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PULSE OXIMETRY SIGNALS: CHAOTIC ANALYSIS IN THE EVALUATION OF NEONATAL ILLNESS SEVERITY

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Background: Assessment of neonatal illness severity is important for quality of care control, unbiased NICU performance comparisons, management studies and rationale use of resources. Emerging evidence indicates that the analysis of heart rate dynamics may provide valuable practical diagnostic and prognostic information. Here, we tested the hypothesis that a reduced dynamics of pulse rate (PR), and perfusion index (PI) is associated with higher illness severity in very low birth weight (VLBW) infants with histologically documented chorioamnionitis (HCA), a leading cause of neonatal morbidity and mortality.

Methods: Two VLBW population with and without HCA were examined [HCA+: gestational age: 27.1 ± 2.3 wk, birth weight 932±300 g, SNAP-II: 39 (29–45), n=15; HCA-: gestational age: 27.4 ± 0.9 wk, birth weight 935±200 g, SNAP-II: 13 (5–17), n=15]. Relative Lempel-Ziv complexity (LZ), Lyapunov largest exponent (̵), correlation dimension (CD) and Hurst exponent (H) were determined for 1000 to 10,000 data set points (Chaos Data Analyzer Pro, The Academic Software Library, North Carolina State University, Raleigh, NC, USA) for PR and PI recorded at 4-s intervals (Masimo RS, Masimo Co., Irvine, CA, USA) for each infant. The predictive accuracy of chaotic analysis was calculated using a receiver operating characteristics (ROC) curve analysis.

Results: HCA+ infants exhibited significantly decreased LZ (PI-LZ: 0.26±0.13 vs. 0.44±0.07, p<0.0001; PR-LZ: 0.18±0.09 vs. 0.41±0.22, p=0.0008), ̵ (PR-̵: -0.14±0.24 vs. 0.44±0.09, p<0.0001; PI-̵: 0.21±0.36 vs. 0.42±0.10, p=0.038) and CD (PI-CD: 1.6±0.9 vs. 2.8±0.7, p=0.0003; PR-CD: 1.0±1.2 vs. 2.7±1.5, p=0.0019), as well as increased H (PR-H: 0.36±0.06 vs. 0.21±0.06, p<0.0001; PI-H: 0.33±0.13 vs. 0.23±0.07, p=0.0139) values were observed. Low PR-CD (≤0.858), PR-̵ (≤0.235), and PI-LZ (≤0.369) adequately identified HCA+ infants (PR-CD and PR-̵:100% sensitivity and 100% specificity; PI-LZ: 87.5% sensitivity; 100% specificity).

Conclusion: These findings suggest that chaotic analysis of pulse oximetry signals may represent a novel, noninvasive, real-time approach for assessing illness severity in high-risk newborns.

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SUBCLINICAL CHORIOAMNIONITIS: AN UNRECOGNIZED RISK FACTOR FOR SEVERE PULMONARY HAEMORRHAGE IN EXTREMELY LOW BIRTH WEIGHT INFANTS

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Background: Clinically apparent pulmonary hemorrhage (PH) occurs in 5%–7% of very low birth weight (VLBW) infants with respiratory distress syndrome (RDS), and is associated with significantly increased mortality rate and severe pulmonary and central nervous system morbidities. To date, little information on the pathogenesis of the condition is available, although recent evidence suggests a key role for inflammation. Here, we tested the hypothesis that subclinical chorioamnionitis (s-CA) is associated with the development of PH in extremely low birth weight (ELBW) newborns.

Methods: The clinical and placental histology findings of ELBW infants died with severe PH (PH+; n=9; M:2, F:7; gestational age[mean ± SD]: 25.7 ± 1.2 weeks, birth weight: 768 ± 179 g; age at death [median; interquartile range]: 4 days; 3–7) were compared to those of a gestational age- and birth weight-matched ELBW population without PH (PH-; n=15; M:7, F:8; gestational age: 26.1 ± 3.1 weeks, birth weight: 787 ± 255 g).

Results: PH+ ELBW newborns showed significantly higher proportions of histological s-CA [8/9 (88.9%) vs. 1/15 (6.7%), p=0.0001; relative risk = 13.3; 95% CI: 1.97–89.8], preterm premature rupture of membranes [9/9 (100%) vs. 5/15 (33.3%), p=0.0020], together with higher frequency of intraventricular haemorrhage degree 3–4 [IVH3–4: 8/9 (88.9%) vs. 2/15 (13.3%), p=0.0049] than the PH- population. Conversely, no statistical differences were observed between the groups regarding the other examined variables, including coagulation screening work-up, antenatal steroids, multiple gestation, emergency caesarean section, 1-min and 5-min Apgar scores, fetal growth restriction, patent ductus arteriosus, air leak, necrotizing enterocolitis, sepsis, I.M.-vitamin K1 supplementation, fresh frozen plasma administration, surfactant replacement and number of surfactant doses, type of assisted ventilation, as well as energy, fluid, glucose protein, and lipid intakes during the first postnatal week (p≥0.21).

Conclusion: These findings appear to support the hypothesis that s-CA, associated with a fetal systemic inflammatory response syndrome, may play a key role in the pathogenesis of severe PH in ELBW infants.

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EVALUATING ILLNESS SEVERITY FOR VERY LOW BIRTH WEIGHT INFANTS: CRIB OR CRIB-II ?

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Background: The clinical risk index for babies (CRIB) is a risk-adjustment instrument used worldwide to determine illness severity in infants born at less than 31 weeks' gestation, or having 1500 g birth weight or lower. However, the appropriateness of CRIB has been questioned, and CRIB has very recently been updated and simplified into a five-items scoring system (CRIB-II) for infants born at less than 32 weeks' gestation, in order to improve its accuracy. Here, we compared the accuracy of CRIB and CRIB-II scores in predicting mortality for VLBW infants in a small unit.

Methods: A total of 147 NICU-admitted VLBW infants with data available for both CRIB and CRIB-II were enrolled in the study (M:70, F:77; mean ± SD: 28.6 ± 2.5 weeks; birth weight: 1070 ± 325 g). Major non-lethal malformations were present in 3 (2.04%) infants and minor birth defects were observed in 7 (4.76%). Extremely low birth weight infants were 59 (40.15% of total; M:27, F:32). Newborns with lethal congenital abnormalities, metabolic disorders or undergoing complex cardiac surgery were excluded. Both CRIB and CRIB-II scores were calculated for each newborn. Neonatal mortality (death before hospital discharge) was selected as the outcome measure.

Results: The median CRIB and CRIB-II scores were 2.0 (range:0–16), and 8.0 (range:3–20), respectively. A significant positive correlation between CRIB and CRIB-II was observed (P <0.0001), with a mortality rate of 11.56% (17/147). Newborns with unfavourable outcome (M:8, F:9) had a significantly lower birth weight (696±205 g vs. 1130±300; p<0.0001), gestational age (25.7±2.9 weeks vs. 29.08±2.1 weeks; p<0.0001), CRIB (median [25th–75th percentiles]: 8.0 vs. 2.0, P<0.0001) and CRIB-II (14.0 vs. 8.0, P <0.0001) than surviving infants. Mean AUCs for CRIB, CRIB-II, gestational age and birth weight in identifying neonatal mortality in VLBW infants ranged from 0.924 (CRIB) to 0.869 (gestational age). No significant differences were observed for the AUCs of CRIB vs. CRIB-II (P=0.34), CRIB vs. gestational age (P=0.18), CRIB vs. birthweight (P=0.24), CRIB-II vs. gestational age (P=0.62), or CRIB-II vs. birth weight (P=0.86).

Conclusion: Our main findings suggest that CRIB and CRIB-II have comparable accuracy in predicting neonatal mortality in VLBW infants. Although our observed mortality rate is higher than that reported for the original CRIB-II population, differences between the two proportions are not statistically significant (P =0.16).

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ABNORMAL ORAL MUCOSAL LIGHT REFLECTANCE IN ACHONDROPLASIA

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Background: Approximately 90% of achondroplasia (ACH) cases are caused by a de novo mutation. No phenotypical or genotypical markers for the unaffected ACH parents are known to date. Here, we assessed the value of oral mucosal color in identifying patients with sporadic mutations and their unaffected parents.

Methods: The study was conducted on ACH children (n=30), unaffected ACH parents (n=60), and a sex- and age-matched controls (control children, n=30; control parents, n=60). Light reflectance of the lower gingival and vestibular oral mucosa were measured using an imaging reflectance system in the optical spectrum (400–700 nm wavelengths).

Results: The oral mucosa of the ACH patients showed significantly higher reflectance values in the 410–630 nm wavelength range of the optical spectrum (P≤0.0063) than that of controls, while unaffected ACH parents showed significantly lower reflectance values over the whole optical spectrum (P≤0.0001). From the ROC curve analysis results, a reflectance cutoff value >9.37% at the 550 nm wavelength identified ACH patients with 100% sensitivity and 100% specificity, while a reflectance cutoff value ≤4.71% at the 430 nm wavelength identified ACH parents with 100% sensitivity and 96.4% specificity.

Conclusion: These findings indicate the presence of previously unrecognized oral mucosal reflectance abnormalities in ACH children and unaffected ACH parents.

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MEDICATION ERRORS IN A NEONATAL UNIT

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Background: The magnitude and consequences of medical errors are controversial issues; nevertheless, there is a consensus on the preventability of medication errors and their frequent occurrence. Aim: To determine the frequency of different types of error in medical prescriptions and to estimate its occurrence as a function of characteristics and circumstances of the prescriptions.

Methods: Cross-sectional study of hand-written prescriptions for newborn infants admitted to a third level neonatal unit during a 5 months study period (July–November 2003). Data were extracted from all prescriptions written on 53 randomly sampled days. Outcome variables: different elements were assessed to describe the correction of a prescription (drug name, dose, units, administration route, interval, legibility); a prescription was considered correct when all its elements were present. Determinants: characteristics and circumstances of the prescriptions (type of drug, day of the week, night/day shift, training of the prescriber and clinical profile of the patient). Data analysis: Proportions and logistic regression adjusted odds ratio (95% confidence interval).

Results: 4132 hand-written prescriptions were reviewed. 58.6% of the prescriptions fulfilled the correction criteria. 88% of incorrect prescriptions were intercepted. No adverse effect was related to a prescription error. Dose calculation was incorrect in 12.3% of the prescriptions. An incorrect abbreviation of the units was used in 8.4%; 4% did not state dose interval and 2.8% stated an incorrect interval. At least one of the elements of the prescription was considered illegible or uncertain in 13.7%. The route of administration was not stated in 12.7%, and it was not correct in 0.7%. The drugs with the higher proportion of incorrect prescriptions were caffeine and erythropoietin. Prescriptions were more frequently correct for newborns admitted to intensive vs. intermediate care, 1.5 (1.3–1.7); birth weight over 2500 g, 1.9 (1.5–2.4); on week-ends vs. rest of the week, 1.3 (1.1–1.5); on afternoon/night vs. morning shifts, 1.8 (1.4–2.3); and when written by in-training vs. staff doctors, 1.5 (1.4–1.8).

Conclusion: More than half of prescriptions written out by hand in a neonatal unit were not considered correct. A higher workload is not related with a higher number of incorrect prescriptions. Professional experience does not reduce, in general, the number of prescription errors. The occurrence of miscalculation of dose was higher for medication prescribed daily or routinely.

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DO TRANS ISOMERIC FATTY ACIDS INTERFERE WITH THE METABOLISM OF LONG-CHAIN POLYUNSATURATED FATTY ACIDS IN EXPECTING WOMEN?

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Background: There are several publications reporting significant associations between trans fatty acids and LC-PUFA status or development in the perinatal period. Significant inverse correlations were reported between trans isomeric and long-chain polyunsaturated fatty acids in cord blood lipids both in healthy full-term infants (Elias & Innis, Am J Clin Nutr 2001; 73: 807–814) and in full-term infants with an atopic trait (Decsi et al., Am J Clin Nutr 2001; 74: 364–368), as well as in cord vessel wall lipids in healthy full-term infants (Decsi et al., Lipids 2002; 37: 959–965), and in plasma lipids in very young preterm infants (Koletzko, Acta Paediatr Scand 1992; 81: 302–306). It was speculated that the inverse association seen at birth should have its origin in the maternal fatty acid status, but the question has not been explicitly addressed as yet.

Methods: Fatty acid composition of erythrocyte membrane phosphatidylcholine lipids was determined by high-resolution capillary gas-liquid chromatography at the 20th week of gestation in expecting women living in Germany (n = 23), Hungary (n = 34) and Spain (n = 44).

Results: The sum of trans isomeric fatty acids was significantly (P <0.01) higher in Spanish (0.71 [0.32], % wt/wt, median [IQR]) than in German (0.49 [0.24]) and Hungarian (0.56 [0.34]) mothers. No correlation was found between trans isomers and LC-PUFA in erythrocyte membrane lipids in German and Hungarian mothers. In Spanish mothers, there was no correlation between trans fatty acids versus linoleic acid (15:96 [3.90]) and alpha-linolenic acid (0.08 [0.11]) (table). In contrast, trans hexadecenoic acid (C16:1; 0.20 [0.15]), trans octadecenoic acid (C18:1; 0.36 [0.18]) and the sum of trans isomeric fatty acids were significantly inversely correlated to both arachidonic acid (7:92 [4.37]) and docosahexaenoic acid (2:50 [1.76]) (table, * = P <0.05, ** = P <0.01).

Fatty acid	Trans hexadecenoic	Trans octadecenoic	Sum of trans
Linoleic acid	r=-0.08	r=+0.28	r=+0.15
Alpha-linolenic acid	r=+0.08	r=-0.02	r=+0.05
Arachidonic acid	r=-0.47**	r=-0.33**	r=-0.48**
Docosahexaenoic acid	r=-0.35**	r=-0.45**	r=-0.43**

Conclusion: 1. The significant inverse associations found between trans isomeric and long-chain polyunsaturated fatty acids in erythrocyte membrane lipids in expecting women support the concept that maternal trans fatty acid intake may be inversely associated to the long-chain polyunsaturated fatty acid status of the foetus. 2. Among three groups of expecting women investigated, the inverse association between trans isomeric and long-chain polyunsaturated fatty acids was seen only in the group with the highest erythrocyte membrane trans fatty acid values. The study was supported by EU grant QLK1-CT-1999–00888