213

CHITOTRIOSIDASE ACTIVITY AND IL-10 LEVELS IN NEONATAL INFECTIONS

J LABADARIDIS, M THEODORAKI, E DIMITRIOU, K SPANO, J SARAFIDOU, G TRIANTAPHYLIDIS, H MICHELAKAKIS ¹NEONATAL INTENSIVE CARE UNIT, GENERAL HOSPITAL NIKAI, ²NEONATAL INTENSIVE CARE UNIT, GENERAL HOSPITAL NIKAI, ³INSTITUTE OF CHILD HEALTH, ⁴AGHIA SOPHIA CHILDREN'S HOSPITAL, ⁵INSTITUTE OF CHILD HEALTH, ⁶NEONATAL INTENSIVE CARE UNIT, GENERAL HOSPITAL NIKAI, ⁷INSTITUTE OF CHILD HEALTH (GREECE)

Background : Increased activity of chitotriosidase, a human enzyme with chitinolytic properties, has been observed to increase in neonates with fungal and microbial infections. IL-10 is an anti-inflammatory cytokine associated with Th-2 response and thus alternative activation of macrophages which are believed to produce chitotriosidase.

Aim : To investigate chitotriosidase activity in relation to IL-10 levels in neonates with fungal and microbial infections.

Neonates-Methods : A total of 20 neonates, 6 with fungal (1 *Aspergillus niger*, 5 *Candida albicans*) and 14 with microbial infections, were studied. In all, chitotriosidase activity (fluorometric method) in urine samples and IL-10 plasma levels (Elisa Diaclone kit) were measured on diagnosis and in 16/20 neonates in serial samples.

Results : A positive statistically significant correlation was observed between chitotriosidase activity in urine and IL-10 plasma levels (chitotriosidase activity: 0–10060, mean: 594.86 nmoles/mg creatinine/hr, n=42, IL-10 : 0.8–263.6 mean : 58.8 pg/ml, n=44; Pearson q=0.411, p=0.008). In fungal, but not in microbial infections, the highest IL-10 levels were observed in neonates that died.

Conclusions : Our results, in agreement with previous studies, support the proposal that chitotriosidase is produced by alternatively activated macrophages. Increased IL-10 levels may be an indicator of adverse outcome in fungal infections.

214

WHOLE-BODY PROTEIN TURNOVER AND UREA PRODUCTION OF PRETERM SMALL FOR GESTATIONAL AGE INFANTS FED FORTIFIED HUMAN MILK OR PRETERM FORMULA.

HA DE BOO¹, A CRANENDONK¹, W KULIK², JE HARDING³, HN LAFEBER¹ ¹DIV. OF NEONATOLOGY, DEPT. OF PEDIATRICS VRIJE UNIVERSITEIT MEDICAL CENTER (THE NETHERLANDS), ²DEPT. OF CLINICAL CHEMISTRY, VRIJE UNIVERSITEIT MEDICAL CENTER (THE NETHERLANDS), ³THE LIGGINS INSTITUTE, UNIVERSITY OF AUCKLAND (NEW ZEALAND)

Objectives: To investigate protein metabolism and urea production in preterm small for gestational age (SGA) neonates fed a preterm formula (PF) or fortified human milk (FHM).

Methods: Ten preterm SGA neonates were fed either their own mothers milk, fortified with a powdered protein mineral supplement or a special preterm formula. Protein metabolism was determined using constant steady-state infusion of L-[ring-2H5]phenylalanine and L-[1-13C]valine. Urea production was determined from steady-state [13C]urea kinetics.

Results: Protein intakes were 24% higher in the PF group than in the FHM group. Both kinetic methods showed no difference in protein turnover, synthesis and breakdown between the two groups, but protein accretion was 71–79% higher in the PF group than the FHM group (significance at p<0.05). Urea production rates were not different between the two groups. There was a strong negative correlation between urea production and protein accretion calculated from phenylalanine kinetics but not when calculated from valine kinetics.

Conclusions: Both PF and FHM appear equally well tolerated by preterm SGA neonates, but protein accretion is higher in the PF group. It is speculated that even SGA preterm infants tolerate higher protein intakes that may improve their early postnatal growth. Protein intake from human milk source will vary but in practice it seems that even SGA preterm infants would benefit from human milk feeding fortified with a higher amount of protein than 0.7 g. per 100ml. In preterm SGA infants, both phenylalanine and valine kinetic methods can be used to accurately determine protein metabolism.

215

PERINATAL NICOTINE EXPOSURE DISRUPTS BREATHING RHYTHM BY INTERFERING WITH O₂ (NOT CO₂) – SENSITIVE RESPIRATORY STABILIZING MECHANISMS.

G COHEN, A BOUSSOAU, J-C ROUX, J-P CHANGEUX, H LAGERCRANTZ ¹KAROLINSKA INSTITUTE, NEONATAL UNIT, ASTRID LINDGREN CHILDREN'S HOSPITAL, 171 76 (SWEDEN), ²KAROLINSKA INSTITUTE, NEONATAL UNIT, ASTRID LINDGREN CHILDREN'S HOSPITAL, 171 76 (SWEDEN), ³KAROLINSKA INSTITUTE, NEONATAL UNIT, ASTRID LINDGREN CHILDREN'S HOSPITAL, 171 76 (SWEDEN), ⁴CNRS UA D1284 RÉCEPTEURS ET COGNITION, INSTITUT PASTEUR, 28 RUE DU DR ROUX, 75724 PARIS CEDEX 15, (FRANCE), ⁵KAROLINSKA INSTITUTE, NEONATAL UNIT, ASTRID LINDGREN CHILDREN'S HOSPITAL, 171 76 (SWEDEN)

There is a strong association between perinatal tobacco (especially nicotine) exposure and poor infant outcome, but the mechanisms linking the two are not well understood. Here we determined how perinatal nicotine exposure compromises neonatal respiratory control by comparing the effects of nicotine in normal (wild-type, WT) and knockout (KO) mice lacking nicotinic acetylcholine receptors (nAChRs) containing the b2 subunit. These nAChRs are a major component of high-affinity nicotine binding sites in the nervous system. Pregnant WT and KO mice were implanted with micro-osmotic minipumps on embryonic day 14. Pups delivered either water or nicotine (6.0 mg.kg⁻¹ day⁻¹). Breathing was measured using dual-chamber plethysmography. Control WT and KO pups had comparable breathing rhythms at rest. Stress, however, unmasked important differences between genotypes. KO pups responded briskly to hypoxia, but breathing became highly irregular, with frequent pauses (apnoeas) during recovery from hypoxia. Irregular breathing and apnoeas were never seen in WT pups post-hypoxia. Control KO and WT pups responded similarly to CO₂, with no evidence of breathing irregularity or apnoea in either genotype during recovery from bouts of intermittent hypercapnia. Nicotine-exposure augmented the response of the WT pups to hypoxia. WT pups also developed an irregular breathing rhythm due to frequent apnoeas between bouts of hypoxia. Nicotine-exposed WT pups consequently resembled the KO. Nicotine-exposure did not alter the hypoxic breathing pattern of KO pups. Moreover, perinatal nicotine exposure did not alter responses of either WT or KO pups to intermittent hypercapnia.

Conclusion: Our findings suggest that nicotine increases the risk of neonatal apnoea by disrupting nAChR-dependent mechanisms that fine-tune breathing rhythm. These mechanisms are particularly sensitive to sudden changes in reflex drive from O₂ rather than CO₂-sensitive chemoreflexes.

216

USE OF REMIFENTANYL FOR PERCUTANEOUS VENOUS LINE INSERTION IN PRETERM INFANTS

P LAGO¹, C TIOZZO¹, T BETTIOL², SO SAI², F ZACCHELLO¹ ¹NICU, DEPT. OF PEDIATRICS, UNIV OF PADUA, ²NICU DEPT. OF PEDIATRICS, TREVISO HOSPITAL (ITALY)

Background: Remifentanyl (R) is a synthetic mu-opioid agonist whose unique metabolism by blood and tissue esterases yields a rapid-onset, ultrashort elimination half-life and short recovery time. Remifentanyl is particularly suitable for invasive procedures, because it is easier to handle than Fentanyl.

Aims: The aim of this study was to define the safety and efficacy of R during percutaneous venous line insertion (PICC) in preterm infants. Patients and methods: Thirty-five preterm (mean gestational age 29 + 3 SD, r. 23–36 wks), who underwent elective positioning of a PICC line at a mean postnatal age of 8 + 4 SD days, were randomly assigned to receive R or non-pharmacological measures (C). R infusion was started at a rate of 0.006 mcg/kg/min and then titrated every 10 minutes according to the level of analgesia. During the procedure, cardiovascular and respiratory responses (blood pressure-NIBP, oxygen saturation-SatO₂, respiratory rate-RR, heart rate- HR) and the Neonatal Infant Pain Scale (NIPS) were monitored.

Results: There was no significant difference between the two groups (R vs C) in clinical variables and outcomes. HR changes (147 + 12 SD vs 166 + 18 SD) and NIPS (1 + 2 SD vs 5 + 2) were significantly different during the procedure, suggesting that R provided more effective analgesia than non-pharmacological measures. NIBP, RR and SatO₂ were comparable, demonstrating the absence of hemodynamic and respiratory effects of R at this dosages. To maintain effective analgesia, the mean R infusion rate was 0.03 + 0.017 SD mcg/kg/min (range 0.006–0.084), albeit with a significant individual variability. The recovery time was 12 + 5 SD min. No side effects were noted.

Conclusions: This study confirm the efficacy and safety of Remifentanyl during PICC in premature newborn. For this procedure the mean analgesic dosage is in the recommended range.

217

GASTRIC AND OESOPHAGEAL 24-H-PH MONITORING IN INFANTS.

A LANGE¹ ¹DEP PED, UNIVERSITY HOSPITAL OF AARHUS, (DENMARK)

Objective: To monitor gastric acidity and esophageal reflux pattern simultaneously with a dual-pH probe in order to see whether pathological gastro esophageal reflux (GER), defined as esophageal reflux index (RI) > 10 %, depends on the buffering capacity of the gastric content in infants suspected of GER.

Background: Acidity of the gastric material is a prerequisite for GER. In milk-fed infants the ingested milk may have a neutralizing effect on the acidity of the gastric content. To which extent frequent milk meals neutralize the gastric acid to a degree that inhibits acid GER is sparsely described.

Design/Material: Sixteen infants, 9 boys and 7 girls, with mean age 150 (range 21–379) days were examined with 24-h-pH monitoring because of suspected GER. Gastric and esophageal pH were measured simultaneously. Esophageal RI is defined as percentage of time with pH < 4.

Results: Overall gastric pH was < 4 in 47 % of the time (range, 15–70 %). Time with gastric pH < 4 was independent of postconceptional age (range, 29–93 post conceptional weeks). In 8 infants with RI < 10 % the percentage of time with gastric pH less than 4 was 41 (range, 16–70) %. In 8 infants with RI > 10 % the percentage of time with gastric pH less than 4 was 50 (range, 15–60) % (P > 0.1). In two patients no difference between percentage of time with pH < 4 in the stomach and esophagus were found.

Conclusion: 1) Mean gastric pH was found below 4 in 47 % of the examined time. 2) No significant difference was found in the gastric pH pattern between infants with and without pathological GER, but a tendency toward increased esophageal RI in infants with higher percentage of time, where gastric pH was lower than 4, was found.

218

COGNITIVE STATUS OF 5 YEARS OLD VERY PRETERM CHILDREN : THE EPIPAGE STUDY

B LARROQUE¹, L MARCHAND¹, M KAMINSKI¹, AND EPIPAGE STUDY GROUP ¹INSERM U 149 (FRANCE)

The prevalence of cognitive deficit at preschool age was investigated in a population based cohort of very preterm children born in nine regions of France. Methods. We compared 5 year old children who had been born less than 33 completed weeks of gestation with a control group of children born at 39 or 40 weeks in the same regions. The children were evaluated by a psychologist with a standardized test : the K-ABC (Kaufmann Assessment Battery for Children).

Results: Out of the 2357 surviving very preterm children, 1624 (68%) were assessed by the psychologist as well as 326 (49%) control children. Among the very preterm children, 5.4% had no results for the mental process scale (PMC) because of refusal and/or tiredness of the child ; this percentage was 1.5% for in the control group. There was a significant difference in the mean PMC scores (12.7; 95 CI 10.5–14.9), between very preterm children (93.7+/-19.3) and the control group (106.5 points +/- 17.8). After taking into account mother's age at birth, parity, maternal study level, social level of the family and family situation, this difference was still significant (10.9; 95 CI 7.7–13.0, p<0.001). When using the test reference norms, 21% of very preterm infants had a PMC between 84 and 70 (<-1SD to >=-2SD) versus 8% of control children; 10% had a PMC between 69 and 55 (<-2SD to >=-3SD) versus 3% of control children ; 2% had a PMC less than 55 (-3SD) versus none for control children. Among very preterm children a significant trend was found for lower scores of PMC or achievement scale with decreasing gestational age.

Conclusions: Cognitive impairment is higher in very preterm children than in term children