	N St	N Rx	N C	OR
NN NEC PPROM	10	698	719	1.1(0.8,1.7)
NN NEC PTL	5	321	320	0.4(0.1,1)

iii) NICU: Stay [days]

	N St	N Rx	N C	WMD
PPROM	4	151	158	-5.0(-9.6,-0.4)*
PTL	3	114	111	-3.0(-3.6,-2.5)*

iv) Perinatal-neonatal Complicatons:

	N St	N Rx	N C	OR
All Perinatal Death	17	1135	1143	0.9(0.7,1.3)
All RDS	17	1077	1098	0.8(0.7,0.9)*
All BPD (O2 28 d)	3	411	427	0.6(0.4,0.9)*
Any IVH PPROM	9	635	660	0.8(0.6,1)
Any IVH PTL	4	278	282	0.5(0.2,1.6)

Conclusion: Treatment prolongs latency in both groups, and reduces maternal and infant infections. A decrease in NN length of stay was seen. Prior Cochrane reviews suggested trends to positive impacts for neonatal outcomes, when antibiotics are used in PROM in up to 36 weeks GA. These findings are confirmed in this higher risk (≤ 34 week GA) group. Prior reviews show no benefit of antibiotics in PTL up to 36 week, in contrast we find in ≤34 weeks some benefits. For preterm infants ≤34 weeks, we conclude that there are significant advantages to be gained from the use of prophylactic antibiotics for both PTL and PPROM.

94

RISKS FOR PERSISTENT PATENT DUCTUS ARTERIOSUS (PDA) AFTER TREATMENT WITH INDOMETHACIN

V Lieb[1], O Genzel-Boroviczény[2] [1]LMU, Neonatology GH, Munich, Germany; [2]LMU, Neonatology IS, Munich, Germany

Aims: The study investigates the influence of gestational age (GA), Apgar, pH-value, blood pressure and indicators for infection on the success of indomethacin in closing a PDA

Methods: All 118 preterm infants treated with indomethacin between 1997–2002 sorted in following therapeutic outcome groups: Success: A haemodynamic sig. PDA was closed by (maybe multiple) treatments with indomethacin or became haemodynamic not sig. At the end of the observation period the PDA was closed. Non-success: A haemodynamic sig. PDA was not closed by (maybe multiple) application of indomethacin. At the end of the observation period the PDA was haemodynamic significant. A logistic model was created to analyse GA, Apgar 10min, minimal pH-value of the day indomethacin was started, elevated CRP as indicator for infection, maximal CRP-value, microbiol growth, endotracheal colonisation with Ureaplasma urealyticum (Uu) and blood pressure. To account for the age dependency of blood pressure a new variable (MAD-deviation) was calculated: The MAD deviation is the difference of mean arterial pressure from the reference value which corresponds to the weeks of GA.

Results:85 (72%) of the 118 preterm infants were treated successfully, 22 (19%) of the 33 treatment failures received surgical ligation, 5 died with PDA, 6 were transferred with PDA (3 because of NEC). Higher GA (p=0,0001) and higher MAD-deviation (p=0,04) increase the chance of a successful medical treatment (Odds Ratio (OR) 2,27/ 1,22). (Mean-Success 27,8±2,3 weeks/ 10,3±6,6mmHg; Mean non-success 25,2±1,8 weeks/ 6,4±3,6mmHg). In non-success group the blood pressure amplitude was significant lower than in the success-group (16±4,8 mmHg vs. 20±6,3 mmHg; p=0,0001).The chance of successful medical treatment will decrease if there is an endotracheal colonisation with Uu (p=0,028/OR= 0,165). Surprisingly pos. microbiological cultures are associated with a higher success rate of indomethacin treatment (OR=7,2/p=0,011). No association with treatment outcome were found for pH, Apgar and CRP.

Conclusion: Gestational age remains the main determining factor for success of indomethacin. The low mean arterial pressure in treatment failures might be indicative of a higher shunt volume. Chronic inflammation with Uu might cause prostaglandin activation which impedes the closure of the PDA. Taking these risk factors for treatment failure in account, might help in the decision whether to ligate the PDA surgically or try repeated courses of indomethacin.

95

MATURITY-DEPENDENT OLIGODENDROCYTE APOPTOSIS CAUSED BY HYPEROXIA

B Gerstner, U Felderhoff-Mueser, M Marcinkowski, M Obladen, C Bührer Charité Virchow-Klinikum, Neonatology, Berlin, Germany

Background: In the developing human brain, periventricular leukomalacia (PVL) is the predominant white matter injury underlying the development of cerebral palsy. PVL has its peak incidence in the premature infant during a well-defined period in human brain development (23–32 weeks, postconceptional age) characterized by extensive oligodendrocyte migration and maturation. We hypothesized that the dramatic rise of oxygen tissue tension associated with mammalian birth may be harmful to immature oligodendrocytes. We therefore investigated the effects of hyperoxia on cultured rat premature, immature and mature oligodendroglia cells.

Methods: Flow cytometry was used to assess apoptosis via annexin-V, anti-active caspase-3 antibody, and propidium iodide staining, while cell viability was measured by metabolism of 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium (MTT).

Results: Apoptosis was detected at various stages (early: annexin-V, effector: caspase-3) after 24–48 h incubation with hyperoxia (80% O2) in preoligodendrocytes, immature oligodendrocytes (OLN-93) but not in mature oligodendrocytes. These results were confirmed in MTT assays.

Conclusion: Hyperoxia directly initiates the apoptotic cascade in immature oligodendrocytes and pre-oligodendroglia cells. This mechanism may contribute to the white matter damage observed in PVL.

96

USEFULNESS OF AN EARLY BREASTFEEDING ASSESSMENT SCORE TO PREDICT EXCLUSIVE BREASTFEEDING FAILURE

M L Gianni[1], C Vegni[2], G Ferraris[2], C Moioli[2], A Mangiaracina[2], F Mosca[2], A Marini[1] [1]University of Milan, Institute of Pediatrics and Neonatology, Milan, Italy; [2]Cl. L. Mangiagalli, ICP, NICU, Milan, Italy

Background: A comprehensive breastfeeding assessment score (BAS) has been recently proposed to identify infants at risk for early cessation of breastfeeding. International guidelines for the infant feeding recommend exclusive breastfeeding during the first 4–6 months of age. This observational study assessed whether BAS evaluated at hospital discharge may be a useful tool to predict stopping exclusive breastfeeding within the first month of life.

Methods: A total of 175 mothers who delivered vaginally at the same hospital healthy full-term infants, and exclusively breastfed in the maternity ward, entered in the study. Mothers practiced 24 hours rooming in, breastfed on demand and started breastfeeding within the first hour of delivery. BAS was evaluated at hospital discharge. BAS includes maternal age (y) (<21, 21–24, >24), previous breastfeeding experience (failure, none, successful), latching difficulty (every feeding, half the feeding, <3 feeding), and breastfeeding interval (hours) (>6, 3–6, <3). Stopping exclusive breastfeeding during the first month of delivery was the outcome measure. Statistical analysis was based on the Mann-Whitney U test or the Chi-square test. Significance was posed at the level of P<0.05.

Results: Mean (SD; median) length of hospital stay was 2.2 (0.2; 2.2) days. At 1 month of delivery 86.9% of babies were still exclusively breastfed; 6.3% were complementary breastfed and 6.9% formula fed. Mean (SD; median) BAS was 9 (1; 9) in mothers exclusively breastfeeding and 8 (1; 8.5) in mothers no more exclusively breastfeeding at 1 month of delivery (P=0.021). No difference in BAS occurred between mothers who switched to complementary breastfeeding or stopped breastfeeding (P=0.88). Mothers without previous successful breastfeeding experience (P=0.001) or exhibiting higher latching difficulty (P=0.001) were at risk for stopping exclusive breastfeeding. No significant association of stopping breastfeeding within 1 month was found with maternal age ((P=0.885) or breastfeeding interval (P=0.219).

Conclusion:BAS index may be an early and useful measure to predict exclusive breastfeeding failure. Supported by AISTMAR

97

COST-BENEFIT ANALYSIS OF PREVENTION OF NEONATAL ANEMIA WITH RECOMBINANT HUMAN ERYTHROPOIETIN IN PREMATURE INFANTS

I Glorieux, J Tricoire, N Afchar, A C Perier, M Rolland, C Casper Neonatology Unit, Children's Hospital, Toulouse, France

Background: Premature infants frequently develop anemia. This results from blood sampling and also from a relatively poor erythropoietic response to anemia. As a result, these infants often receive multiple transfusions with the risk of disease transmission. The aim of this study was to determine the efficacy and cost effectiveness of recombinant human erythropoietin (r-HuEPO) in reducing erythrocyte transfusion needs in preterm infants.

Methods: 93 premature infants of gestational age less than 34 weeks and birth weight less than 1500g were admitted in our unit from March 1998 to June 1999 and received r-HuEPO 750 U/kg per week intravenously or subcutaneously from day 5–15 to day 40–55. They also received oral iron 3–6 mg/kg per day from day 10. These infants were compared to 81 iron supplemented premature infants born during 1997 before the protocol r-HuEPO was introduced in 1998.

Results: Gestational age (30.2 vs 30.5), birth weight (BW) (1220 vs 1229g), hemoglobin upon admission (15.6 vs 15.6 g/dl), and phlebotomy losses (20.9 vs 20.2 ml/kg) were similar in both groups. The mean number of transfusions per infant was 0.8 compared with 1.9 transfusions per control infant (p <0.0001). Volume of erythrocytes transfused was 17.5 mL/kg in r-HuEPO-treated infants and 45.8 mL/kg in control infants (p <0.0001). The number of infants without transfusion was significantly higher in the r-HuEPO-treated group (64.8 vs 27.2% ; p <0.0001). The cost per patient for transfusion and r-HuEPO was 188 euros for r-HuEPO recipient and 281 euros for control infant. Blood pressure, neutrophil count, platelet count and complications of prematurity were not significantly different in both groups of infants. Of infants with gestational > 32 weeks (18 vs 17 infants) or weight >1200g at birth (46 vs 57 infants), mean number of transfusions was not significant.

Conclusion: R-HuEPO is cost-effective in the prevention of anemia of prematurity for children born before 32 weeks or with BW <12000 g. This treatment doesn't exclude other procedures to prevent transfusion requirements.

98

GENETIC POLYMORPHISMS AS DETERMINANTS OF INTRAVENTRICULAR HAEMORRHAGE, PERIVENTRICULAR LEUKOMALACIA AND HYDROCEPHALUS IN VERY-LOW-BIRTH-WEIGHT-INFANTS

W Gopel, P Ahrens, A Entenmann, C Hartel University of Lubeck, Department of Pediatrics, Lubeck, Germany

Background: Genetic polymorphisms might influence the development and severity of brain diseases of very-low-birth-weight-(VLBW)-infants, like intraventricular haemorrhage (IVH), periventricular leukomalacia (PVL) and hydrocephalus.

Methods: Genetic association study. 1136 infants were studied: 150 VLBW-infants with IVH and/or PVL, 696 VLBW-infants without IVH or PVL and 290 healthy term born infants. Subgroups of VLBW-infants who were compared to VLBW-infants with normal brain-ultrasound-studies included VLBW-infants with IVH grade IV or PVL (n=54), VLBW-infants with IVH grade I-III (n=96) and VLBW-infants who subsequently developed hydrocephalus requiring ventriculoperitoneal shunting (n=27). Polymorphisms which were determined: factor-V-Leiden, prothrombin-G20210A, factor-VII-del/ins, toll-like-receptor4–896G, toll-like-receptor-2-Arg753Gln, NOD2–3020insC, interleukin-6-G(-174)C, plasminogen-activator-inhibitor-4G/5G, stromelysin1–6A/5A, CD14–159T, interleukin-4-C582T and lymphotoxin-alpha-A252G.

Results: Two polymorphisms were more frequent in VLBW-infants with abnormal ultrasound-studies. The homozygous lymphotoxin-alpha-A252G-polymorphism was more frequently found in VLBW-infants with hydrocephalus (33%) than in VLBW-infants without hydrocephalus (12.7%, OR 3.4, 95%CI 1.5–8, p=0.002) and in healthy infants born at term (10.1%). The heterozygous or homozygous prothrombin-G20210A-polymorphism was more frequently found in VLBW-infants with IVH grade IV or PVL (9.1%) compared to VLBW-infants without IVH (2.9%, OR 3.3, 95%CI 1.2–9.3, p=0.03) and healthy infants born at term (2.2%).

Conclusion: Although the majority of polymorphisms selected by our group was previously reported to be associated with intracranial haemorrhage or infarction in adults or VLBW-infants, we detected significant associations only for two polymorphisms. Our study underlines the importance of large cohorts in candidate gene association studies for severe diseases of VLBW-infants.