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IDENTIFYING TISSUE ACIDOSIS IN EXTREMELY LOW BIRTHWEIGHT INFANTS: HYPOALBUMINAEMIA IS A CONFOUNDING FACTOR

G LEE[1], G FOX[1], A DURWARD[2] [1]NEONATAL UNIT, GUY'S & ST THOMAS' HOSPITAL TRUST , [2]PAEDIATRIC INTENSIVE CARE, GUY'S & ST THOMAS' HOSPITAL TRUST (UK)

Background: Identification of tissue acidosis (TA) is important in the management of sick, extremely low birthweight infants (ELBW). Previous work has suggested that anion gap may be a more accurate reflection of tissue acidosis than base deficit (Stewart, 1983). Hypoalbuminaemia leads to underestimation of anion gap (Durward et al, 2003).

Aims: To estimate the incidence of hypoalbuminaemia in ELBW infants during the first 72 hours of life, and its effect on estimation of TA in a retrospective, observational study.

Methods: Infants with birthweight <1000g admitted to a tertiary neonatal intensive care unit were studied. Blood gas samples were pooled with results of laboratory electrolyte, albumin and haematology assays at 0, 24, 48 and 72 hours of life. The base deficit (BD) and anion gap (AG) were calculated and then corrected for albumin using Figges formula (Corrected AG = AG + 0.25*(40 - albumin g/L)). TA was quantified by strong ion gap + lactate, a method which has been validated previously (Stewart, 1983), and raised TA defined as >3mEq/L.

Results: 104 samples were collected from 26 infants (median birthweight 708g; median gestation 25+6 weeks). The incidence of hypoalbuminaemia (<25g/l) on admission was 100% and extreme hypoalbuminaemia (<20g/L) 50%. BD had the weakest correlation with TA (r2=0.25, p<0.0001). Correction of the AG demonstrated the best correlation with TA (r2=0.91, p<0.0001). Due to the incidence of hypoalbuminaemia, AG underestimated the corrected AG by 5.1mEq/L. Of 95 samples demonstrating TA, 46.3% had BD >5mEq/L, whereas 75.8% had corrected AG of >16mEq/L. Corrected AG identified TA on 28 occasions where BD <5mEq/L.

Conclusions: Base deficit is a poor marker of TA in ELBW infants. Hypoalbuminaemia is a universal finding in this population. Failure to correct the anion gap for hypoalbuminaemia may lead to underestimation of TA, which may have treatment implications.

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THUMUS SIZE AND ITS RELATIONSHIP TO THE RESPIRATORY DISTRESS SYNDROME AND CORD BLOOD CORTISOL LEVEL IN THE PRETERM INFANTS

JA LEE[1], BI KIM[2], SY SHIM[2], EK KIM[2], HS KIM[2], JH CHOI[2] [1]SEOUL NATIONAL UNIVERSITY BORAMAE HOSPITAL , [2]SEOUL NATIONAL UNIVERSITY COLLEGE OF MEDICINE (SOUTH KOREA)

Purpose: Thymic size can be affected by glucocorticoids. Glucocorticoids increase surfactant synthesis in preterm infants. We assessed the hypothesis that fetal lung maturity in preterm infants correlates with thymus size detected at birth on routine chest radiograph. We also searched for a possible relationship between thymus size, respiratory distress syndrome, and the cord blood cortisol level.

Methods: The cardiothymic/thoracic ratio within 3 hours after birth and cord blood cortisol level were measured in 42 preterm infants admitted to the neonatal intensive care unit of Seoul National University Children's Hospital from June 2002 to December 2003. Multiple linear regression analysis was done to assess the relationships between cardiothymic/thoracic ratio, perinatal events and cord blood cortisol. The receiver operation characteristic curve analysis was done to evaluate the cardiothymic/thoracic ratio in the prediction of respiratory distress syndrome.

Results: 8 infants (19.0%) developed respiratory distress syndrome. The cardiothymic/thoracic ratio positively correlated with birthweight (R=0.416, P=0.044), but not with gestational age. The cardiothymic/thoracic ratio were significantly larger in preterm infants with respiratory distress syndrome than those without respiratory distress syndrome (0.419¡3/4 0.058 versus 0.358¡3/4 0.069, P=0.019). After multiple linear regression, birthweight and respiratory distress syndrome were all independently associated with cardiothymic/thoracic ratio (R2=0.252, P=0.048 for RDS, P=0.012 for birthweight). The cord blood cortisol levels were significantly lower in preterm infants with respiratory distress syndrome than in those without respiratory distress syndrome [median 1.550 microgram/dL(range 0.400–13.600 microgram/dL) versus median 3.450 microgram/dL(range 1.000–18.200 microgram/dL), P=0.016]. The cord blood cortisol levels were negatively correlated with cardiothymic/thoracic ratio (R2=0.212, P=0.002). The cardiothymic/thoracic ratio less than 0.37 identified infants with respiratory distress syndrome with 87.5% sensitivity and 61.8% specificity.

Conclusion: The larger thymus at birth can be used to identify respiratory distress syndrome. The lower cord blood cortisol levels may be associated with larger thymus in respiratory distress syndrome.

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FACTORS INFLUENCING SOCIAL MATURITY AMONG OBESE CHILDREN AT ELEMENTARY SCHOOL IN SURAKARTA

ED LESTARI[1], D HIDAYAH[1], MK SUCI[1], M RIZA[1], S MARTUTI[1] [1]DEPARTMENT OF CHILD HEALTH, MEDICAL SCHOOL, UNIVERSITY OF SEBELAS MARET, MOEWARDI HOSPITAL , [2]DEPARTMENT OF CHILD HEALTH, MEDICAL SCHOOL, UNIVERSITY OF SEBELAS MARET, MOEWARDI HOSPITAL, [3]DEPARTMENT OF CHILD HEALTH, MEDICAL SCHOOL, UNIVERSITY OF SEBELAS MARET, MOEWARDI HOSPITAL, [4]DEPARTMENT OF CHILD HEALTH, MEDICAL SCHOOL, UNIVERSITY OF SEBELAS MARET, MOEWARDI HOSPITAL, [5]DEPARTMENT OF CHILD HEALTH, MEDICAL SCHOOL, UNIVERSITY OF SEBELAS MARET, MOEWARDI HOSPITAL (INDONESIA)

OBJECTIVE: TO EXAMINE THE PREVALENCE OF SOCIAL MATURITY AND THE INFLUENCE FACTORS AMONG OBESE CHILDREN FROM ELEMENTARY SCHOOL IN SURAKARTA.

METHODS: THE STUDY WAS A CROSS SECTIONAL CONDUCTED FROM JANUARY TO FEBRUARY 2005. TWENTY PERCENT OF THE AMOUNTS OF THE ELEMENTARY SCHOOL IN EVERY SUB-DISTRICT WERE RANDOMIZED SELECTED. ALL OF OBESE CHILDREN FROM SELECTED SCHOOL WERE RECRUITED TO THE STUDY AFTER OBTAINING THE INFORMED CONCERN. THE CRITERIA OF OBESITY IN CHILDREN WERE BASE ON BMI >= 95TH PERCENTILE RELATED TO AGE AND SEX. SOCIAL MATURITY WAS MEASURED USING VINELAND SOCIAL MATURITY SCALE, WHICH CONTAINED OF 8 CATEGORIES I.E. SELF-HELP GENERAL, SELF-HELP EATING, SELF-HELP DRESSING, SELF-DIRECTION, OCCUPATION, COMMUNICATION, LOCOMOTION AND SOCIALIZATION. SOCIAL MATURITY SCORE WAS DETERMINED USING AGE GROUP. THE TOTAL SCORE DIVIDED INTO TWO CATEGORIES I.E. IMMATURE AND MATURE. THE POSSIBLE ASSOCIATED FACTORS WITH THE SOCIAL MATURITY SUCH AS SEX, MATERNAL EDUCATION, INTELLIGENCE, AND CHILDCARE WERE ANALYZED USING SPSS 10.0 FOR WINDOWS.

RESULTS: THERE WERE 158 OBESE CHILDREN RECRUITED IN THE STUDY. THE PREVALENCE OF SOCIAL IMMATURITY WAS 32.5%. THE ODDS RATIO (OR) FOR CHILDCARE WAS 2.32 (95%CI: 1.01–5.31); OR FOR INTELLIGENCE WAS 3.93 (95%CI : 1.42–10.89); OR FOR SEX WAS 2.41 (95%CI; 1.08–5.38) AND OR FOR MATERNAL EDUCATION WAS 1.22 (95%CI: 0.61–2.41). AFTER CONTROLLING USING MULTIVARIATE REGRESSION, THE SIGNIFICANT RESULT WERE FOUND IN SEX(OR=2.44; 95%CI : 1.06–5.58) AND INTELLIGENCE (OR=3.31; 95%CI : 1.12–9.84).

CONCLUSION: THE PREVALENCE OF SOCIAL MATURITY OF OBESE CHILDREN IS HIGH. THE FACTOR ASSOCIATED WITH SOCIAL MATURITY ARE INTELLIGENCE AND SEX. THE INFLUENCE OF OBESITY IN THE OCCURENCE OF SOCIAL MATURITY.

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ENHANCED TLR4 EXPRESSION AND IL-8 RELEASE IN PRETERM NEONATES

E LEVI[1], A MOUCHTOURI[1], K XINI[1], K KARALIS[2], S FOTOPOULOS[1], M XANTHOU[1] [1]B NICU AGHIA SOPHIA CHILDREN'S HOSPITAL , [2]INSTITUTE OF BIOMEDICAL RESEARCH OF ACADEMY OF ATHENS (GREECE)

Sepsis related morbidity in neonates is mediated through innate inflammatory responses. The initial step in inflammation is the recognition of the invading microorganisms by immune cells which leads to their activation and the clearance of pathogens. Toll-like receptors expressed on immune cells bind to pathogens and trigger the release of pro-inflammatory cytokines. Aim: To investigate the innate immune response to Gram negative bacteria in healthy neonates and adults by evaluating the effect of in vitro LPS administration on: a) TLR4 surface expression on peripheral blood monocytes and b) IL-8 and TNF-alpha release from blood cultures. Materials and Methods: Peripheral blood from 10 preterm, 10 term neonates and 10 adults was incubated for 4 hours with or without 100ng/ml LPS. For blocking experiments, blood was pre-incubated with anti-TLR4 antibody for 30 minutes. Double staining with anti-CD14 and anti-TLR4 antibodies was performed by FACS and TLR4% expression as well as mean fluorescence intensity were estimated. IL-8 and TNFalpha release were assessed by ELISA in culture's supernatant. Results:TLR4 surface expression on monocytes before LPS stimulation was significantly higher in preterm neonates as compared to adults. Following LPS administration, TLR4 expression increased in all three groups, however the increase in adults was significantly higher to that found in preterms. TNF-alpha release was similar in all three groups. IL-8 release was significantly higher in full terms and preterm neonates as compared to adults. Blocking experiments with anti-TLR4 antibody partially decreased LPS-induced IL-8 release. Conclusions: Preterm neonates have higher baseline expression of TLR4 than adults and thus may be more susceptible to bacterial infections. Although TLR4 increase following LPS was lower in preterms as compared to adults, IL-8 release was higher. The partial inhibition of TLR4 by blocking antibody suggests that IL-8 production in newborns is also mediated through TLR4 independent pathways.

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PLACENTAL TRANSFER OF THE PROTEASE INHIBITOR NELFINAVIR IN THE DUAL IN VITRO PLACENTA PERFUSION MODEL

K LINNEMANN[1], D MEHLTRETTER[2], K MAY[1], N SIEBERT[1], M KUROWSKI[3], H.K. KROEMER[2], W SIEGMUND[2], C FUSCH[1] [1]DEPT. OF NEONATOLOGY AND PEDIATRIC INTENSIVE CARE, UNIV. OF GREIFSWALD , [2]INST. OF PHARMACOLOGY, UNIV. OF GREIFSWALD, [3]HIV-LAB C/O AUGUSTE-VIKTORIA-KRANKENHAUS (GERMANY)

Intro: The protease inhibitor nelfinavir is a common drug for treatment of HIV in pregnancy. Pairs of serum samples of maternal vein - and umbilical cord blood show very low levels of nelfinavir in umbilical cord blood. These results could be caused by an backward efflux of Nelfinavir into the maternal circulation by p-glycoprotein, which is highly expressed in the placenta. Nelfinavir is a known substrate of p-glycoprotein.

Aim: Measurement of placental transfer of nelfinavir and determination of an active transport Material and Methods: Placentas were obtained after written informed consent. Dual closed loop in vitro perfusion of isolated cotyledons (n=12): Perfusion experiments in 4 phases: 1. stabilization and control phase (1h); 2. addition of nelfinavir into first circuit (either maternal or fetal) and measurement of nelfinavir transfer (3h); 3. washout phase (0.5h) followed by; 4. addition of nelfinavir into the second circuit. The order of nelfinavir administration (first maternal or first fetal) was randomized. These transfer data were normalized with the antipyrine permeability to correct for diffusional differences between the experiments. Control parameters for vital placental tissue were glucose consumption, lactate production, leptin production and permeability of creatinine and antipyrine.

Results: The permeability ratio of nelfinavir:antipyrine in materno-fetal direction was not significant different from the permeability ratio in fetal-maternal direction (0.5±0.5 v 0.3±0.4). Glucose consumption (0.23±0.07 μmol/g/min), lactate production (0.42±0.12 μmol/g/min) and leptin release (225pg/g/min) indicated a normal metabolism of the tissue. Feto-maternal leakage was below 4ml/h.

Conclusion: It is unlikely that active directional transporters are involved in the placental transfer of nelfinavir. The observed low fetal serum concentrations in treated pregnancies are rather caused by other mechanisms like high plasma protein binding or drug metabolism.

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INCREASED PREVALENCE OF OBESITY IN CHILDREN WITH FUNCTIONAL CONSTIPATION WITH AND WITHOUT FECAL INCONTINENCE

V LOENING-BAUCKE[1], DS PASHANKAR[2] [1]UNIVERSITY OF IOWA, IOWA CITY, IOWA , [2]YALE UNIVERSITY, NEW HAVEN, CONNECTICUT (USA)

Recently, it was shown in 90 children attending an obesity clinic that 23% had constipation and 15% fecal incontinence.

Aim: To evaluate if constipated children are more obese than controls. Materials and Methods: We evaluated all children, over 4 years of age, seen for functional constipation during a 2-year period in the Pediatric Clinics at the Children Hospital of Iowa. The control group consisted of all children, over 4 years of age, who had came for a well child visit during a 6-month period. Obesity was defined as a BMI >95th percentile and morbid obesity as BMI >5 kg/m2 above the 95th percentile for age and gender.

Results: We evaluated 719 constipated children (390 boys and 329 girls) and 930 controls (480 boys and 450 girls). These two groups were similar regarding mean age and gender ratio. The constipated children were significantly more obese (22%) and morbid obese (8%) than the controls (12% and 2%; P <0.001). The higher prevalence of obesity and morbid obesity was seen in both constipated boys and constipated girls compared to the control boys and girls (P <0.001). Constipated boys were more obese (25%) and morbid obese (10%)than constipated girls (19%, 6%; P <0.03). Rates of obesity and morbid obesity were not different between constipated children with and without fecal incontinence (P >0.5). Constipated children with fecal incontinence as well as children with constipation only were significantly more obese and morbid obese than the controls (P <0.01).

Conclusion: Obesity was more prevalent in both constipated boys and constipated girls. More constipated boys were obese than constipated girls. Constipated children with fecal incontinence were not more obese than children with constipation only. Reasons for the increased prevalence of obesity in constipated children could be multifactorial, including diet, activity level, or hormonal influences and require further studies.