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URINARY BETA2-MICROGLOBULIN AS AN INDICATOR OF RENAL LESION IN ASPHYXIATED NEONATES

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BACKGROUND:Perinatal asphyxia can cause transient renal impairment or acute renal failure in neonates. Proximal tubular cells are extremely vulnerable to hipoxia.The ischemic injury results in elevated concentration of beta2microglobulin (beta2M) in urine.Urinary beta2M concentration increases with degree of tubular dysfunction.The aim of the study was to determine a concentration of beta2M in urine of asphyxiated and healthy neonates of varying gestational and postnatal age.

STUDY AND THE CONTROL GROUPS:The study and the control groups were 141 neonates.The study group were 66 asphyxiated neonates,16 term and 50 preterm. Mean [SD] gestational age (GA) of term newborns was 38 (37 to 42) with mean [SD] birth weight 3290 g [703] and mean GA [SD] of preterm was 32 (30 to 36) mean [SD] birth weight 2070 g [548]. Criteria for inclusion were umbilical cord arterial pH less than 7.1 and BE less than minus 12 mmol/l. The control group were 75 neonates clinically stable 14 term (GA 37–42 mean [SD] 39 [1] mean birth weight [SD] 3440 g [500] and 57 preterm (GA 30- 36 mean [SD] 33 [2] mean [SD] birth weight 2061 g [552]. Both study and control group were divided into three subgroups of different maturation (A > 35 , B-33–35, C 30–32 GA).

METHODS:Urine samples were frozen at minus 20 C until assay. Beta2M was estimated in five samples on day 1, 3, 7, 14, 28 using competitive radioimmunoasay.

RESULTS: We found statistically significant elevation of mean values of beta2M in urine of asphyxiated neonates compared to controls in all samples.The level of beta2M in preterm infants was significantly higher than that in term ones, both in study and control group during the entire first month of life.The highest values were observed in most immature neonates (GA 30–32). In group of asphyxiated and most immature neonates very high level of beta2M was still detected on day 28 while in fullterm it was almost normal.The beta2M excretion in asphyxiated neonates showed an increase on 1 and 3 day with a peak level at 7 day of age and than a slow decrease.Transient elevation of urinary beta2M were noted also in control group on day 3 with no significant differences between values of beta2M in the other samples in control group. We observed also correlation of beta2M with severity of perinatal asphyxia. The levels of beta2M were significantly increased in severe asphyxia group (pH less or equal 6.9) compared to mild asphyxia group.

CONCLUSIONS:Measuring of beta2M can be non invasive method for determining a severity of perinatal asphyxia and renal maturation as well.

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PPHN - THE COURSE WITH RESPECT TO BIRTH WEIGHT

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Objective: Persistent Pulmonary Hypertension of the Newborn (PPHN) constitutes a serious neonatal disorder occurring in 1–2 cases per 1000 live births with mortality of 10–20%.To our knowledge, no research in Poland has been conducted to study the course of this disorder with respect to birth weight.

Aim: to assess the severity of PPHN within various ranges of birth weights.

Material and method: All mechanically ventilated newborns with diagnosed PPHN admitted to the Department of Neonatology in Poznan between 1998 to 2003 were consecutively collected (n=166) and analyzed in 3 groups depending on their birth weight: group I (n = 35) <= 1500 g, group II (n = 32) 1501 g - 2500 g, and group III (n = 99) >=2501 g. We measured severity of PPHN at the time of admission evaluated by mean pulmonary artery pressure - MPAP (mmHg) and oxygenation index - OI (primary outcomes) followed by assessment of duration of mechanical ventilation (days), length of hospital stay (days), and prognosis (secondary outcomes). We analyzed coexisting disorders in all groups.

Results (mean+/-SD): Primary outcomes are comparable between groups with the exception of significantly higher MPAP in group I (58+/-8) in comparison to group III (53+/-7) - p=0,0006. Newborns in group III were ventilated for a significantly shorter amount of time (7+/-6) than in groups I (17+/-24) - p=0,0002 and II (10+/-7) - p=0,02. Similarly, newborns in group III were hospitalized for a significantly shorter amount of time (17+/-10) than in groups I (32+/-36) -p=0,0002 and II (25+/-17) -p=0,001. Number of full recoveries is significantly lower in group I (7) in comparison to groups II (16) - p=0,01 and III (72) - p<0,0001 and in group II when compared to group III -p=0,02. The need for further treatment is significantly lower for group II (9) than group III (13) -p=0,049. Number of deaths is highest in group I (21) and significantly different from groups II (7) -p=0,002 and III (14) -p<0,0001. The most common diagnosis in group I was respiratory distress syndrome (32 cases) and in groups II and III pneumonia (21 and 52 cases, respectively).

Conclusions and discussion: Birth weight seems to influence the course of PPHN, with worse outcomes in groups of low and very low birth weights. However, all coexisting disorders must be considered as PPHN is only one among various causes of fatal prognosis.

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PREDICTIVE VALUE OF CARDIAC TROPONIN T (CTNT) IN THE DIAGNOSIS OF CARDIAC DYSFUNCTION IN ASPHYXIATED FULL-TERM INFANTS

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In the last years several reports on exploiting cardiac troponin T in the retrospective diagnosis of perinatal asphyxia have been published. Application of these method in neonates still stays open. Aim of the study was to evaluate usefulness of cTnT determination in the diagnosis of hypoxic myocardial injury in full-term infants.

Material and method: 105 neonates >37 weeks of gestation were enrolled into the study. We separated study group of 45 asphyxiated neonates (umbilical pH<7,10, BE<-12mmol/1), with mean gestational age 38,7±1,3 weeks and birth weight 3246,4±587,0 g and control group (60 non-asphyxiated infants) with mean gestational age 38,6±1,5 weeks and birth weight 3374,8±496,9g. Quantitative determinations of cTnT in blood serum were performed between 12th and 24th hour of life using Elecsys cTnT STAT Immunoassay, that contains specific monoclonal antibodies against human cTnT.

Results: cTnT levels were higher in the asphyxiated infants comparing to controls (0,21+/-103ng/ml and 0,054+/-0,039ng/ml, respectively) (p<0,00001). ROC curve proved that cTnT had high value in the diagnosis of posthypoxic myocardial injury in newborn. Discriminate value of cTnT was 0,060ng/ml (sensitivity 71,1%, specificity 66,7%, positive predictive value 61,5%). cTnT levels correlated with pH and BE in umbilical blood (p<0,00001 and p<0,00001, respectively), Apgar score in the 1min and 5 min (p<0,0002 and p<0,0002, respectively), abnormal fetal heart pattern on cardiotocography (p<0,01).

Conclusions: cTnT determination is useful method of myocardial injury diagnosis in full-term infants after perinatal asphyxia. Serum blood levels of cTnT indicate, that cardiac dysfunction in neonates who suffered intrauterine hypoxia is more frequent than would be diagnosed based solely on clinical symptoms.

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EFFICACY OF IBUPROFEN FOR TREATMENT OF PATENT DUCTUS ARTERIOSUS (PDA) IN NEONATES < 34 WEEKS OF GESTATION

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Patent ductus arteriosus (PDA) in premature neonates is less likely to close spontaneously comparing to full-term infants. Pharmacological treatment with nonsteroidal anti-inflamatory drugs are mainly used for closure of PDA. Although the use of Ibuprofen (IBU) in PDA treatment have not yet been examined in detail The aim of this study was to evaluate the efficacy of IBU therapy in premature infants (<34 weeks of gestation) treated for PDA.

Materials and methods: Thirty five neonates neonates born between 25–33 weeks of gestation (mean 29+/-2.5 weeks) and with birth weights between 820-2090g at birth (mean 1338.3+/-380.5g) were enrolled into the study. All infants were diagnosed as having hemodynamically significantPDA confirmed by ECHO between 3rd and 7th day of life. Intravenous IBU (first dose of 10mg/kg followed by next doses of 5mg/kg at 24-hour intervals) was administred by a 15 minute intravenous infusions. The patients serum platelet counts were >60,000uL and blood urea nitrogen <40mg/dL. Head ultrasound, enteral feeding tolerance, urine output were assesed before and after IBU.

Results: IBU was administered at mean 5.8+1.3 days of life. Mean size of PDA was 2+/-0.8 mm. In 31 of 35 patients (88.6%) PDA was closed after IBU therapy. 3 neonates (8.6%) with a clinically closed ductus developed a recurrent, symptomatic PDA and 2 of them needed surgical ligation. The treatment was ineffective in 4 infants (11.4%) of which 3 neonates underwent surgical ligation. Pulmonary hemorrhage occured in one patient and another one showed gastric hemorrhage. Twenty infants (57%) were enterally fed during the treatment. We have not shown an increase in the incidence of necrotizing enterocolitis, IVH, renal failure and bleeding from puncture sites.

Conclusions: Our findings suggest that IBU is of high efficacy when used for PDA tratment in neonates < 34 weeks of gestation. The treatment had no influence on incidence of intraventricular hemorrhage and did not impaire food tolerance and urine output.

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LONG-TERM OUTCOMES OF LUCINACTANT (SURFAXIN) VS. ANIMAL-DERIVED AND SYNTHETIC, NON–PROTEIN-CONTAINING SYNTHETIC SURFACTANTS IN VERY PRETERM INFANTS

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Background: We have published results of two randomized, controlled trials comparing lucinactant (Surfaxin®), a new generation, peptide-based synthetic surfactant, with non-protein-containing synthetic colfosceril (Exosurf®) and bovine-derived beractant (Survanta®) (SELECT trial), and with porcine-derived poractant (Curosurf®) (STAR trial) for prevention of respiratory distress syndrome (RDS). In the SELECT trial, Surfaxin significantly reduced the incidence of RDS at 24 h, 14-d RDS-related mortality and bronchopulmonary dysplasia (BPD) at 36 wk post menstrual age (PMA) compared with Exosurf. All-cause mortality at 36 wk PMA and 14-d RDS-related mortality were decreased compared with Survanta. The STAR trial demonstrated similar results for 36-wk mortality without BPD for Surfaxin and Curosurf. Objective: To compare long-term outcomes including mortality and morbidity at 1 year corrected age for Surfaxin vs. synthetic and animal-derived surfactants across the STAR and SELECT trials.

Methods: Infants with gestational age of 24–32 wk and birth weight (BW) of 600-1250 g were randomized to treatment with Surfaxin (175 mg/kg), Exosurf (67.5 mg/kg), Survanta (100 mg/kg), or Curosurf (175 mg/kg). An analysis of outcomes through 1-year corrected age across the two studies was performed for all randomized patients. Treatment differences were compared using the Wilcoxon test, stratified by BW strata, country, gender, and race.

Results: At 1-year corrected age, survival still favored Surfaxin (73.4%) vs. the animal-derived surfactants (71.2%; p=0.05) and Exosurf (69.0%). These observations were consistent with the difference in all-cause mortality at 36 wks PMA for Surfaxin-treated patients (20.3%) vs. the animal-derived products (24.1%; p=0.01), and Exosurf (23.8%). Overall health and gross neurological outcomes trended in favor of Surfaxin over the comparator surfactants.

Conclusion: The early survival advantage observed through 36-wks PMA in premature infants treated with Surfaxin compared with animal-derived surfactants as well as a synthetic, non-protein-containing surfactant was maintained through 1-year corrected age.

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COMPARISON OF THE EXPRESSION OF CD11B RECEPTORS OF NEUTROFILS IN PRETERM NEONATES AND TERM HEALTHY NEONATES ASSESSED IN UMBILICAL ARTERY BLOOD.

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Objectives: An intrauterine infection of bacterial origin is the most frequent cause of preterm births. Promising marker of the intrauterine infection in preterm neonates seems to be an assessment of the expression of CD11b receptors of neutrofils.

Aim of the work: To compare the expression of CD11b receptors of neutrophils assessed in umbilical artery blood in preterm neonates and healthy term neonates.

Material and methods: Expression of CD11b receptors of neotrophils was assessed in umbilical artery blood by flow cytometric analysis in 17 preterm neonates (average gestational age - 28,9 week) and 11 healthy term neonates (average gestational age - 38,9 wek). Additionally, in group of preterm neonates the expression of CD11b receptors of neutrophils was assessed twice, every 24 hours, in 2nd and 3rd day of life. Expression assessment was done with FACScalibur BD analyser and with CD11b (BD) monoclonal antibodies. For statistical significance p<0,01 level was admitted.

Results: There was no statistically significant difference between the expression of CD11b receptors of neutrophils in umbilical artery blood in group of preterm neonates and term healthy neonates (p=0,3930). However, increase of the expression of CD11b receptors of neutrophils in group of preterm neonates between 1st day of life and 2nd and 3rd day of life (p<0,0000004 and p<0,00015 respectively) was statistically significant.

Conclusions: 1. Expression of CD11b receptors of neutrophils assessed in umbilical artery blood in preterm neonates does not show a statistical significant difference in comparison to term healthy neonates. 2. Statistically significant increase of the expression of CD11b receptors of neutrophils in preterm neonates in the 2nd and 3rd day of life in comparison to the 1st day of life can be consider as a marker of the inflammation due to an intrauterine infection, but assessed only after 24 hours of life of preterm neonate.