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EFFECT OF COLONIC SHORT CHAIN FATTY ACIDS, LACTATE AND PH ON THE GROWTH OF COMMON GUT PATHOGENS

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Background: It has been demonstrated that the addition of a specific prebiotic mixture of galacto- and fructo-oligosaccharides to an infant formula can change the intestinal flora of formula-fed infants. The microbial composition, the metabolic end products and the pH of the feces shift in the direction of values typical for breast-fed infants. To test the relevance of the observed changes, the effect of the different short chain fatty acids, lactate and pH on the growth of opportunistic pathogens and gut commensals was tested *in vitro*.

Methods: Representative concentrations of D- and L-lactate and SCFA's (acetate, propionate and butyrate), either individually or in combinations, were tested in Tryptic Soy Broth in a pH-range of 5 to 7.5. Inhibition of several opportunistic pathogens (*Salmonella typhimurium*, *Staphylococcus aureus*, *Escherichia coli*, *Enterococcus faecalis*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*) and some gut commensals (*Lactobacillus rhamnosus*, *Lactobacillus plantarum* and *Bifidobacterium breve*) by these metabolic end products was tested by comparing the individual growth curves as determined by turbidity measurements (OD₆₀₀).

Results: The different SCFA's, and especially acetate, gave a concentration dependent inhibition of the different pathogens. The growth inhibition was most pronounced at lower pH values. The combination of lactate (12.5 mM), SCFA's (Acetate 25 mM, Butyrate 2.5 mM, Propionate 5 mM) and a low pH (5.5) as found in the feces of breast- and prebiotic-fed infants, almost completely inhibited all tested pathogens. The tested commensal bacteria were only slightly affected by these combinations, and in these cases sometimes even a stimulation of growth was observed.

Conclusion: Acetate, an end product of bifidobacteria in the gut of breast-fed and prebiotic-fed infants, is an efficient growth inhibitor of many common pathogens. Especially at lower pH values the growth *in vitro* is strongly reduced. The other SCFA's and lactate have an additive effect on the inhibition of the pathogens tested. Growth of commensals, like bifidobacteria and lactobacilli, is hardly affected under these conditions. The physiological changes induced by a mixture of galacto- and fructo-oligosaccharides can therefore be considered as an important mechanism for the inhibition of pathogens in the gut.

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EARLY IBUPROFEN INTERVENTION FOR PRETERM INFANTS UNDER 28 GESTATIONAL WEEKS

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Background: Three cases of pulmonary hypertension with severe hypoxaemia were reported in 2002 after prophylactic ibuprofen administration during a randomized controlled trial of prophylactic treatment of patent ductus arteriosus (PDA) in very preterm infants (Gourmay et al., Lancet 2002; 359: 1486-88). In a monocentre open study we investigated whether curative treatment with ibuprofen for a haemodynamically significant PDA induced pulmonary hypertension when administered between 24 and 72 h of life in preterm infants under 28 weeks of gestational age (GA).

Methods: 29 preterm newborns below 28 weeks of GA were screened between 24 and 72 h of life for the presence of a haemodynamically relevant PDA, defined as one or more of the following criteria: left atrium/aortic root ratio > 1.4, reduction in diastolic flow in the anterior cerebral artery (resistance index > 0.8) or respiratory step back. Exclusion criteria were: ductus-dependent cardiopathy, right-to-left shunt over the PDA, intra-ventricular haemorrhage grade III or IV or thrombocytopenia <50,000/nl. Intravenous ibuprofen was started after confirmation of a relevant PDA with 10 mg/kg bodyweight and was continued with two doses of 5 mg/kg in 24 h intervals. Besides determination of a haemodynamically relevant PDA echocardiographic measurements included the following parameters for the evaluation of pulmonary vascular resistance: shunt direction and flow velocity via the ductus and foramen ovale, estimation of the right systolic ventricular pressure (RSVP) in the presence of a tricuspid regurgitation and mean pulmonary artery pressure. In the treated infants these measurements were obtained serially during the ibuprofen course.

Results: Of the 29 screened patients 14 were excluded from the study: 3 patients with severe IVH, 3 with pulmonary hypertension, and 8 due to non-relevant PDA. Among the 15 treated infants 8 showed a tricuspid regurgitation before the first ibuprofen dose with an estimated pulmonary vascular pressure (RSVP median 31 mmHg; range 23-43 mmHg) below systemic systolic pressure (median 41 mmHg; range 32-51 mmHg). The RSVP resolved during ibuprofen administration. In the treatment group PDA-closure rate 24 h after the third ibuprofen dose was 53.3%.

Conclusion: In preterm infants below 28 weeks GA curative treatment with ibuprofen for a haemodynamically significant PDA was not associated with the occurrence of pulmonary hypertension when administered after 24 h of life.

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CESAREAN SECTION AND NEONATAL OUTCOME

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Background: To investigate the neonatal outcome after cesarean sections in Norway

Methods: Prospective survey using information provided by clinicians at 24 maternity units. A specially designed form for each delivery was used and the neonatal data were derived from birth logs and infant journals. Data from vaginal births were derived from the Medical Birth Registry of Norway. 2380 singleton cesarean sections were included in the survey from January 1, 1999 to July 1, 1999 representing 70.1% of all cesarean sections and 71.2% of all births in Norway in the same period.

Results: The cesarean section rate in singleton pregnancies was 12.5%. 63% of the cesarean sections were unplanned operations. Bagging, intubation and chest compression were carried out in 8.5%, 4.3% and 1.9% of the cesarean sections, respectively. A comparison between elective cesarean sections and vaginal deliveries disclosed: 1) significant more children admitted to the neonatal intensive care unit (NICU) (p=0.00), 2) increased risk for pulmonary disorders (TTN and RDS) (p=0.00) and respiratory treatment (p=0.00) after cesarean section, 3) no difference in the risk for cerebral irritation and cerebral depression (p=0.58) and for neonatal convulsions (p=0.58).

Conclusion: This prospective study represents more than two thirds of all deliveries in Norway in the study period. The most important findings were that a vaginal delivery resulted in reduced risk for transferring to the NICU and for pulmonary disorders compared to an elective section. We stress the importance to try to limit the use of an elective operation to cases where an operation gives benefit to the mother or the child.

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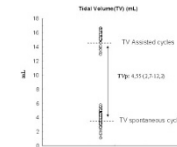
A NON INVASIVE APPROACH TO ASSESS COMPLIANCE OF PRETERM NEWBORNS WITH PERSISTENT ACTIVE RESPIRATORY MOVEMENTS DURING SYNCHRONIZED INTERMITTENT MANDATORY VENTILATION: PRELIMINARY RESULTS

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Background: The evaluation of respiratory mechanics of the preterm infant requiring mechanical ventilation is used to optimize the assisted ventilation settings and reduce baro-voluo-traumatisation. This is a difficult task when using synchronized intermittent mandatory ventilation (SIMV). Indeed the SIMV is currently used when weaning very preterm infants from assisted ventilation.

Aims: We present preliminary results to assess a new, non invasive, approach to evaluate compliance, when active respiratory movements persist during synchronized intermittent mandatory ventilation. **Design/Methods:** Four premature newborns (1 male, 3 female, gestational age: 27.3 (26-33) wks, birth weight: 975 (635-1940) g, postnatal age: 3 (1-9) days), hospitalized for treatment of hyaline membrane disease (HMD), were explored for the evaluation of total respiratory compliance. The technique we used is non invasive and does not need any adaptation of the usual preterm care in the NICU. The airways pressure (Paw) and pulmonary flow were recorded from the respirator Babylog 8000®, Dräger. Tidal volume (TV) was obtained by numerical integration from the pulmonary flow signal for each respiratory cycle. Since patient inspiratory effort during spontaneous and mechanical assisted respiratory cycles are considered equal, we estimated the mean tidal volume of passive cycles (TVp) as: TVp = mean TV assisted cycles - mean TV spontaneous cycles. The mechanical compliance of the respiratory system (Csr) was calculated by the relation: Csr = TVp / (max Paw - PEEP). Results are expressed as median (extremes).

Results: TVp: 4.55 (2.7-12.2) ml; max Paw: 14.6 (14.3-19.6)cmH2O; PEEP: 3(2.6-3.6) cmH2O; Csr: 0.4 (0.33-0.57)ml/cmH2O/kg.



Conclusions: These preliminary results agree with expected data for premature newborns with HMD. This new and non invasive technique could be used for further studies to evaluate the compliance during synchronized intermittent mandatory ventilation.

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PRENATAL INFLAMMATION AND FETAL RESPONSE IN PREMATURE AND TERM INFANTS

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Background: Histological findings of chorioamnionitis and funisitis are frequent in both premature and term deliveries. Aims: (i) to study the difference between the degree and the localization of inflammation in placenta and umbilical cord, and (ii) the difference in cytokine response in premature and mature newborns.

Methods: In 94 premature newborns born between 23+0 - 30+6 (median 28+6) g.a. and 20 term newborns 39+1 - 41+6 (median 40+3) g.a., histological examinations of placenta and umbilical cord were performed with special regard to the localization and the degree of inflammatory infiltration (criteria by Salafia - modified). Umbilical serum levels of IL-1beta, IL-6 and IL-8 were measured (ELISA) and compared between groups.

Results: Histological signs of prenatal inflammation occurred more frequently in premature than in mature newborns: chorioamnionitis 70 vs 55% (p<0.05) and funisitis 44 vs 25% (p<0.05). The difference was even more pronounced in severe chorioamnionitis 57 vs 30% (p<0.01) and severe funisitis 26 vs 0% (p<0.01). Umbilical serum IL-1beta, IL-6 and IL-8 levels were higher in premature newborns (all p<0.05).

Discussion: Higher occurrence of chorioamnionitis and funisitis in premature infants and particularly higher occurrence of their more advanced stages signals higher risk of fetal inflammation in this population. This finding is further supported by higher levels of umbilical serum proinflammatory cytokines. Fetal inflammatory response interferes with adaptation and development of premature infants. Speculation: Histological semi-quantitative scoring of inflammation in placenta and umbilical cord with special regard to more advanced stages may be useful in evaluation of the perinatal treatment strategies like ATB use, timing of delivery etc. Study was supported by the grant of IGA MZ ER No. NE 6435.

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ESTIMATE SCORES OF IQ IN ADOLESCENTS WITH LOW BIRTHWEIGHT. THE CHOICE OF SHORTFORMS MAKE A DIFFERENCE

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Background/Aim: In adolescents with low birth weight, specific deficits in cognitive abilities have been reported. For practical purposes it is customary to estimate IQ by using short forms in larger studies. If few tests are used and some of them tap into specific difficulties in these adolescents, IQ estimates may be artificially low compared to controls. The aim of this study was to compare the estimated IQ of two short forms of the WISC-III in adolescents with low birth weight and controls. **Design/methods:** At age 14, two groups of adolescents with low birth weight (54 premature with birth weight <1500 g (VLBW), and 60 small for gestational age born at term (SGA)) were compared to 83 controls with normal birth weight at term. IQ was estimated using four subtests from WISC-III: arithmetic and vocabulary from the verbal subscales and picture arrangement and block design from the performance scales (Kaufman 1976) or by using two subtests: vocabulary and block design (Sattler 1992). Except for vocabulary, these subtests are associated with perceptual and spatial abilities.

Results: Both ways of estimating IQ resulted in significantly lower scores in the VLBW group than the SGA and the control group (p<0.001). The score on vocabulary was similar in all groups, the VLBW group scored lower on the three other subtests than the two other groups. Estimating IQ by four subtests resulted in a reduction of 8.2 points in the VLBW group, 3.7 in the SGA group and 2.5 in the controls.

	VLBW	SGA	Control group
Two subtests	86.4(19.9)	94.1(14.6)	97.1(14.3)
Four subtests	78.2(22.0)	90.4(17.7)	94.6(16.5)

Conclusion: Estimates of IQ in VLBW adolescents are influenced by the choice of short forms of WISC-III. Using several subtests that load on perceptual and spatial abilities may indicate a level of intellectual functioning in these adolescents that may be too low. Caution is therefore warranted when using short forms of IQ tests.