Background and aims Acute kidney injury (AKI) is a common consequence of perinatal asphyxia (PA). Therapeutic hypothermia (TH) used for neuroprotection in hypoxic-ischaemic-encephalopathy (HIE) may also ameliorate kidney injury. AKI can be associated with more severe PA, but association with worse neurological outcome remains to be proven. We aim to evaluate the incidence of AKI in neonates under TH and the association with HIE grades and outcome.

Methods A total of 51 cooled infants were reviewed using a prospectively collected database. Modified AKIN criteria were used to classify AKI. We studied perinatal, resuscitation and clinical data during admission to the NICU. Outcome of interest was duration of NICU stay, predictable neurologic outcome and mortality.

Results AKI was found in 17 of 51 neonates (33%). Based on the modified AKIN criteria, 13, 1, and 3 patients had stages I, II, and III, respectively. AKI was more frequent in HIE 2/3 than in the rare HIE 1 infants that were cooled ($p < 0.03$) and in those with worse base deficit at birth ($p < 0.05$). A significant association was found between vancomycin and gentamicin use and AKI ($p < 0.01$). Renal replacement therapy was needed in 2/3 of AKIN stage III infants. NICU stay, mortality and predicted adverse neurologic outcomes were not associated with AKI.

Conclusions AKI was less frequent in our cohort than the one previously described in non-cooled newborns. More severely asphyxiated neonates were more likely to experience AKI, but AKI was not related to worse outcomes.

PO-0395 SCAVENGING OF EXTRACELLULAR HAEMOGLOBIN MODIFIES THE MONOCYTE-MACROPHAGE RECRUITMENT AND DIFFERENTIATION IN THE INTRAVENTRICULAR SPACE FOLLOWING IVH

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10.1136/archdischild-2014-307384.1041

Introduction Severe cerebral intraventricular haemorrhage (IVH) in preterm infants continues to be a major clinical problem. To date, no available therapy prevents infants from neurologic sequel following IVH. Recruitment of monocytes-macrophages and periventricular infiltration is a key step in the inflammatory response leading to brain damage. The sequence of the recruitment and profiling of monocytes-macrophages following IVH is not well characterised. We have previously shown that extracellular haemoglobin induces chemotactic cytokines following IVH. Haptoglobin is a haemoglobin scavenger and could potentially protect the immature brain from the detrimental effects of haemoglobin.

Objective To characterise the recruitment and differentiation of monocytes-macrophages in the intraventricular space following IVH and to investigate if haemoglobin scavenging with haptoglobin alters the recruitment and differentiation.

Methods Using a preterm rabbit pup model of IVH we characterised the immune cell recruitment and differentiation in intraventricular cerebrospinal fluid (CSF) at 24 to 72 h following haemorrhage. Using flow cytometry, immunohistochemistry and mRNA and protein analysis we characterised the systemic and CSF infiltrating macrophages in animals with IVH, sham controls and animals treated with intraventricular injections of haptoglobin.

Results Following IVH, there is an infiltration of M1 macrophages into the intraventricular CSF. Intraventricular introduction of the haemoglobin-scavenger haptoglobin modifies them

into alternative M2 macrophages, expressing CD163. This causes a subsequent *in vivo* clearance of the accumulated haemoglobin.

Conclusion Following IVH, intraventricular haptoglobin treatment modifies macrophage differentiation, initiating clearance of extracellular haemoglobin. Treatment of haptoglobin might be a feasible approach to protect the immature brain following IVH.

PO-0396 THE SIGMA-1 RECEPTOR AGONIST PRE-084 PROTECTS AGAINST GLUTAMATE INDUCED NEUROTOXICITY IN PRIMARY HIPPOCAMPAL NEURONS

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10.1136/archdischild-2014-307384.1042

Background Prematurity is a major determinant of neonatal mortality and morbidity. The number of preterm birth is still on the rise. Recently we and others could demonstrate neuroprotective effects of sigma-1 receptor ligands in adult and newborn animal models of brain injury. Since sigma-1 receptor agonists are already undergoing clinical trials in adult neurological disease, they might be considered a promising therapeutic option also in preterm brain injury. We have previously shown that the selective sigma-1 receptor agonist PRE-084 (2-(4-morpholinethyl)-1-phenylcyclohexane-carboxylate) protects against neonatal excitotoxic brain injury *in vivo*. The aim of the present study was to investigate whether PRE-084 is able to prevent neurotoxicity following glutamate exposure *in vitro*.

Methods Cultured primary hippocampal neurons (day *in vitro* 10) were pre-treated with PRE-084 before glutamate was applied. Subsequently cell death was quantified by means of PI/calcein – AM staining using live confocal microscopy. Neurons were randomly assigned to one of the following groups: i) control, ii) glutamate or iii) glutamate+PRE-084. PRE-084 was applied in two dosages (10 and 100 μ M) prior to glutamate.

Results The application of PRE-084 significantly reduced the percentage of dead cells (PRE-084 10 μ M: 22.09 (20.50;28.84) and 100 μ M: 25.87 (18.77;33.40)) compared to the untreated glutamate control group 43.56 (39.86;46.02).

Conclusion Our data show that administration of PRE-084 protects against glutamate induced cell death in primary hippocampal neurons. PRE-084 shows considerable promise as a therapeutic strategy in preterm brain injury and might provide an adequate means of combating this major cause of neurological disability in infancy.

PO-0397 THE NEUROPEPTIDE SECRETONEURIN IS PROTECTIVE IN ESTABLISHED *IN VIVO* AND *IN VITRO* MODELS OF NEONATAL BRAIN INJURY

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10.1136/archdischild-2014-307384.1043