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EARLY-ONSET NEUTROPENIA IS ASSOCIATED WITH HEAVY FUNGAL COLONIZATION IN THE 1ST MONTH OF LIFE IN VERY LOW BIRTH WEIGHT NEONATES

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Background: Fungal Colonization (FC), mostly by Candida spp., and subsequent invasive fungal infection are increasingly frequent features in preterm neonates in NICUs, and several risk factors have been found associated to them. The objective of this study was to evaluate the role of Early-Onset Neutropenia (EON) in the development of FC in preterm very low birth weight (VLBW) neonates in NICU.

Methods: Medical records of all <1500 g birth weight neonates admitted to our 3rd level Facility between 1997 and 2003 and survived more than 1 week were reviewed. Neonates with baseline fungal colonization were excluded, thus final number of considered neonates was n=424. For all neonates we recorded: a) the presence of neutropenia in the first week of life (EON), diagnosed with Manroe (J Pediatr 1979) and Mouzinho (Pediatrics 1994) reference values (n=52, 12.2%); b) the presence of FC (at least one site), the number and the type of sites colonized during the first month of life. In 25 on 52 neutropenic infants, a 3-days course of Filgrastim (10 mg/kg/die) was performed during the 1st week of life with normalization of the neutrophil count always before the 8th day of life. In neutropenic not treated neonates neutrophil count became spontaneously normal before the beginning of 3rd week of life. Statistical analysis was performed by Chi-square, ANOVA and T-test using SPSS 8.0 for Windows.

Results: Statistical analysis did not show significant differences between neutropenic and not neutropenic neonates as for mean gestational age and birth weight, sex, race, outcome and presence of the most common risk factors associated with FC. Incidence of FC in the 2nd, 3rd and 4th week of life was significantly higher in neutropenic (n=32/52, 61.5%) than in not neutropenic patients (n=134/372, 36%) (Chi-square 14.288, OR 0.32; p<0.001). Intensity (as number of different sites affected) and severity (as number of risk sites affected) of FC were as well higher in the neutropenic patients (p<0.002 and p<0.001 respectively). Treatment with Filgrastim did not change the relative risk for colonization: FC was present in 60% of neutropenic treated neonates and 64% of not treated (p<0.28, NS).

Conclusion: EON in VLBW neonates significantly influences the rate of colonization by fungal spp. in the first month of life, causing a higher risk that cannot be corrected by filgrastim therapy. VLBW neonates with EON should be carefully monitored for fungal colonization during their stay in NICU, and should undergo prophylactic measures to prevent it.

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DIFFERENTIATION-DEPENDANT SENSITIVITY OF NEURONAL PRECURSOR CELLS TOWARDS OXIDATIVE STRESS

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Background: Apoptosis is an endogenous cell suicide mechanism triggered in response to biological factors and genotoxic stimuli often resulting from oxidative stress. Neuronal apoptosis especially in the developing brain may cause long-term brain dysfunction. Cognitve deficits in the later childhood are frequent in preterm infants. Preterm infants are exposed to high oxygen due to their premature lungs. At the same time their nutritional regimens are deficient in antioxidant precursors. In cell cultures a relation between oxidative stress and cell death could be found. This study tested the hypothesis that differentiated rat adrenal medullary pheochromocytoma PC12 cells are less sensitive to hyperoxia than undifferentiated cells.

Methods: PC12 cells differentiated with nerve growth factor protein (NGF) and undifferentiated cells were exposed to an atmosphere of 80% oxygen and treated with buthionine sulfoximine (BSO), a glutathione synthesis inhibitor. Control cells did not receive BSO. Cell viability was tested by reduction of MTT (3-(4,5-dimethylthiazol-2-yl)2,5-diphenyltetrazoliumbromide). Apoptosis was measured by flow cytometry (annexin/ propidiumjodid, caspase-3-activity).

Results: Undifferentiated cells treated with BSO exposed to hyperoxia showed an increase in apoptosis (cytometry) and a significant decrease in viability (BSO+normoxia 81±5,1%, hyperoxia 95±3,1%, BSO+hyperoxia 22±3,0%, means ± S.E.M. for 4–6 experiments, p< 0,05, cell viability assay). Differentiated cells showed reduced sensibility towards BSO and hyperoxia (BSO+normoxia 101±3,3%, hyperoxia 97±1,9%, BSO+hyperoxia 87,6±2,5%, cell viability assay). BSO alone did not induce apoptosis.

Conclusion: We conclude that exposure to high oxygen in combination with limited antioxidant protection is responsible for increased cell death via apoptosis in undifferentiated neurons. This finding may contribute to longterm cognitive deficits in preterm infants exposed to high oxygen.

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BIRTH ASPHIXIA CHANGES THE CONCENTRATION OF VASCULAR ENDOTHELIAL GROWTH FACTOR

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Objectives: To investigate whether birth asphyxia acute or chronic can stimulate secretion of VEGF (vascular endothelial growth factor) Study designe: We evaluated VEGF protein level in the umbilical blood in 44 healthy neonates (19 term and 25 preterm) and 79 hypoxic neonates. Among the hypoxic newborns 40 was born at term (28 with birth weight appropriate for gestational age - AGA, and 12 with birth weight below 10 percentile-SGA) and 39 was born before 32 week of gestation (25 AGA and 14 SGA). ELISE assay for VEGF was purchased from R&D Systems and used according to instructions.

Results: In the healthy newborns VEGF level was 78,45±152,12 pg/ml in the term and 45,41±23,46 in the preterm. The level of VEGF was higher in the hypoxic neonates. The levels of VEGF in the hypoxic term newborn with AGA and SGA birth weight were 658,99±360,89 and 741,26±332,67 respectively. The levels of VEGF in the hypoxic preterm neonates with AGA and SGA birth weight were 833,41±276,62 and 847,63±276,21 respectively. There were no differences between newborns with AGA and SGA birth weight. The levels of VEGF were highest in the neonates who developed PVL, NEC, BPD, ROP or HIE. In the term neonates we have found positive correlation between the level of VEGF and oxygenation index and medium airway pressure during the first day of life. We have found also positive correlation between the level of VEGF and duration of TPN, katecholamine treatment and hospital stay.

Conclusions: The vascular endothelial growth factor is releases in the response for either acute or chronic hypoxia and is assumed to be early indicator of birth asphixia.

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NEONATAL INFECTION AFTER CENTRAL CATHETERIZATION, ACCORDING TO ANTIBIOTICAL THERAPY

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Objectives: The aim of this study is to determine the efficacy of administrating antibiotics to prevent central catheter-related infections in newborns (NW).

Methods: We report a survey of 122 patients of our Neonatal Unit over a two years period. Criteria for inclusion: at least 24 weeks gestation or 500 grams, no mortal congenital malformations, catheter inserted in the first 72 hours after labor, no infection (possible or confirmed), and absence of mechanical ventilation. At the beginning and at the end of the technique, blood is extracted for blood culture. A betalactamic and an aminoglucoside agents are administered intravenously when canalizing the central way, and for 7 days to one of every two newborns. Both groups are compared, not receiving antibiotics (A) and receiving antibiotics (B), evaluating positive cultures and diagnosis of infections. Statistical method: Odds Ratio (OR) and i2 test.

Results: Selected NW: 122. Valid NW for the study: 117 (61 in group A and 56 in group B) Pre-catheterization: NW with positive cultures: Group A: 8. Group B: 7 (OR: 1,06; IC95%: 0,32–3,55) NW with positive blood cultures: Group A: 4. Group B: 3 (OR: 1,22; IC95%: 0,22–7,39) Post-catetherization: NW with positive cultures Group A: 18. Group B: 18 (OR: 0,88; IC95%: 0,37–2,09) NW with positive blood cultures: Group A: 3. Group B: 3 (OR: 0,91; IC95%: 0,14–5,99) NW with infection: Total infections: Group A: 10. Group B: 16 (OR: 0,49; IC95%: 0,18–1,30) 0–7 days: Group A: 5. Group B: 6 (OR: 0,74; IC95%: 0,18–2,98) 7 days: Group A: 5. Group B: 10 (OR: 0,41; IC95%: 0,11–1,43) Sepsis: Group A: 6. Group B: 7 (OR: 0,76; IC95%: 0,21–2,76) 0–7 days: Group A: 3. Group B: 4 (OR: 0,67; IC95%: 0,11–3,78) 7 days: Group A: 3. Group B: 3 (OR: 0,91; IC95%: 0,14–5,99) Other infections: Group A: 4. Group B: 9 (OR: 0,37; IC95%: 0,09–1,42) 0–7 days: Group A: 2. Group B: 2 (OR: 0,92; IC95%: 0,09–9,50) 7 days: Group A: 2. Group B: 7 (OR: 0,24; IC95%: 0,03–1,33)

Conclusion: In our hospital, central catheterised newborns receiving profilactically antibiotics seem to have a major probability, with no statistical differences, of having more nonseptical and later infections, than those who don't receive antibiotics. There are very few differences in the incidence of sepsis and early infections in both groups. Therefore, it doesn't seem useful the use of profilactical antibiotics when catheterising a non infected newborn.

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NEONATAL INFECTION AFTER EXCHANGE TRANSFUSION ACCORDING TO ANTIBIOTICAL THERAPY

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Objectives: The aim of this study is to determine the efficacy of administrating antibiotics to prevent exchange transfusion-related nosocomial infections in newborns.

Methods: We report a survey of 36 patients of our Neonatal Unit over a two years period. Criteria for inclusion: at least 24 weeks gestation or 500 grams, no mortal congenital malformations, no infection (possible or confirmed), absence of mechanical ventilation during the exchange transfusion, and survival of more than 24 hours after the admission. At the beginning and the end of the technique blood is extracted for blood culture. A betalactamic and an aminoglucoside agents are administered intravenously when canalizing the central way, and for 7 days to one of every two newborns. Both groups are compared, not receiving antibiotics (A) and receiving antibiotics (B), evaluating positive cultures and/or diagnosis of infections. Statistical method: Odds Ratio (OR) and proves of i2 test.

Results: NW with exchange transfusion: 36 RN (18 in every group). - RN with positive cultures pre-exchange transfusion: - Group A: blood culture: 2 (staphilococcus). Others: 1: (staphilococcus). - Group B: blood culture: 1 (streptococcus B). Others: 1: (not usual gram-negative). - RN with positive cultures post- exchange transfusion: - Group A: blood culture: 1 (not identified germ). others: 5: umbilical: 1(staphilococcus), skin: 4 (2 staphilococcus, 2 klebsiella). - Group B: blood culture: 1 (staphilococcus). others: skin: 3 (2 not usual gram-negative and 1 not identified). - RN with diagnosis of infection: - Group A: -1st week of life: none. - >1week of life: 1 bacteraemia (not identified germ) and 1 onfalitis (staphilococcus). - Group B: -1st week of life: 1 septicemia (streptococcus B). - >1week of life: 1 septicemia (staphilococcus) None of these differences are, and are very far to be, statistically significant, therefore we elude to show the results of the odds ratio and of the i2 test.

Conclusion: In our means, in newborns with exchange transfusion, there are no noticeable differences for infections or positive cultures, with or without using prophylactic antibioticotherapy. Therefore, it doesn't seem useful the use of profilactical antibiotics when realizing exchange transfusion in a noninfected newborn.

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SERUM C-REACTIVE PROTEIN AND THE DETECTION OF SIGNIFICANT BACTERIAL INFECTION IN CHILDREN

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Background: Serum C-reactive protein(CRP) is a nonspecific, acute phase protein which rises in response to infection. Consequently, it is a widely used tool in investigating the febrile child with the aim of distinguishing bacterial from viral illness. Aim : To determine the utility of serum CRP in the detection of significant bacterial infection(SBI) in children.

Methods: A retrospective chart review of children investigated for possible infection, over a six month period. Any child who had a white cell count, blood culture and CRP obtained concurrently was included. The positive and negative predictive values and risk ratio(RR) of CRP in relation to significant bacterial infection were calculated.

Results: 395 patients were included in the study. Age range 6 days to 15 years. 71 had either laboratory or radiologically proven SBI. The CRP was significantly higher in the SBI group compared to the non SBI group. A CRP of >100 is the best predictor of SBI, with a positive predictive value of 45% and a RR of 2.96(p=0.00006). Conversely, a normal CRP was found to occur in 10% of patients with SBI.

Conclusion: Serum CRP is a useful screening tool in identifying those febrile children most at risk of SBI. However, it is worth highlighting that some children with a normal CRP will also have SBI. Hence it must always be used in conjunction with a thorough clinical examination.