim: To review the effect of TH on the prognostic value of clinical grading of HIE and its course.
Methods Systematic review and meta-analysis of studies on the ability of Sarnat stage at defined times to predict death/disability at ≥18 m in normothermia and TH-treated term neonates with HIE. Pooled risks were estimated, with random effect models, according to HIE stage and treatment.
Results Data on encephalopathy stage at <6 h were available from seven TH trials including 1214 newborns with moderate/severe HIE. Post-hoc studies of two trials (381 infants) provided 72 h data.

The proportion of infants with moderate encephalopathy at <6 h who had poor outcome was 52% (95% CI:44–60; I^2 = 48%) in normothermia-treated and 35% (95% CI:28–41; I^2 = 51%) in TH-treated neonates. The proportion for severe encephalopathy was 83% (95% CI:72–93; I^2 = 81%) in normothermia and 67% (95% CI:58–76; I^2 = 74%) in TH. At <6 h, the OR for severe vs moderate HIE to predict unfavourable outcome was 4.14 (95% CI:2.40–7.13; I^2 = 35%) in normothermia and 3.77 (95% CI:2.62–5.41; I^2 = 0%) in TH.

TH did not affect HIE grade at 72 h. No improvement of encephalopathy at 72 h increased the risk of poor outcome (OR 8.21, 95% CI:2.01–33.6; I^2 = 74%). The ORs for persistent moderate and severe encephalopathy at 72 h to predict unfavourable outcome were 5.09 (95% CI:1.53–16.92; I^2 = 66%) and 42.83 (95% CI:13.55–135.37; I^2 = 44%).

Conclusions While TH has changed the predictive values of initial HIE grades, clinical staging at <6 h correlates with outcome. The course of encephalopathy throughout TH is valuable in outcome prediction.

PS-155 COMPARISON OF CLINICAL AND ELECTROPHYSIOLOGICAL SIGNS OF ENCEPHALOPATHY IN NEONATES WITH PERINATAL ASPHYXIA QUALIFYING FOR HYPOTHERMIA

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Background and aims Early prediction of neurodevelopmental outcome following hypoxic-ischaemic encephalopathy remains a challenge. The aim of this retrospective study was to evaluate the aEEG background patterns and Thompson score on admission in asphyxiated neonates receiving hypothermia regarding outcome and neonatal variables.
Methods After excluding congenital malformations and muscle paralysis, 89 neonates (January 2008 to June 2012) were included (GA: 39.7 ± 1.8 wks; BW: 3504 ± 640 g). On admission the Thompson score and aEEG were recorded. aEEG was scored as Continuous Normal Voltage (CNV), Discontinuous Normal Voltage (DNV), Burst-Suppression (BS), Continuous Low Voltage (CLV) or Flat Trace (FT). The combination of one or more of the following event (s): death, cerebral palsy, and Griffiths DQ less than 85 at 18 months were considered an adverse outcome. ANOVA, correlation, and binary logistic regression analyses were performed.
Results Thompson scores (in mean ± sd) were associated with aEEG pattern (CNV: 8.3 ± 1.7; DNV: 8.9 ± 1.9; BS: 11.6 ± 3.6; CLV: 12.0 ± 2.1; FT: 13.1 ± 3.2; $p < 0.001$). Also, both aEEG and Thompson score were statistically correlated with Apgar 1 and 5 min scores ($p < 0.05$). Using a logistic regression model, both Thompson score (OR = 1.43; 95% CI = [1.15;1.77]) and aEEG pattern (BS: OR = 4.06; 95% CI = [0.74;22.16]; CLV: OR = 11.10; 95% CI = [1.38;89.66]; FT: OR = 13.35; 95% CI = [1.87;95.31]; reference group: CNV +DNV) were significant predictors of an adverse outcome.
Conclusions Both Thompson scores and aEEG are associated with outcome in neonates receiving hypothermia for perinatal asphyxia and with 1 min Apgar scores. Further studies are needed to identify which method is preferable for selection of neonates for hypothermia.

PS-156 ASSESSMENT OF MYOCARDIAL FUNCTION IN INFANTS RECEIVING THERAPEUTIC HYPOTHERMIA USING TISSUE DOPPLER IMAGING

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Introduction Hypoxic ischaemic encephalopathy (HIE) may lead to cardiovascular dysfunction in newborn infants and conventional echocardiographic measures such as fractional shortening (FS) and left ventricular output (LVO) may not accurately detect cardiac dysfunction in these patients.[1]
Objective To evaluate cardiac dysfunction in HIE using tissue Doppler imaging (TDI).[2]
Methods 20 infants born at ≥36 w gestation with HIE requiring therapeutic hypothermia (TH) were examined with serial conventional echocardiography and TDI on days 1, 2, 3 and after re-warming. Structural integrity of the heart was confirmed before obtaining measures of myocardial function (peak systolic (S'), early (E') and late diastolic (A') velocities, myocardial performance index (MPI) [using TDI], and FS and LVO). Measurements were also obtained from 10 healthy term infants as controls. Ethical approval and written parental consent were obtained.
Results Median gestation and birth weights of infants with HIE vs. controls was 39.6 w vs. 40 w and 3110 g vs. 3170 g. On days 1, 2, 3 all myocardial velocities (MV), except left ventricular A' on day 3, were significantly lower (<0.05) and MPI was significantly higher ($p \leq 0.05$) in the HIE group. After re-warming all MVs and MPIs were similar between the two groups. FS and LVO were similar between both groups on all days, except LVO on day 1 which was significantly lower in HIE infants ($p < 0.05$).
Conclusions TDI, compared to FS and LVO, may be better at detecting myocardial dysfunction in this group of babies and hence improve management of cardiac dysfunction.

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PS-157 MODERATE TO SEVERE NEONATAL ENCEPHALOPATHY IS PREDICTED BY RISING SERUM BUT NOT CSF BIOMARKERS

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Background Term infants with NE of hypoxic-ischaemic origin, have been exposed to generalised oxidative injury which may cause excessive cytokine production and release in serum and CSF. Cytokine levels may correlate with severity of brain injury and aid in outcome prediction.
Objective To investigate the relationship between serum and CSF biomarkers and NE in a group of term infants exposed to perinatal hypoxia-ischaemia compared to controls.
Design/Methods Levels of serum and CSF biomarkers [VEGF, IL-8, Epo, GM-CSF] were serially measured over day 1–11 in a group of term newborns with NE and controls (serum only). These values were compared to grade of encephalopathy defined by Sarnat score.
Results Twelve control and 82 cases had serum samples collected (Grade 0 NE = 6, Grade I NE = 23, Grade II NE = 42, Grade III NE = 11). Thirty-nine infants underwent TH, 4 infants died. Controls had significantly lower serum Epo on day 1–2 compared with cases (p-values < 0.05). Grade II/III NE was significantly associated with elevated serum Epo (Day 2), IL-8 (Day 2 and 6–8) (p-values < 0.05) and with decreased VEGF (Day 1). Grade II/III NE was best predicted by Epo and IL-8 (Day 2) and VEGF (Day 1) (p-values < 0.05). CSF biomarker levels (n = 34 infants) were not significantly associated with abnormal NE grade.
Conclusions Term infants exposed to perinatal hypoxia-ischaemia have elevated levels of serum biomarkers compared to