Conclusions Children with syndromic craniosynostosis are at risk of elevated ICP due to a complex interaction of risk factors. The relationship between mild and moderate OSA and elevated ICP is weak, however in individual patients OSA may be the decisive factor. Severe OSA significantly increases the risk of elevated ICP.

Intervention/Hypothermia

PS-149 INITIATION OF THERAPEUTIC HYPOTHERMIA BY REFERRING HOSPITALS DURING NEONATAL TRANSPORT – EXPERIENCE IN VICTORIA, AUSTRALIA

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10.1136/archdischild-2014-307384.445

Background Hypothermia is an effective treatment for moderate-severe hypoxic-ischaemic encephalopathy (HIE) in term newborns. Non-tertiary units (NTUs) may initiate controlled whole-body hypothermia to a target rectal temperature of 33–34°C in consultation with the Newborn Emergency Transport Service (NETS) by removing external heat sources prior to arrival of the NETS team. We aimed to evaluate temperature outcomes during neonatal transport when hypothermia was initiated by the referring NTU.
Method We retrospectively audited NETS records of infants with HIE treated with hypothermia from September 2008–August 2012. Infants in whom hypothermia was initiated by the NTU were compared with those in whom the NETS team started cooling.
Results Demographics of the 123 included infants were comparable between groups. Infants cooled by NTUs began cooling earlier (1.10 vs. 3.25 h after birth, $p < 0.01$) and reached the target temperature (33–34°C) sooner (3.35 vs. 4.54 h, $p < 0.01$) than infants cooled by NETS. There was no difference in time of referral, stabilisation, or arrival at receiving hospital. There was a trend towards more infants cooled by NTUs achieving the target temperature (33–34°C), OR 2.19 (0.96, 4.96). Infants cooled by NTUs were more likely to have temperatures <33°C, OR (95% CI) 5.39 (1.64, 22.83), but had fewer temperatures >37°C, OR (95% CI) 0.25 (0.07, 0.85).
Conclusions Controlled whole body-hypothermia initiated by regional NTUs, with guidance from NETS, allows earlier initiation of cooling, and attains the target 33–34 °C sooner to optimise neuroprotection in newborns with HIE. Clinical practice should focus on avoiding temperatures <33°C and preventing hyperthermia.

PS-150 CAN CEREBELLAR AND BRAINSTEM APPARENT DIFFUSION COEFFICIENT (ADC) VALUES PREDICT NEUROMOTOR OUTCOME IN TERM NEONATES WITH HYPOXIC-ISCHAEMIC ENCEPHALOPATHY (HIE) TREATED WITH HYPOTHERMIA?

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10.1136/archdischild-2014-307384.446

Objective To evaluate apparent diffusion coefficient (ADC), measured in specific infratentorial brain structures in the first weeks of life, as prognostic indicator of neuromotor outcome for HIE neonates both treated and not with whole-body hypothermia (TH).
Methods We retrospectively evaluated 71 MRI studies of term neonates, born between 2010 and 2013 at Boston Children's Hospital. Selected cases were classified into three groups: 1) HIE neonates who underwent TH, 2) HIE normothermics (TN), and 3) controls. The neuromotor outcome was categorised as normal, abnormal and death. The ADCmean was calculated for six infratentorial brain regions.
Results 51 infants were included: 29 HIE TH treated, 11 HIE TN, and 11 controls (mean gestational age of 39.07 weeks; 62% male; 11.7% non-survivors). Mean age at first MRI was 3.6 days (range, 1–14 days). Statistically significant correlation was shown between motor outcome and the ADC mean in the vermis ($p = 0.002$), cerebellar left hemisphere ($p = 0.035$), midbrain ($p = 0.028$), and pons ($p = 0.008$). In patients treated with TH, only in the vermis did ADC mean remained significantly lower than controls ($p = 0.03$). There were significant correlation between infant survival and ADC mean in all ROIs except the pons and medulla.
Conclusions ADC mean values during the first week of life in vermis, cerebellar left hemisphere, midbrain and pons are correlated with the motor outcome in infants with HIE. Therefore, this objective tool could be used to detect particularly severe cases of HIE for assessing prognosis at the first week of life.

PS-151 ALTERED MICRORNA EXPRESSION IN UMBILICAL CORD BLOOD OF INFANTS WITH HYPOXIC ISCHAEMIC ENCEPHALOPATHY

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10.1136/archdischild-2014-307384.447

Background To guide the neuroprotective management of infants with hypoxic ischaemic encephalopathy (HIE), early identification is essential. MicroRNAs are small non-coding RNA molecules with potential for use as biological markers for disease. The aim of this study was to investigate the expression profile of miRNA in umbilical cordblood (UCB) from infants with HIE.
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. Degree of encephalopathy was defined using both continuous multichannel-EEG in the first24 hours, and modified Sarnat score. In total, 70 infants, 52 cases (32 PA without HIE, 20 with HIE) and 18 controls, were included in the study. miRNA was extracted from UCB and the expression profiles of 866 miRNAs were determined using a microarray assay. Significant findings (fold change > ± 1.3) were validated using quantitative RT-PCR (qRT-PCR).
Results On microarray 70 miRNAs were differentially expressed between the HIE and the control group. Of these hsa-miR-374a was the most significantly downregulated in HIE vs controls ($p < 0.001$). Validation of expression using qRT-PCR confirmed a significant reduction in expression among HIE vs. perinatal asphyxia vs. controls (mean RQ (SD) = 0.5215 (0.374) vs 1.1022(1.521) vs 1.755 (1.689), $p < 0.02$).
Conclusion To our knowledge, this is the first study to describe the miRNA profile present in umbilical cord blood following

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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10.1136/archdischild-2014-307384.448

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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10.1136/archdischild-2014-307384.449

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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10.1136/archdischild-2014-307384.450

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%).