Background and Aims A recent RCT suggested improved neurological outcome at discharge for moderate to severe perinatal asphyxia babies given iv magnesium sulphate. However, this trial was performed in babies who were not cooled.

Methods We present a pilot case series of 3 patients with moderate to severe HIE who satisfied the criteria for cooling and received both cooling and iv magnesium sulphate loading of 200mg/kg. Serum Magnesium levels were monitored at 0, 12, 24, 48, 72 hours of cooling.

The babies were reviewed for adverse effects of magnesium sulphate in terms of hypotension, arrhythmia, feed intolerance, respiratory depression and hypocalcemia.

Results One patient received systemic cooling and two other patients received selective head cooling. In addition to iv magnesium sulphate loading, decision was made to institute continuous infusion of iv magnesium sulphate in one of these patients for 4 days at 20–40 mg/kg/h for PPHN. All babies achieved serum magnesium levels of > 1.2 mmol/l within 24h of the loading dose, which was similar to the level aimed for in the previous RCT.

Magnesium sulphate was well tolerated with only mild hypotension requiring one day of dopamine (max 5 mcg/kg/min) in one patient. No babies had respiratory depression, arrhythmia, feed intolerance or hypocalcemia. Neurodevelopmental outcome to date is also presented.

Conclusions Magnesium sulphate is well tolerated in babies with moderate to severe HIE in the cooling era. A large RCT is required to assess its efficacy, long term impact and further look into adverse effects.
Abstracts

Methods Newborn piglets underwent hypoxia following a standardized model. They were randomly assigned for 30 min resuscitation with air (21% O₂) (n=12) or 2.1% Hydrogen gas mixed into synthetic air, H₂ (n=14) and then observed for 9 hours. One control group (n=6) went through the same procedures and observation time (anesthesia, surgery, ventilation and sample collection). The left hemisphere was used for histopathology. Tissue from prefrontal cortex and liver were snap frozen in liquid nitrogen and stored by –70°C until analysis. The tissue samples were homogenized and the protein extracted. A Quantikine KM 300 immunoassay was used to measure activated caspase-3 protein. Gene expression for Casp-3, BDNF, MMP-2, MMP-9 and VEGFR2 was measured in tissue from prefrontal cortex and liver.

Results The use of 2.1% hydrogen gas mixed into synthetic air decreased activated caspase-3 vs. air. In liver tissue piglets resuscitated with air: 12.6 pg/mg protein SD (9.1) vs. H₂: 5.3 (4.9), p<0.051 whereas in cortex piglets resuscitated with air 26.3 pg/mg protein (14.9) vs. H₂: 15.4 (13.0), p<0.05.

There were no significant changes in gene expression in liver and cortex. Histopathology showed a tendency to less brain damage in the hydrogen group.

Conclusions Hydrogen gas used for newborn resuscitation may reduce apoptosis.

The neuroprotective effects of valproic acid, an histone deacetylase inhibitor in a neonatal hypoxic-ischemic rat model

doi:10.1136/archdischild-2012-302724.1115

Introduction Neurodegenerative diseases were associated with a decrease in histone acetylase transferase (HAT) activity, resulting in relative over-deacetylation. Histone deacetylase (HDAC) inhibitors were suggested as potentially neuroprotective agents. The aim of this study was to evaluate the neuroprotective effects of valproic acid (VPA), an histone deacetylase inhibitor, in neonatal hypoxic ischemic rat model.

Methods After being anesthetized, 7-day-old pups underwent ischemia followed by exposure to hypoxia. The pigs were divided into 5 groups: sham group, vehicle group (saline group) and VPA group. VPA was administered intraperitoneally for three times; 24 and 48 hours after the first dose, respectively. After sacrifice, brain infarct volume, apoptosis, HDAC activity, acetylated H4 protein and caspase 3 expression, and proinflammatory cytokine concentrations were evaluated in brain tissue of rat pups.

Results Percent infarcted brain volume and number of TUNEL positive cells per unit area in hippocampus and cortex CA1 were markedly reduced with VPA treatment. HDAC activity was found to be significantly reduced in VPA group, whereas acetylated H4 protein expression was significantly increased with VPA treatment. The caspase-3 activity in VPA group was significantly lower than the control group. The proinflammatory cytokine levels also significantly decreased with VPA treatment.

Conclusions This is the first study that showed the neuroprotective effects of VPA treatment as an HDAC inhibitor by reducing percent infarcted brain volume, histone deacetylation activity, inflammation and apoptosis while increasing acetylated H4 protein levels in a neonatal hypoxic-ischemic rat model.

Hypoglycaemia and insulin-induced alterations in the retina of rat pups

doi:10.1136/archdischild-2012-302724.1116

A Pig Model of the Preterm Neonate: Anthropometric and Physiological Characteristics

doi:10.1136/archdischild-2012-302724.1117

Background and Aims Rat pups are applicable to investigate specific role of the factors which are implicated in the pathogenesis of retinopathy of prematurity (ROP) including hyperglycaemia and insulin treatment.

Methods The aim of our study was to investigate specific effect of streptozotocin-induced hyperglycaemia, insulin-treatment and intravitreal injection of a potential retinoprotective agent, pituitary adenylyl cyclase activating polypeptide (PACAP) on the rat pups’ retina. We made a comparative analysis between the following treatment-groups: controls (Stz-/Ins-), insulin-treated (Stz-/Ins+), hyperglycaemic (Stz+/Ins-), insulin-treated hyperglycaemic (Stz+/Ins+), all animals were treated with intravitreal PACAP or vehicle. Blood glucose levels were monitored. The retinas were processed on P21 for routine histology and immunohistochemistry for glial fibrillary acidic protein (GFAP), GLUT1 and tyrosine hydroxylase (TH).

Results Standard histological methods revealed no major differences between the groups. Increased expression of GFAP – as an specific marker of metabolic insults in the retina- was detected from the inner retina in the Stz-/Ins+ group, although hypoglycaemia didn’t develop. Similar alteration of the GFAP staining was found in the hyperglycaemic (Stz+/Ins-) and insulin-treated hyperglycaemic (Stz+/Ins+) groups. Intravitreal PACAP resulted in suppression of the elevated GFAP expression in the Stz-/Ins+ group, but not in the Stz+/Ins- and Stz+/Ins+ ones. None of the groups showed alteration in the anti-TH immunoreactivity (dopaminergic amacrine cells) or GLUT1 expression of pigment epithelial cells.

Conclusions In our model hyperglycaemia or insulin did not induce ROP; however, sign of metabolic insult was detected in the neural retina, which was partly prevented by intravitreal PACAP application.