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THE EFFECT OF VITAMIN K SUPPLEMENTATION ON BMD IN CHILDREN AND ADOLESCENT WITH CYSTIC FIBROSIS

P NICOLAIDOU¹, H GEORGIOULI¹, I STAVRINADIS², J LOUKOU³, A PAPADOPOULOU¹, K DOUROU¹, D GOURGIOTIS², A ANTONIOU⁴, S DOUDOUNAKIS³ ¹3RD DPRT OF PEDIATRICS, ²2D DPRT OF PEDIATRICS, ³CYSTIC FIBROSIS DPRT, ⁴RADIOLOGY DPRT (GREECE)

As the life span of patients with cystic fibrosis (CF) has gradually increased, a variety of problems, like osteoporosis, have been recognized. Hypovitaminosis D, hypogonadism, lack of physical activity and chronic inflammation are some of the factors that contribute to the pathogenesis of bone disease in CF patients. Decreased absorption of vitamin K because of pancreatic insufficiency could be another risk factor for osteoporosis. The aim of the study was to determine the implication of vitamin K in the pathogenesis of osteoporosis in CF children and adolescent. We studied 20 patients with CF (ten boys) aged 6 to 7 years old and 25 healthy subjects of similar age and sex. All patients were evaluated before and 1 year after vitamin K supplementation. In all patients and controls serum carboxy-terminal propeptide of procollagen type I (PICP), amino-terminal propeptide of procollagen type I (PINP), bone alkaline phosphatase (sALP), osteocalcin (OC), cross-linked carboxy terminal telopeptide of type I collagen (ICTP), vitamin D, parathormone (PTH) and undercarboxylated osteocalcin (GLU-OC) were determined. Urine deoxypyridinoline/creatinine was also determined. Bone density was measured only in the patients using dual-energy x-ray absorptiometry (DEXA). Our results indicated that 55% of CF patients had osteoporosis. The supplemented patients showed: a) increase of bone density (0.789 ± 0.149 than 0.737 ± 0.151 , $p < 0.0001$), b) increase of PINP (579.35 ± 275.11 microg/l than 341.65 ± 270.77 microg/l, $p < 0.0001$) c) increase of PICP (341.30 ± 140.53 microg/l than 290.06 ± 117.64 microg/l, $p < 0.011$) d) increase of sALP (51.75 ± 14.94 microg/l than 45.28 ± 20.48 microg/l, $p < 0.024$) e) increase of oc (26.22 ± 14.25 ng/ml than 15.45 ± 11.62 ng/ml, $p < 0.004$) f) decrease of GLU-OC (2.28 ± 3.93 ng/ml than 6.60 ± 6.24 , $p < 0.004$). According to our results, vitamin K supplementation in CF children and adolescent improves BMD by enhancing osteoblast activity.

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ESTROGEN ATTENUATES OLIGODENDROCYTE APOPTOSIS CAUSED BY HYPEROXIA

B GERSTNER¹, A SCHÜLLER¹, M BERNIS¹, C BÜHRER², M OBLADEN¹, U FELDERHOFF-MUESER¹ ¹DEPARTMENT OF NEONATOLOGY, CHARITÉ VIRCHOW HOSPITAL, UNIVERSITY MEDICAL CENTER (GERMANY), ²DEPARTMENT OF NEONATOLOGY, BASEL UNIVERSITY CHILDREN'S HOSPITAL (SWITZERLAND)

Background: In the developing human brain, periventricular leukomalacia (PVL) is the predominant white matter injury underlying the development of cerebral palsy. Our group recently showed that a rise of oxygen tissue tension is a powerful trigger to initiate apoptosis in premature and immature, but not in mature oligodendrocytes (OL). Estrogen plays an important role in the development and function of the cerebral nervous system, and estrogen receptors show a specific distribution with high density around the third ventricle, the region where OL progenitors are generated. We therefore examined the effects of estrogen on hyperoxia-induced cell death in cultured rat immature oligodendroglia cells.

Methods: OLN-93 cells, derived from spontaneously transformed cells of 5- to 10-day-old primary rat brain oligodendrocytes were subjected to 24–72 h of hyperoxia (80% O₂) in the presence or absence of estrogen (17beta-estradiol) at various concentrations. These immature oligodendrocytes resemble an intermediate stage between oligodendrocyte precursors and mature oligodendrocytes. Flow cytometry was used to assess apoptosis via annexin-V, anti-activated caspase-3 antibody, and propidium iodide staining. Oligodendrocyte maturation status and caspase-3 activation were confirmed by immunocytochemistry.

Results: In immature rat oligodendrocytes (OLN-93), apoptosis was detected at various stages (early: annexin-V, effector: caspase-3) after 24–72 h of hyperoxia (80% O₂). Cell death was reduced up to 30% by preincubation with estrogen at a concentration optimum of 10–7 M estrogen.

Conclusion: Estrogen reduces apoptosis in immature oligodendrocytes exposed to hyperoxia. The sudden drop in circulating estrogen of placental origin after mammalian birth may aggravate the susceptibility of immature oligodendrocytes to increased oxygen tension. Supported by grants from the German Federal Department of Education and Research (BMBF, # 01 ZZ 0101), Bonn, and the Ernst Schering Research Foundation, Berlin.

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EVALUATION OF METABOLIC & RESPIRATORY DISORDERS IN INFANTS OF DIABETIC MOTHERS (IDM)

S GHAEMI¹, M MOHAMADY MASOUDI¹ ¹S GHAEMI ISFAHAN UNIVERSITY OF MEDICAL SCIENCES, ²M-MOHAMADY MASOUDI ISFAHAN UNIVERSITY OF MEDICAL SCIENCES (IRAN)

Background: Control of diabetes mellitus with insulin during pregnancy has led to improved outcomes in children. Poorly controlled maternal diabetes is associated with problems in the fetus and neonate. Fetal and neonatal hyperinsulinism is central to many of these problems. The incidence of respiratory, metabolic, hematologic and cardiac problems is higher in IDM. The aim of this research was to detect the prevalence rate of some common metabolic & respiratory problems in IDM.

Material & methods: The research involved a descriptive analytic study carried out on 200 neonates of diabetic mothers admitted to the Al-zahra & Beheshti hospitals in Isfahan, Iran, between July 1995 and August 1999.

Results: A group of 100 (50%) out of 200 IDM had metabolic disorders, (53% females and 47% males). Hypoglycemia, hyperbilirubinemia and hypocalcaemia were common metabolic complications with a frequency of 37.5%, 30% and 10% respectively. 48 (24%) of the 200 IDM had respiratory distress, (52.1% males, 47.9% females). All complications were more common in preterm infants than term infant, metabolic disorders were 75% in preterm versus 25% term, and respiratory disorders were 70.8% in preterm versus 29.2% term. Hypocalcaemia & respiratory distress were more common in male than in female infants and hypoglycemia & hyperbilirubinemia were more common in females than males.

Conclusions: Metabolic and respiratory disorders were more common in IDM than infants of non-diabetic mothers. Preterm status was a predisposing factor for developing complications in IDM.

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EVALUATION OF SURFACTANT THERAPY IN HMD AND REDUCTION OF MORTALITY

S GHAEMI¹, M MOHAMADY MASOUDI¹ ¹ISFAHAN UNIVERSITY OF MEDICAL SCIENCE, ISFAHAN ISFAHAN, (IRAN)

HMD Occurs Primarily in premature infants, and its incidence is inversely proportional to gestational age and birth weight. HMD is a Major cause of morbidity and mortality in preterm neonates. (about 30%) Surfactant deficiency is the primary cause of HMD in Previous studies, surfactant therapy has reduced mortality from HMD approximately 40% the aim of this research was determined the incidence of mortality in neonates with HMD after treatment with surfactant. **Methods & materials:** In this study that was a descriptive analytic study, we evaluated 450 neonates with HMD, who were admitted to NICU in Beheshti Hospital Isfahan Iran , between Mar 2003 to Aug 2004. After diagnosis of HMD by clinical signs of Respiratory distress, and radiological findings of the chest , 89 Patients received surfactant (Males 58 and females 31)

Results: A group of 34 (38.2%) out of 89 neonates who received surfactant survived HMD , on the other hand , in this study surfactant therapy has reduced mortality from HMD (38.2%), 42% were females and 36.2% were males. The most efficacy of surfactant therapy and low mortality were observed on gestational age more than 32 weeks, and therapy in the 1st 24 hr of life (47.5% and 43.3% respectively). Also the most efficacy of surfactant were showed in APGAR score at 1 , 5 min more than 7/10 and in birth weight more than 1500 Gr (48% and 52.5% respectively). In this study , mothers who received steroid before delivery and their neonates who took surfactant after birth , had the most efficacy and reduction of mortality (41.7% with steroid and 34.15% without steroid).

CONCLUSIONS: The purpose of this study was detection the prevalence rate of reduction of mortality after surfactant therapy in HMD, our study was showed reduction of mortality and also was concluded the most efficacy of surfactant therapy on some condition which associate with HMD.

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PERINATAL HYPHOSPHATASIA - PRENATAL DIAGNOSIS

J GHIEA¹, C ROLL¹, U KUHN², B ALBRECHT³, G GILLESSEN-KAESBACH³ ¹DEPARTEMENT OF PEDIATRICS, UNIVERSITY HOSPITAL, ²DEPARTMENT OF PERINATOLOGY, UNIVERSITY HOSPITAL, ³INSTITUT FÜR HUMANGENETIK, UNIVERSITÄTSKLINIKUM, (GERMANY)

Background: Hypophosphatasia is a rare autosomal recessive disorder characterized by defective bone and teeth mineralization, and deficiency of bone and serum alkaline phosphatase activity (ALP). The clinical expression is highly variable and ranges from stillbirth without mineralized bone to pathologic fractures developing only in late childhood. The responsible gene encoding the tissue non-specific alkaline phosphatase (TNSALP) consists of 12 exons and is localized on chromosome 1p36.1. More than 138 distinct mutations including a great number of compound heterozygous genotypes have been described.

Case report: The patient was the first child of unrelated healthy Turkish parents. At 30 weeks of gestation ultrasound examination showed polyhydramnion, short limbs, reduced mineralization of the skull, and short ribs with a hypoplastic chest. Hypophosphatasia was suspected. Analysis of fetal cord blood showed absence of ALP-activity. These findings prompted us to initiate molecular analysis of the TNSALP-gene which revealed compound heterozygous mutations in the TNSALP-gene (G203V and R206Q) (E. Mornet, Versailles, France). The girl was born at 36 weeks gestational age and died of respiratory failure 30 minutes after birth. Clinically, she presented with a large head, soft calotte, muscular hypotonia, short and hyperflexible limbs. X-ray examination proved a severely reduced mineralisation of the bones with marked shortening of the long bones, very short and thin ribs and a hypoplastic chest and lungs.

Conclusion: Reduced mineralization especially of the skull and the absence of ALP led to the clinical diagnosis of hypophosphatasia. The mutations found in the fetus predicted a lethal outcome. Prenatal molecular diagnosis is important for the perinatal management.

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BEHAVIORAL OUTCOMES AND ACADEMIC PERFORMANCE IN LOW BIRTH WEIGHT CHILDREN IN SCHOOL AGE

T TSEKOURA¹, M GIANAKAKI², M THEODORAKI³, I DAKANAL⁴, M FILIPIDIS⁵, A TSILIMIGAKI⁶ ¹PEDIATRIC DEPARTMENT, BENIZELIO GENERAL HOSPITAL HERAKLION CRETE, ²BENIZELIO GENERAL HOSPITAL NEONATAL INTENSIVE CARE UNIT, ³NEONATAL INTENSIVE CARE UNIT, BENIZELIO GENERAL HOSPITAL HERAKLION CRETE, ⁴BENIZELIO GENERAL HOSPITAL, HERAKLION, CRETE, GREECE, ⁵NEONATAL INTENSIVE CARE UNIT, BENIZELIO GENERAL HOSPITAL HERAKLION CRETE, ⁶PEDIATRIC DEPARTMENT, BENIZELIO GENERAL HOSPITAL HERAKLION CRETE, (GREECE)

Background: Preterm very low birth weight infants are at an increase risk for the subsequent development of both cognitive and behavioral problems in childhood.

Objective: To examine the prevalence of clinically significant behavior problems in preterm very low birth weight infants (VLBW) in school age

Methods: We compared a cohort of 39 survivors among VLBW (mean gestational age at birth: 30.5 weeks, mean birth weight 1220 gr.), 19 of whom were boys and 20 girls, mean age 8.5+ 3.5 years, with 45 control subjects who had normal birth weight, (22 boys and 23 girls, mean age 9.2+3.7 years). The parents and tethers completed a questionnaire on their behavioral and school performance.

Results: VLBW children had a higher prevalence of hyperactivity and attention problems (23%) than controls (4.4%) $P < 0.01$. VLBW children had a higher prevalence of school difficulties (41%) than controls (15%) p

Conclusions: VLBW children have an increase risk of exhibiting hyperactive behavior, attention problems and school difficulties. VLBW children