11

OPTICAL IMAGING OF THE NEONATAL BRAIN

T Austin[1], J C Hebden[2], A Gibson[2], R M Yusof[2], S R Arridge[3], J H Meek[1], D T Delpy[2], J S Wyatt[1] [1]University College London, Paediatrics and Child Health, London, United Kingdom; [2]University College London, Medical Physics and Bioengineering, London, United Kingdom; [3]University College London, Computer Science, London, United Kingdom

Background: Perinatal brain injury remains an important problem for critically ill newborn infants. Optical methods provide a means of monitoring brain oxygenation safely in an intensive care environment. Information on light absorption and scattering throughout the brain can be obtained by measuring the time of flight of photons from multiple sources and detectors. The aim of this study was to reconstruct three dimensional images of regional cerebral oxygenation from newborn infants using a time resolved optical imaging system.

Methods: Ten infants were studied with a median (range) postmenstrual age of 30 (26–37) weeks. The median age at study was 28 (3–40) days. Three infants had evidence of unilateral intraventricular haemorrhage (IVH) on cranial ultrasound examination. One infant had suffered an acute hypoxic-ischaemic injury following uterine rupture and was studied whilst receiving ventilatory support. Optical data were collected using a custom built 32 channel optical imaging system. Static data sets were acquired from each infant; in addition, data from the ventilated infant were acquired following induced changes in PaO2 and PaCO2. Three dimensional images of tissue absorption were reconstructed and were then converted into maps of regional [Hb], and [HbO2].

Results: Movement artifact and poor optode contact limited the ability to obtain a complete data set from 5 of the infants. Images were reconstructed from the remaining five, including the infant who had suffered the hypoxic-ischaemic insult. Dynamic images of volume change and oxygenation change were obtained from this infant following changes in the PaCO2 and PaO2 respectively. A large increase in [Hb] and [HbO2], corresponding to an increase in cerebral blood volume, was seen following an increase in PaCO2. An increase in [HbO2] was seen following an increase in PaO2. Of the remaining 4 infants for whom images were reconstructed, 2 had evidence of unilateral IVH; these infants were found to have increased absorption of light on the side of the haemorrhage, corresponding to an increase in [Hb] and decrease in [HbO2] in that region.

Conclusion: Using a time resolved optical imaging system we have obtained novel information on regional cerebral blood volume and oxygenation and been able to assess regional oxygenation in the presence of a unilateral IVH. These images demonstrate the feasibility of this technique and the potential to provide unique information on regional cerebral oxygenation in the developing brain.

12

EFFECT OF ANTICYTOKINE TREATMENT IN A MOUSE MODEL FOR PERINATAL WHITE MATTER LESIONS

U Ådén[1], F Plaisant[2], J Lampa[3], P Gressens[2] [1]Karolinska Institutet, Woman and Child Health, Stockholm, Sweden; [2]INSERM E9935, Hopital Robert Debré, Paris, France; [3]Karolinska Institutet, Rheumatology, Stockholm, Sweden

Background: White matter lesions in neonates can result in motor handicaps such as cerebral palsy. Ischemia/reperfusion and excitotoxic injuries have been considered probable aetiologies, but epidemiological data implicate that maternal-fetal infection and associated increase in circulating cytokines most likely also contributes to cerebral palsy. Tumor necrosis factorá (TNFá) is a cytokine that has a central position in the inflammatory cascade in many tissues and controls the release of other pro-inflammatory cytokines such as interleukin-1â (IL-1â). Numerous studies of systemic inflammatory diseases show that neutralization of TNFá with antibodies or soluble receptors inhibits the production of proinflammatory cytokines. Less is known about the effect of TNFá blocking agents in neonatal brain injury. In a study using lipopolysaccharide-induced brain injury, TNFá antibody had no effect whereas IL-1 receptor antagonist attenuated brain damage. Here, we have investigated the role of TNFá and in model of excitotoxic white matter lesion.

Methods: The glutamate analog ibotenate was injected into the periventricular white matter of 5-day-old mice. At postnatal day 10, brains were sectioned in the coronal plane and the number of sections with brain damage was evaluated using cresyl-violet staining. The following groups of pups (n=8–10) were exposed to ibotenate: pretreatment (P1–5, i.p.) with IL-1â (10ng/kgx2), TNFá soluble receptor (etanercept, 100 μg/kgx1), IL-1 receptor antagonist (anakinra 0.3 g/kgx1) or PBS. Posttreatment (P5–7) with etanercept (1–500μg/kgx1), anakinra (0.3–1,0 g/kgx1) or PBS. In addition, TNFá knockouts (Jackson lab) and corresponding wild type mice were subjected to ibotenate intracerebral injection and pretreatment with IL-1â (10ng/kgx2).

Results: TNFá soluble receptor or IL-1 receptor antagonist did not affect white matter lesions induced by ibotenate alone. Likewise, excitotoxic lesion did not differ between TNFá knockouts and wildtypes. However, if the excitotoxic lesion was enhanced by pretreatment with IL-1â, TNFá soluble receptor entirely attenuated this exacerbation ($p<0.05$).

Conclusion: White matter damage induced by a combination of excitotoxicity and inflammation is reduced by a TNFá neutralizing agent. This indicates that TNFá is a key cytokine also in the brain and suggests a role for TNFá blocking drugs in preventing neonatal white matter lesions.

13

ULTRASTRUCTURE OF PLACENTAL TISSUE AFTER 6H OF DUAL IN VITRO PLACENTA PERFUSION

N Bachmaier[1], K Linnemann[1], R Warzok[2], K May[1], N Siebert[1], C Fusch[1] [1]Neonatology and Pediatric Intensive Care, University of Greifswald, Greifswald, Germany; [2]Institute of Pathology, University of Greifswald, Greifswald, Germany

Background: The dual in vitro placenta perfusion model allows the separated ex vivo perfusion of the maternal & fetal circulation and the investigation of the different functions of the placenta. The vitality and integrity of the perfused tissue up to the end of the perfusion experiment is essential for valid experiments. There is no systematic study about the ultrastructural integrity of the perfused placental tissue. Aim of the investigation: Estimation of placental ultrastructural intergrity after 6h of perfusion for extended evaluation of the dual in vitro placenta perfusion model using electron microscopy.

Methods: Placentas (n=10) after uncomplicated pregnacies at term, the mothers gave their written informed consent. Sampling of villous tissue before and after 6h of dual in vitro placenta perfusion and deposition in fixation buffer. Preparation of semithin and ultrathin sections. Systematic investigation of the substructures rough and smooth endoplasmatic reticulum (ER), mitochondrium, nucleus, mikrovilli of syncytio- and cytotrophoblast by a blinded investigator. Control parameters for placental function: glucose consumption, lactat production, creatinine- and antipyrin permeability as well as leptin- and hCG release.

Results: We found no significant differences of the substructures before and after 6h of dual in vitro placenta perfusion with stable placental function (constant glucose consumption and hormone release). We found in perfusion experiments with poor placental function (glucose consumption <0,1μmol/min/g, feto-maternal leakage) a distended rough ER and swelling of the mitochondria in syncytio- and cytotrophoblasts.

Conclusion: 6h of dual in vitro placenta perfusion preserves the integrity of the cellular substructures. The used function parameters are correlated with substructural changes and they are therefore appropiate control parameters for vitality and integrity of the placental tissue.

14

A COMPARISON OF PERINATAL CHARACTERISTICS BETWEEN TWO REGIONS: TRENT, UNITED KINGDOM AND NEW SOUTH WALES AND AUSTRALIAN CAPITAL TERRITORY, AUSTRALIA, 2000–2002

B Bajuk[1], D Field[2], T Vincent[1], E Draper[2], B Manktelow[2], D Henderson Smart[1] [1]University of Sydney, NSW Centre for Perinatal Health Services Research, Sydney, Australia; [2]University of Leicester, Health Science, Leicester, United Kingdom

Background: To compare perinatal characteristics of very preterm births between two regions, the state of New South Wales/Australian Capital Territory (NSW/ACT) in Australia and the Trent Health Region (Trent) in the United Kingdom.

Methods: Study population: NSW/ACT: Ongoing prospective population based cohort study of all infants 22–31 weeks gestation born 1/1/2000 to 31/12/2002 admitted to a tertiary neonatal intensive care unit (NICU) in NSW (n=9) or the ACT (n=1). Infants born in non-tertiary hospitals near the northern, southern and western borders of NSW are transferred interstate for intensive care. Total births obtained from NSW Midwives Data Collection and ACT Maternal-Perinatal Data Collection. Population characteristics obtained from Australian Bureau of Statistics, 2001 Census. Trent: The Trent neonatal Survey is an on-going prospective study of neonatal care established in 1990. Data was available for all babies <33 weeks gestation for the study period who entered a neonatal unit. All stillbirths and live born babies not admitted to an intensive care unit (non viable) at this gestation were identified by the Trent Confidential Enquiry into Stillbirths and Deaths in Infancy (CESDI).

Results: Population characteristics for NSW/ACT and Trent respectively: 5146 (2938 v 2208) infants 22–31 weeks gestation, were live born of whom 4766 (2681; 91.3% v 2085; 94.4%) were admitted to a NICU in the study area between 1/1/2000 and 31/12/2002. Infant characteristics for NSW/ACT and Trent respectively: There was no difference in mean birth weight (1226.4+/-387.5 v 1224.1+/-388.5) and gestational age (28.5+/-2.2 v 28.6+/-2.3). NSW/ACT had significantly more multiple births than Trent (OR 1.45; 95%CI 1.27–1.65). Management practices and outcomes: NSW/ACT babies were more likely than Trent babies to be transported after birth (OR 3.44; 95%CI 3.05–3.88), to receive antenatal corticosteroids (OR 1.38; 95%CI 1.17–1.63) and to have continuous positive airway pressure [CPAP] (OR 2.50; 95%CI 2.21–2.82). They were less likely to receive surfactant (OR 0.49; 95%CI 0.44–0.55). There was no difference in caesarean section, mechanical ventilation, oxygen (infants alive at 28 days), and mortality (neonatal and total). NSW/ACT babies were sicker CRIB II - 8 (IQR 5,11) v 6 (IQR 4,9) and hospitalised for longer (survivors) 55 (IQR 42,78) days v 48 (IQR 33,71) days than Trent babies.

Conclusion: The differences in the two regions can be accounted for by management practices geographical variations.

15

TRANSFERRING BETWEEN NEONATAL INTENSIVE CARE UNITS ON DAY ONE. DOES IT MATTER?

T Vincent[1], B Bajuk[1], L Downe[2] [1]University of Sydney, NSW Centre for Perinatal Health Services Research, Sydney, Australia; [2]Nepean Hospital, Neonatal Intensive Care Unit, Sydney, Australia

Background: Despite Australia's regionalised system of perinatal care it is still necessary to transfer very preterm infants between neonatal intensive care units (NICUs). Many NICUs have a policy of 'last in first out' when beds are scarce. The aim was 1) to compare risk factors for very preterm infants born in a tertiary hospital and transferred between NICUs during in the first 24 hours of life (early transfer) with those who remain in the tertiary hospital of birth (non transfer) and those who are born in a non tertiary hospital (outborn) and 2) to evaluate the risk factors associated with this policy.

Methods: Ongoing prospective population based cohort study of all infants 22–31 weeks gestational age born 1/1/1992 to 31/12/2002 admitted to a tertiary neonatal intensive care unit. All infants were transferred by a specialist neonatal team.

Results: There were 8654 infants of 22–31 weeks gestation, admitted to a NICU between 1/1/1992 and 31/12/2002. Of these 7674 remained in the hospital of birth, 143 had early transfer and 837 were outborn. Early transfer infants were more likely to have a birth weight <3rd centile ($p=0.0006$), a major congenital anomaly ($p<0.0001$), hydrocephalus ($p=0.03$), cystic leukomalacia ($p=0.004$) or patent ductus arteriosus (PDA) ($p=0.01$) requiring major surgery. They were also more likely to die before discharge ($p=0.001$) or during the first year ($p=0.0006$) than non transfer or outborn infants. Outborn infants were more likely to have a 5 minute Apgar score <5 ($p<0.0001$), be treated with surfactant ($p<0.0001$), require indomethacin for a PDA ($p=0.003$), require surgery for necrotising enterocolitis ($p=0.02$), have an intraventricular haemorrhage ($p<0.0001$) or require treatment for fits ($p<0.0001$). Their mothers were more likely to be teenaged ($p<0.0001$), Aboriginal and/or Torres Strait Islander ($p<0.0001$), live in a rural area ($p<0.0001$), have preterm labour ($p=0.007$) and antepartum haemorrhage ($p=0.0001$). Non transfer infants were more likely to be multiple births ($p=0.0002$) and have antenatal corticosteroids ($p<0.0001$). Their mothers were more likely to be aged 35 years or more ($p<0.0001$), have assisted conception ($p<0.0001$), pregnancy induced hypertension ($p<0.0001$) and a caesarean section ($p<0.0001$).

Conclusion: A policy for transferring well stable infants may be more appropriate than a 'last in first out' policy when there are insufficient neonatal intensive care beds. Antenatal transfer to a tertiary unit may result in improved long term outcomes for very preterm babies.

16

PREDOMINANT BREASTFEEDING IN THE MATERNITY WARD AND INFANT'S FEEDING PRACTICES THROUGH THE FIRST YEAR OF LIFE

M Giovannini[1], E Riva[1], G Banderali[1], M Sala[1], G Radaelli[2], C Agostoni[1] [1]San Paolo Hospital, University of MIlan, Department of Pediatrics, Milan, Italy; [2]San Paolo Hospital, University of MIlan, Unit of Medical Statistics Systems, Milan, Italy

Background: There is lack of population-based studies evaluating whether predominant (Pr) vs exclusive (Ex) breastfeeding (BF) at the maternity ward may influence infants' feeding practice through the first year.

Methods: A total of 1656 Italian-speaking mothers of healthy full term singleton infants among those who delivered during November 1999 in Italy entered the study. Mothers were telephonically interviewed within 1 month of delivery and when infants were 3, 6, 9, 12 months-old. Feeding practices were classified according to the WHO criteria. Introducing formula within one month after delivery was defined "early introduction". Outcome measures were duration of BF and time at introduction of formulas and solids. Maternal and infants' characteristics at birth and the WHO's ten steps to successful BF were considered as confounding variables.

Results: In the maternity ward ExBF was found in 57.2% (95% confidence interval [CI], 54.4–59.6%) and PrBF in 42.8% (95%CI, 40.4–45.2%) of infants. Duration (SD) of postpartum hospital stay (days) was 2.8 (1.4) and 3.0 (1.6) for infants respectively ExBF or PrBF ($P=0.10$). Caesarean section ($P<0.0001$), maternal overweight ($P<0.01$), non adherence to WHO's steps 6 ($p<0.01$), 7 ($P<0.01$) and 8 ($p<0.01$) were independently associated with PrBF. The median, 95%CI, duration (mos) of full (Ex+Pr) BF was 3.8, 3.6–4.0, in ExBF infants and 3.4, 3.2–3.6, in PrBF infants ($P=0.02$), but the difference was no longer significant after adjusting for confounders ($P=0.32$). The median, 95%CI, age (mos) at the first introduction of formula was 4.3, 4.1–4.5, in ExBF infants and 3.4, 3.2–3.6, in PrBF infants ($P<0.05$). The median, 95%CI, age (mos) at introduction of solids was, respectively, 4.7 and 4.6, 4.4–4.8, ($P=0.59$). After adjusting for confounders, no significant difference was found between ExBF and PrBF in the maternity ward as far as duration (mos) of both BF (median, 95%CI, 6.3, 5.9–6.7, vs. 6.1, 5.7–6.6, $P<0.01$), and full BF (3.8, 3.6–4.0, vs 3.4, 3.2–3.6, $P<0.01$), and age (mos) at introduction of formula (4.3, 4.1–4.5 vs 3.4, 3.2–3.6, $P<0.01$) or solids (4.7, 4.5–4.9 vs 4.6, 4.4–4.8, $P<0.01$). PrBF infants were more likely to have formula introduced before the age of 1 month (adjusted odds ratio, 1.54, 95%CI 1.14–2.09, $P<0.01$).

Conclusion: In an industrialized country supply of non-milk liquids in the maternity ward may not be a major determinant for stopping BF or timing to introduce solids, but may be associated with an earlier use of formula.