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WHITE MATTER ABNORMALITY IS ASSOCIATED WITH VOLUME REDUCTION IN DEEP GREY NUCLEI FOLLOWING PRETERM BIRTH

JP BOARDMAN¹, S COUNSELL¹, O KAPPELOU¹, D RUECKERT¹, JV HAJNAL¹, KK BHATIA¹, P ALJABAR¹, M RUTHERFORD¹, J ALLSOP¹, AD EDWARDS¹ ¹IMPERIAL COLLEGE (UK)

Background: Diffuse white matter disease, which can be seen on MRI as Diffuse Excessive High Signal Intensity (DEHSI) and quantified using apparent diffusion coefficient (ADC) values is the most common abnormality in preterm infants at term equivalent age. We used a computational anatomic approach to survey the brain for structural alterations associated diffuse white matter disease.

Methods: Subjects: 62 preterm infants without parenchymal cerebral lesions, born at median 29.7 weeks GA were studied at term equivalent age (median 40.4 weeks GA) together with 12 term born controls. Image acquisition: a 1.5 Tesla MR system was used to acquire high resolution T1-weighted volume datasets with a voxel size 1x1x1.6mm, in addition to conventional and diffusion weighted imaging. Diffuse white matter disease was defined as ADC values > 2 standard deviations above the mean of the control group in one or more white matter region. Image processing: non-rigid image registration was used to transform all images to a reference subject, and voxel-wise volume change values extracted from transformations were analysed with a correction for multiple comparisons.

Results: Preterm infants showed volume loss within lentiform and thalamic nuclei (p<0.05), particularly among infants with diffuse white matter disease (p<0.05) and with increasing prematurity at birth (p<0.05), but ADC values in the thalamus and lentiform nuclei were similar to controls.

Conclusions: Growth failure within deep grey nuclei occurs in association with diffuse white matter disease and without evidence of acute injury. This suggests deep grey matter connectivity is altered by preterm birth.

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THE -866A/A BUT NOT THE -866G/A GENOTYPE OF UNCOUPLING PROTEIN 2 GENE IS ASSOCIATED WITH REDUCED DIHOMO-GAMMA-LINOLENIC ACID VALUES IN OBESE CHILDREN

SZ BOKOR¹, K CSERNUS¹, É ERHARDT¹, I BURUS¹, D MOLNÁR¹, T DECSI¹ ¹DEPARTMENT OF PAEDIATRICS, UNIVERSITY OF PÉCS (HUNGARY)

Introduction: Previously we found significantly higher values of the n-6 long-chain polyunsaturated fatty acids, gamma-linolenic acid (C18:3n-6), dihomogamma-linolenic acid (C20:3n-6) and arachidonic acid (C20:4n-6) in plasma lipids in obese children than in nonobese controls (Decsi et al, Lipids 31: 305-311, 1996). Recently, an association between obesity, lipid metabolism disorders and the G-allele of the -866G/A polymorphism in the promoter region of uncoupling protein 2 gene (UCP2) was reported (Le Fur et al, Diabetes 53: 235-239, 2004). Here we report data on the association of the -866G/A polymorphism of UCP2 to the fatty acid composition of plasma lipids in obese children.

Subjects and methods: Obese children (n = 80, age: 13 [2.7] years, body mass index: 41.7 [4.4] kg/m², body fat: 39.1 [4.2] %, mean [SD]) were investigated. Genotyping was performed by polymerase chain reaction with subsequent restriction fragment length polymorphism analysis. Fatty acids were determined by high-resolution capillary gas-liquid chromatography.

Results: The frequencies of the different genotypes were as follows: -866G/G: 42.5%, -866G/A: 42.5%, -866A/A: 15%. Anthropometric characteristics did not differ among the 3 groups. Values of eicosadienoic acid (C20:2n-6) in phospholipids and values of C20:3n-6 in sterol esters were significantly lower in children with the -866A/A genotype than in the other two groups (Table). Values of C20:3n-6 were also significantly lower in children with the -866A/A than in those with the -866G/A genotype in plasma phospholipids (Table). Table: Fatty acid composition of plasma phospholipids and sterol esters in 80 obese children stratified according to genotype of the UCP2. Data are median [IQR], a, b = P < 0.05

| | Phospholipids | | | | Sterol esters | |
|----------|--------------------------|--------------------------|---------------------------|--------------------------|--------------------------|---------------------------|
| | -866 G/G (n = 34) | -866 G/A (n = 34) | -866 A/A (n = 12) | -866 G/G (n = 34) | -866 G/A (n = 34) | -866 A/A (n = 12) |
| C18:2n-6 | 18.50 (3.47) | 18.26 (2.46) | 19.10 (2.89) | 53.35 (5.93) | 52.83 (6.38) | 53.85 (4.73) |
| C18:3n-6 | 0.07 (0.05) | 0.06 (0.04) | 0.07 (0.04) | 0.87 (0.51) | 0.81 (0.38) | 0.86 (0.44) |
| C20:2n-6 | 0.51 (0.17) ^a | 0.50 (0.10) ^b | 0.41 (0.11) ^{ab} | 0.12 (0.05) | 0.14 (0.05) | 0.11 (0.02) |
| C20:3n-6 | 3.33 (0.84) | 3.36 (1.01) ^a | 3.01 (0.42) ^a | 0.94 (0.25) ^a | 0.92 (0.23) ^b | 0.73 (0.22) ^{ab} |
| C20:4n-6 | 11.34 (2.54) | 10.79 (1.74) | 11.40 (1.69) | 8.28 (3.12) | 8.14 (2.90) | 7.78 (1.38) |

Conclusion: In this study, we found significantly lower values of dihomogamma-linolenic acid, an important eicosanoid precursor, in plasma lipids of -866A/A homozygote compared with -866 G/A heterozygote and -866G/G normal obese children.

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DIAGNOSIS AND MANAGEMENT OF PATENT DUCTUS ATERIOSUS IN PREMATURE INFANTS: A CANADA WIDE SURVEY OF NEONATOLOGISTS

E. BOLSTER¹, A. KAKADEKAR¹, K. SANKARAN¹ ¹UNIVERSITY OF SASKATCHEWAN (CANADA)

Background/Aims: Patent ductus arteriosus (PDA) is common in preterm infants and is inversely related to gestational age. The incidence is 40-55% in infants of 23-28 weeks gestation but drops to 0.1% for full term infants. PDA management appears to be variable; from conservative waiting to pharmacotherapy and surgery. We undertook a national survey among neonatologists to determine if there was any consensus regarding the management of PDAs.

Methods: We surveyed all 133 active neonatologists working in level 2 or 3 centres with 29 questions regarding the diagnosis and management of PDA. The results were reviewed with a descriptive analysis.

Results: Out of the 79%(105/133) who responded, 75% of neonatologists wanted echocardiographic confirmation before initiating treatment. 71% waited until the PDA became a clinical problem before initiating treatment. Prior to initiating pharmacotherapy, 78% of neonatologists assessed creatinine levels and 94% assessed platelet counts. 68% decreased fluid intake and 52% stopped feeding. Medical treatment is the first line of treatment for everyone. Indomethacin was the drug of choice with only 5% using ibuprofen. Only 31% of neonatologists used indomethacin prophylactically. The dosage for indomethacin varied widely. Surgery is primarily done when medical treatment was contraindicated and/or after medical treatment had failed. Surgical ligation was performed by pediatric cardiac surgeons in 64% of centres and by pediatric general surgeons in 26% of centres.

Conclusion: Management of PDA varied across Canada. Echocardiographic confirmation was sought before treatment. Similarly, the majority waited until the PDA became a clinical problem before intervention. Indomethacin was the first line of treatment. Creatinine and platelets were measured and fluid was restricted prior to treatment. Prophylactic indomethacin use was rare. Surgical ligations were done by pediatric surgeons. These findings suggest that a systematic approach to the management of PDA appears to be necessary so that treatment effects can be assessed.

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POSTNATAL GROWTH KINETICS OF VERY LOW BIRTH WEIGHT INFANTS

E BERTINO¹, A COSCIA¹, L BONI¹, G ROSSETTI¹, M MOMBRO¹, C MARTANO¹, F GIULIANI¹, E SPADA², S MILANI², C FABRIS¹ ¹CATEDRA DI NEONATOLOGIA-UNIVERSITÀ DI TORINO, ²ISTITUTO DI STATISTICA MEDICA E BIOMETRIA-UNIVERSITÀ DI MILANO (ITALY)

General agreement has been achieved on the need for longitudinal studies to evaluate growth of VLBWIs: these could provide data suitable to trace distance growth charts and also velocity charts so to detect earlier whether a child is growing unsatisfactorily. For this reason aim of this study has been to analyse weight growth kinetics of VLBWIs from birth up to 2 years.

Data were prospectively collected on 262 VLBWIs admitted to Turin University NICU. During hospitalization body weight was recorded daily up to 28 days, then weekly up to discharge. Follow-up examinations were at 1-3-6-9-12-18-24 months of corrected age. The large number of weight measures per neonate allowed us to design an exponential-logistic function suitable for driving average weight growth and growth velocity curves.

Weight growth curve of post-natal age has been plotted on the neonatal reference chart for N-W Italy and on the Italian longitudinal growth charts for children: weight is between the 10th and 25th centile at birth, at 42 weeks it is slightly below the 10th centile and it remains between the 10th and 25th centile up to 24 months. At 2 years population fails to achieve catch-up growth. The very complex pattern of weight growth is better described by the growth velocity curve: it shows a negative value of velocity in the first week, subsequently velocity increases and reaches a first narrow peak at 20.5 days and a second higher peak at 87.5 days. Then velocity decreases slowly and regularly.

The function allowed us to describe some milestones of growth process. Growth velocity curve allowed us to demonstrate a non-linear growth kinetics for VLBWIs so it does not seem appropriate to report only a mean value of velocity as most authors do. Future studies should be performed to evaluate effects on growth kinetics exercised by individual pathologic variables.

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ANXIETY AND DEPRESSION IN CHILDREN AND ADOLESCENTS AFFECTED BY ACUTE LINFOBLASTIC LEUKAEMIA

S. BONINI¹, C. CIAMPI¹, A. LIPPI¹, G. GIUNTOLE², G. BERNINI¹ ¹OSPEDALE PEDIATRICO A. MEYER, ²OSPEDALE PEDIATRICO A. MEYER, ³OSPEDALE PEDIATRICO A. MEYER, ⁴UNIVERSITÀ DEGLI STUDI DI FIRENZE-FACOLTA' DI PSICOLOGIA, ⁵OSPEDALE PEDIATRICO A. MEYER (ITALY)

BACKGROUND: IN THE LAST YEARS, THE HIGHEST PROBABILITIES OF SURVIVAL FOR CHILDREN AFFECTED BY CANCER HAVE STIMULATED A MAJOR INTEREST IN PATHOLOGY'S PSYCHOLOGICAL CONSEQUENCES BY THE HEALTH CARE PROFESSIONALS. ALL RESEARCHERS UNDERLINE THE DIFFICULTIES CAUSED BY CANCER AND THE RISKS FOR THE CHILDREN'S DEVELOPMENT, BUT ONLY SOMEONE HAS SURVEIRED THAT CANCER IS CAUSE OF PSYCHOLOGICAL DISORDERS AND THAT ANXIETY AND DEPRESSION ARE COMMON SYMPTOMS. AIMS: AIM OF THIS RESEARCH HAS BEEN TO EVALUATE, BY SPECIFIC TESTS, THE ANXIETY AND DEPRESSION'S LEVELS OF CHILDREN AFFECTED BY LEUKAEMIA, ONE YEAR AFTER THE DIAGNOSIS (ONCO-HAEMATOLOGY UNIT, 'A. MEYER' HOSPITAL, FLORENCE).

METHODS: FROM JANUARY TO JUNE 2004, THE 'ANXIETY SCALE QUESTIONNAIRE FOR EVOLUTIVE AGE' (BUSNELL, DALL'AGLIO & FAINA, 1974) AND THE 'CHILDREN'S DEPRESSION INVENTORY - C.D.I.' (KOVACS, 1982) HAVE BEEN ADMINISTERED TO 8 CHILDREN (9-13 YEARS OLD) AFFECTED BY ACUTE LINFOBLASTIC LEUKAEMIA AND A GROUP OF HEALTHY CHILDREN (9-14 YEARS OLD), ATTENDING THE SAME SCHOOLS OF ILL CHILDREN. THE QUANTITATIVE DATA OBTAINED HAVE BEEN ANALYSED BY DESCRIPTIVE STATISTIC ANALYSES.

RESULTS: THE RESULTS DON'T SHOW SIGNIFICANT DIFFERENCES BETWEEN THE GROUPS. IN THE FIRST RELAPSE OF THE PATHOLOGY, ONLY ONE CHILD OF CLINIC SAMPLE OBTAINED A HIGH 'C.D.I.' SCORE, HIGHER THAN THE 'PATHOLOGIC CUT-OFF' ONE. IN THE LITERATURE IT ISN'T EVIDENT THAT THERE IS INFLUENCE OF THE 'SOCIAL-DEMOGRAPHIC' VARIABLES ON ANXIETY AND DEPRESSION'S LEVELS AMONG CHILDREN WITH CANCER.

CONCLUSIONS: THE RESEARCH FOCUSES THE ATTENTION ON THE 'GLOBAL CARE' IMPORTANCE IN PAEDIATRIC ONCOLOGY, THANKS TO A MULTIDISCIPLINARY TEAM CONSTITUTED BY ONCOLOGISTS, PSYCHOLOGISTS FOR THE PARENTS CARE, INFANT NEUROPSYCHIATRISTS FOR THE CHILD ASSESSMENT AND EDUCATIONAL PSYCHOLOGISTS, FOR THE PASTIME DURING HOSPITALIZATION AND DAY-HOSPITAL CHECKUPS. THE 'GLOBAL CARE' MAY INFLUENCE THE CHILDREN'S HEALTH, NOT DEFINED AS A SIMPLE ABSENCE OF ILLNES, BUT AS 'A STATE OF PHYSICAL, MENTAL AND SOCIAL WELL-BEING'.

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PROPHYLAXIS OF CHRONIC LUNG DISEASE WITH LOW-DOSE HYDROCORTISONE: A RANDOMISED, PLACEBO CONTROLLED TRIAL. PRELIMINARY REPORT

F BONSANTE¹, G LATORRE², S IACOBELLI², V FORZIATTI², N LAFORGIA¹, M DELVECCIO¹, L ESPOSITO², A MAUTONE¹ ¹DEPARTEMENT OF PEDIATRICS, NICU, UNIVERSITY OF BARI, ²NICU AND NEONATOLOGY SECTION, MIULLI HOSPITAL (ITALY)

BACKGROUND: Several reports showed decreased cortisol response to adreno-corticotropic hormone in preterms developing chronic lung disease (CLD). Administration of prophylactic low-dose hydrocortisone (HC) may allow for beneficial effects, particularly in infants with histologic chorioamnionitis. However, there are concerns regarding short and long-term effects of corticosteroid therapy in preterms.

OBJECTIVE: Evaluation of effectiveness and safety of prophylactic HC in improving survival without CLD in preterms.

METHODS: Double blind randomised placebo-controlled trial in 2 centres. After parental consent mechanically ventilated infants (birth weight 500-1249) were entered within 48 hours of life and randomized to receive treatment (HC: 0.5 mg/Kg/12 hrs for 9 days, then 0.5 mg/Kg/ 24 hrs for 3 days) or placebo for 12 days. The major outcome was assessed as survival without CLD (oxygen dependency at 36 weeks of postmenstrual age). The protocol was approved by Ethical Committee at each institution and notified to the National Observatory on Human Drug Experimentation.

RESULTS: 41 patients were enrolled since April 2003. Birth weight, gestational age, chorioamnionitis, CRIB and FiO₂ requirements at entry were similar between the two groups. Survival without CLD was 61% in HC group versus 30% in controls (p<0.05). Mortality rate was 22% in HC group vs. 43% in controls (p=ns). Chorioamnionitis occurred in 51% of patients. In chorioamnionitis group survival without CLD was 42% in HC group vs. 16% in controls (p=ns). Incidence of sepsis, IVH, PVL, NEC, ROP, PDA, hyperglycaemia, hypertension, gastrointestinal perforation, head circumference and weight at 36 weeks were similar between the two groups. Hyperkalemia in the HC group was significantly higher.

DISCUSSION: HC prophylaxis improved survival without CLD in our population, without important short term effects. Neurodevelopmental outcomes will be assessed at 2 years.