

**Methods** 31 babies born between 28 and 36 weeks' gestation were studied. 19 babies were IUGR with individualised birth weight (normalised for sex, ethnicity, parity, maternal BMI) below 3<sup>rd</sup> centile. 12 babies were appropriately grown with individualised birth weight between the 25<sup>th</sup> and 75<sup>th</sup> centile. Blood neurotrophin concentrations were measured using protein chip technology in 30 babies (19 IUGR and 11 controls) between 2 and 7 days after birth. In 14 babies (7 from each group) MRI brain was performed at term equivalence.

**Results** Fractional anisotropy (FA) was lower in IUGR babies compared to controls in 7 out of 8 regions with no statistical significance. Apparent diffusion coefficient (ADC) was lower in IUGR babies compared to controls in 6 out of 8 regions, reaching significance in frontal lobes. 7 out of 8 regions were smaller in IUGR babies compared to the control babies, reaching significance in the dorso-medial pre-frontal cortex. Differences did not persist when normalised for intracranial volume. Serum neurotrophin concentrations were elevated in IUGR babies but did not reach statistical significance. Using multiple regression only FA of right frontal lobe was significantly related to BDNF ( $R=0.65$ ;  $p=0.012$ ).

**Conclusion** IUGR babies showed no differences in neurotrophin concentrations and decreased ADC in frontal lobes when compared with controls.

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#### PREDICTIVE VALUE OF VASCULAR ENDOTHELIAL GROWTH FACTOR IN PRETERM NEONATES WITH INTRAVENTRICULAR HAEMORRHAGE

doi:10.1136/archdischild-2012-302724.1091

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**Objective** Intraventricular haemorrhage (IVH) is a major problem in premature infants. Our objective is to assess the early predictive value of vascular endothelial growth factor (VEGF) for development of IVH and management of its sequel in preterm neonates.

**Methods** We prospectively studied 150 preterm neonates (PT) less than 34 weeks gestation. Fifty of them completed the study. 30/50 developed IVH during follow up, and 20 did not. First 24 hours, and 3rd day serum samples were collected. Cerebrospinal fluid (CSF) samples were withdrawn for 10 IVH patients.

**Results** Serum VEGF; both samples were increased in IVH compared to non-IVH group, ( $P=0.001$ ). PHVD-group ( $n=10$ ) had higher VEGF in both samples than resolved IVH ( $P=0.004$ ), ( $P=0.005$ ). While, VEGF increased in the IVH group 2nd sample compared to 1st ( $P=0.000$ ), it decreased in non-IVH group, ( $P=0.033$ ). Each 1 unit increase in 1ST VEGF increased the risk of occurrence of IVH by 1.6%. 3rd day VEGF at a cut-off value of 135pg/ml is 96% sensitive and 100 specific to predict post haemorrhagic ventricular dilatation (PHVD). Serum VEGF inversely correlated with TLC, pH, PO<sub>2</sub> and HCO<sub>3</sub>, and positively correlated with PCO<sub>2</sub> and FiO<sub>2</sub>.

**Conclusion** Serum VEGF predicts development of IVH and PHVD in PT neonates. Also, high CSF level of VEGF could predict the need for permanent shunt placement.

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#### NEONATAL HYPOGLYCEMIA IS ASSOCIATED WITH INCREASED ALBUMIN NITRATION IN SMALL FOR GESTATIONAL AGE TERM NEWBORNS

doi:10.1136/archdischild-2012-302724.1092

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**Background and Aims** Neonatal hypoglycemia is a frequent event in small for gestational age (SGA) term newborns. Its clinical significance is a highly controversial issue but in experimental models, hypoglycemia has been reported to cause oxidative stress. Among the reactive species, peroxynitrite is responsible for protein nitration, lipid peroxidation and DNA damage, a process referred to as nitro-oxidative stress which can induce apoptosis. The aim of the present study was to investigate whether hypoglycemia is associated with plasma albumin nitration as a marker of nitro-oxidative stress in SGA term newborns.

**Methods** Using a highly sensitive ELISA we quantified plasma nitroalbumin (PNA) as a marker of peroxynitrite generation in 26 SGA term newborns with close glucose monitoring. We compared PNA concentrations in 9 normoglycemic (glycemia  $\geq 2.5$  mmol/L) newborns and in 17 hypoglycemic (glycemia  $< 2.5$  mmol/L) newborns.

**Results** PNA measured during the first hours of life was inversely correlated with glycemia ( $r=-0.63$ ,  $p=0.01$ ) and significantly higher in hypoglycemic compared to normoglycemic patients (7.4ng/mL [5.0–7.9] in normoglycemic patients vs. 20.8ng/mL [9.9–77.7] in hypoglycemic patients,  $n=14$ ,  $p<0.01$ ). PNA measured at day 1 of life was significantly higher in patients with recurrent hypoglycemia compared to patients with transient hypoglycemia and normoglycemic patients. We observed significant correlations between PNA at day 1 and the area under the curve of the glycemia measured before PNA sampling for several threshold values of glycemia.

**Conclusions** These results indicate that recurrent hypoglycemia is associated with systemic protein nitration in SGA term newborns, suggestive of a significant nitro-oxidative stress.

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#### HYPOGLYCEMIA INDUCES A NITRO-OXIDATIVE STRESS IN PRETERM NEWBORNS

doi:10.1136/archdischild-2012-302724.1093

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Recent data suggest that free radical injury occurs in the neonatal brain after hypoglycemia in animal models. We developed an ELISA allowing the quantitative determination of nitrated plasma albumin (nitroalbumin, PNA) as a biomarker of peroxynitrite generation and investigated the potential nitro-oxidative stress induced by hypoglycemia ( $< 2.5$  mmol/L) in premature newborns.

We measured PNA concentrations at days 0, 1 and 4 of life in 72 preterm infants without any other obvious cause of nitro-oxidative stress such as infection, asphyxia and hyperglycemia. Glucose levels were monitored every 3–4 hours using a strip method. For each patient, we calculated the AUCs for glycaemia measured during the 12, 18 and 24 hours preceding blood sampling as an index of the severity, the number and the duration of hypoglycemic events during the first day of life. Statistical analysis was performed using non-parametric tests.

PNA concentrations were significantly higher in hypoglycaemic than in normoglycemic infants at days 0, 1 and 4. A significant inverse correlation was found between PNA at D<sub>1</sub> and AUGs. PNA concentration at D<sub>1</sub> is related to the number of hypoglycemic events. Gender, term, oxygen exposure, respiratory and hemodynamic parameters were not correlated with PNA concentrations.

Thus, low glycemia levels during the first day of life are specifically associated with increased albumin nitration in preterm newborns, especially in case of recurrent hypoglycemia. This suggests the occurrence of systemic nitro-oxidative stress implying a risk of end-organ damage due to protein nitration, lipid peroxidation and DNA damage, in particular to the brain.