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EFFECTS OF BODY POSITION ON GASTROESOPHAGEAL REFLUX IN PRETERM INFANTS: STUDY USING COMBINED PH-IMPEDANCE MONITORING

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Introduction: Gastroesophageal reflux (GER) is frequent in preterm infants and conservative postural treatment is recommended. Few studies are available on the effects of body positioning on GER in preterms. Only one study use the impedance thecnique combined to manometric, but not pH-metric relevament. This is the first study that uses the combined pH-impedance thecnique to evaluate the effects of body position on GER in premature babies.

Methods: Ten premature neonates (median GE 31 ws, range 25–32 ws; mean BW 1429 g, range 725-2250 g) with recurrent regurgitation and/or postprandial apnoeas were studied. They were on full enteral feeding with preterm formula. In each patient a 24 hours combined pH-impedance monitoring was performed. The study time was divided in four periods of 6 hours with a randomly assigned position: left (LS) and right side (RS), prone (P), supine (S). Each position period contained two meals (20–30 minutes) and two post prandial period (2.5 h). The % of time with acidic and not acidic GER were evaluated in the different positions.

Results: The percentage of time with acidic reflux is lower in left side and prone position, with statistical difference in the latter when compared with supine (2.87% vs 11.03%) and right lateral (2.87% vs 13.07%) position. Also the percentage of time with not acidic GER is lower in prone and left side position with a different statistical significances (P vs S 0.47% vs 1.66%, p=0.011; P vs RS 0.47% vs 1.44%, p=0.0001; LS vs RS 0.75% vs 1.44%, p=0.004). No difference were found between prone and left side position.

Conclusions: Prone position (with cardio-monitor) or left side position may be used to reduce both the early post-prandial not acidic refluxes and the later acidic refluxes.

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EFFECTS OF THICKENING OF HUMAN MILK ON GER IN PRETERM INFANTS: A CROSSOVER STUDY USING SIMULTANEOUS INTRALUMINAL IMPEDANCE AND PH-MONITORING

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Introduction: Regurgitation and gastroesophageal reflux (GOR) are often observed among preterm infants. A recent study indicates that the use of thickened milk reduces the number and intensity of buffered GOR detected by intraluminal impedence among term neonate. The aim of our study was to evaluate the efficacy of thickening expressed HM in preterm infants, using simultaneous intraluminal impedance and ph-monitoring.

Methods: Five preterms (GE range 27–32 ws. BW 570 g-1900 g) were studied. They were on full enteral feeding and presented frequent regurgitations and/or post prandial desaturations. All infants received 8 meals/day using HM fortified with EOPROTIN 3% and added, in alterned meals, with 1.5 % of starch (70% sweet corn/ 30 % potato). A simultaneos intraluminal impedence (IIM) and pH monitoring was perormed for 24 hours. No difference was observed for number of GOR IIM episodes (170 in thickened milk TM vs 146 in not thickened milk NTM) , total length (seconds) of GOR (3689 in TM vs 3262 in NTM), mean duration (seconds) of GOR (21.3 in TM vs 23.4 in NTM) and GOR height (5.54 cm in TM vs 6.1 cm in NTM)

Conclusions: These preliminary data show that thickening HM by starch does not reduce GOR in preterms

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LOW DOSE LIPOPOLYSACCHARIDE (LPS) EXPOSURE POTENTIATES HIGH-TIDAL VOLUME VENTILATION (HTVV)-INDUCED PROINFLAMMATORY CYTOKINE EXPRESSION IN NEWBORN RAT

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Background: Proinflammatory cytokines are associated with increased risk of chronic lung disease in premature patients. Chorioamnionitis as well as mechanical ventilation have been shown to increase cytokine expression in lung tissue and blood. Objective: To test the hypothesis that low-dose LPS exposure would modify the cytokine response to HTVV in newborn rats.

Methods: Newborn (3–6 days) rats were randomly assigned to four groups (I-IV: 12–14 animals/group). Group III and IV were injected 24h prior ventilation with 3 mg LPS/kg while I and II received saline. Group II and IV were subjected to HTVV (25ml/kg, 60/min, 3h). Lung IL-6, MIP-2, IL-1beta and TNF-alpha mRNA was determined by realtime RT-PCR. Cytokine protein content was measured in bronchoalveolar lavage fluid (BALF). Statistical analysis: one-way ANOVA and t-test (significance: $p<0.05$).

Results: LPS injection reduced weight gain within the 24h following injection from 17.9% (saline) to 11.4% ($p<0.05$). Pre-treatment with LPS did neither affect lung compliance nor blood gas values. LPS alone did not change cytokine expression. In contrast, HTVV alone increased mRNA expression of IL-6 by 7.2 fold, MIP-2 by 7.9 fold and IL-1beta by 1.8 fold ($p<0.05$). The combination of HTVV and LPS further increased the expression of IL-6 (II vs IV; 10.5 fold) and IL-1beta (II vs IV; 2.3 fold). IL-6 protein content in BALF increased with HTVV and LPS+HTVV treatments (I 19.4, II 34.0, III 17.5, IV 43.7 pg/ml).

Conclusions: Whereas low grade systemic inflammation alone does not change the proinflammatory cytokine expression, its combination with HTVV potentiates the proinflammatory cytokine response in the newborn lung. Therefore, we speculate that newborn patients born in a context of chorioamnionitis are at higher risk to develop ventilator associated lung injury than those without association with inflammation/infection.

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ALPHA-TOCOPHEROL TRANSFER PROTEIN IS EXPRESSED IN FIRST-TRIMESTER AND TERM HUMAN PLACENTA

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Background: Alpha-Tocopherol Transfer Protein (a-TTP) is a 30kDa cytosolic protein first described to be present in the liver and is important for alpha-tocopherol trafficking. Expression of a-TTP has been described in animal model liver as well as diverse other tissues such as rat brain and pregnant mouse uterus, the latter finding stressing the importance of a-TTP for embryogenesis and foetal development. In mouse placenta, though, a-TTP is not present, while in pregnant mouse uterus, a-TTP is seen in intrauterine endometrial columnar and glandular cells immunohistochemically, with a peak in Northern blot mRNA analysis on day 4 of mouse pregnancy.

Aim: Determination if a-TTP is expressed in first-trimester and/or term human placenta. Methods: Preparation of human a-TTP-specific rat monoclonal antibodies and rabbit polyclonal antibodies, followed by immunohistochemical staining of first-trimester and term human placenta.

Results: a-TTP could be localized immunohistochemically in villous trophoblast (syncytiotrophoblast) as well as in extravillous trophoblast and decidual cells in first-trimester and term placentas.

Conclusions: a-TTP is required for adequate alpha-tocopherol equilibrium not only prior to delivery, but also most likely throughout pregnancy. Alpha-tocopherol as the major ligand of a-TTP is delivered to the foetus via a-TTP and serves as an eminent substrate for maintenance of pregnancy as well as foetal development in humans.

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LOW MORTALITY IN NECROTIZING ENTEROCOLITIS ASSOCIATED WITH COAGULASE-NEGATIVE STAPHYLOCOCCUS INFECTION

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Background/aims: Necrotizing enterocolitis (NEC) remains a major disease in infants. Prevalence and severity of NEC varies greatly among centres. Our purpose was to asses the impact of epidemiology, clinical course and current therapeutic policies on survival. Methods. The medical records of all newborn infants who developed NEC between January 1998 and December 2001 were reviewed for risk factors, clinical signs, laboratory findings and management. NEC was categorized by modified Bell's classification; only proven NEC (= stage II) was included.

Results: During the study period, 2181 infants were admitted to the Neonatal Intensive Care Unit of La Paz University Hospital. A total of 44 infants developed NEC (= stage II): 25 as stage II and 19 as stage III. The incidence of NEC was 0.024% of live births in the hospital per year and 1.4% of admissions to the Unit per year. 4 infants died, an overall mortality rate of 9%. No patients grade II died and the mortality in Bell stage III was 21%. The main risk factor was prematurity (84%). The most frequent clinical features were abdominal distension and guaiac positive stools or gross hematochezia. Gastric residuals were reported in 25% of patients. Age at onset was significantly earlier in term infants versus preterm infants (median 8 days vs. 24 days); no other clinical features were different in preterm and term infants. Blood cultures were positive in 36% and in 75% of these coagulase-negative Staphylococcus was present. Neither Clostridium nor Bacteroides species were isolated. No patient with NEC grade II had thrombocytopenia, whereas all patients with grade III NEC had platelet counts <100.000 cell/mm3. The most frequent antibiotics used were Cefotaxime in 73% of the patients, Vancomycin in 68% and Clindamycin in 66%. 43% of patients with NEC grade III required laparotomy. In 33% of them primary peritoneal drainage was used but all required further operative procedures. Delayed surgical intervention was significantly correlated with mortality (mean time 15 hours in the patients who died vs 7 hours in those who survived)

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HYPOTHYROIDISM AND HIGH PLASMA AND URINE IODINE LEVELS RELATED TO THE USE OF GASTROGRAFIN

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Background/aims: Perinatal exposure to excess iodine can lead to transient hypothyroidism. Gastrografin contains an iodine concentration of 370 mg/mL. It is used as a contrast media and for the treatment of uncomplicated meconium ileus. The aim of this study was to examine whether Gastrografin influences iodine and thyroxine concentrations.

Methods: The effects of the use of Gastrografin on serum and urine iodine concentrations and thyroid function were investigated in 4 patients treated in our Neonatal Unit from July 2002 to June 2003. Serum and urine samples to measure iodine concentrations were collected from each subject before, if possible, and within 24 hours of administration of Gastrografin. Thyroid function was measured within 7 days of the administration.

Results: Transient hypothyroidism was seen in 1 patient (TSH 33.14 mUI/mL; free thyroxine 0,51 ng/dL) after Gastrografin exposure (iodine administered as enema 10.4 g/kg and orally 4.2 g/kg). In this patient no thyroid dysfunction was found with the neonatal screening program for congenital hypothyroidism before the administration of Gastrografin and thyroid antibodies were not present. In other three infants urine and serum iodine concentrations were elevated after Gastrografin administration, with normal thyroid function.

		IODINE PLASMA CONCENTRATION (N: 4-8 µg/dL)		IODINE URINE CONCENTRATION (N <400 µg/L)	
	GASTROGRAFIN DOSE	Before Gastrografin	After Gastrografin	Before Gastrografin	After Gastrografin
CASE 2	2.4 mL/kg as enema	8.5	>100	35	6000
CASE 3	1.9 mL/kg as enema	---	45	---	2000
CASE 4	2 mL/kg as enema	---	64	---	760

Conclusions: We suggest monitoring thyroid function when Gastrografin is used either as an enema or orally due to the paradoxical effect of the iodine excess on the thyroid gland. Although Gastrografin is suitable for the treatment of uncomplicated meconium ileus it would be advisable to use enemas with less, or without, iodine.