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DOES HUMAN MILK ACCELERATE EARLY ENTERAL FEEDING ADVANCEMENT IN VLBW INFANTS?

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Background: Human milk (HM) is believed to improve feeding tolerance in very low birth weight (VLBW) infants compared to formula feeding thereby accelerating early enteral feeding advancement. **Objective:** The present secondary analysis of a controlled randomized trial was to investigated whether human milk accelerates early enteral feeding advancement compared to formula feeding.

Methods: In 129 VLBW infants non-pasteurized HM was fed whenever available and fortification was started after 100ml/kg/day had been achieved. Early enteral feeding advancement was performed following a strict feeding protocol. If HM was not available, hydrolyzed protein or standard protein preterm formula were fed. The hypothesis was tested (Mann-Whitney test) that infants who received ≥10% of HM achieved full feeds faster than infants for whom HM was not available (<10%). Multiple regression backward selection analysis was performed to analyze the effect of the available HM volume measured as percentage of total feeding volume on the time to achieve full feeds. Other variables whose effects were analyzed in the model were birth weight, gestational age, age at starting milk feeds, type of formula, prenatal Betametason treatment, umbilical artery ph, and Apgar scores. Data is shown as median (p25-p75).

Results: 42 Infants received ≥10% of HM (75%(37–96%)) and 87 infants <10% HM (0% (0–0%)). Infants with ≥10%HM infants were significantly more mature (gestational age 29.4 (27.1–31.0) vs. 27.0 (25.2–29.3) weeks; p=0.012), but there was no significant difference with regard to birth weight (980 (740–1280)g vs. 870 (695–1190)g; p=0.40), first day of milk feeding (day 3 (2–4) vs. 3 (2–5); p=0.96), and the age at full feeds (day 14 (12–21) vs. 15 (12–24); p=0.37) . Multiple linear regression analysis confirmed this result since HM (p=0.82) was not associated with the time to achieve full feeds, in opposition to birth weight (p<0.001), type of formula (p<0.011), age at starting milk feds (p<0.001) and prenatal Betametason treatment (p=0.03).

Conclusion: The data did not support the hypothesis that human milk increases early enteral feeding tolerance. Randomized trials in VLBW infants are required to analyze hypothesized beneficial effects of properly fortified human milk.

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NEW AND IMPROVED POPULATION-BASED GERMAN REFERENCE DATA FOR PRETERM INFANTS GROWTH

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Background: Preterm infants growth is best described in form of standard deviation scores (SD scores or z–scores). Effects of nutritional interventions are assessed easily with z–scores. The z–score of a measurement such as weight indicates how far and in what direction that measurement deviates from its distribution's mean, expressed in units of its standard deviation. However, there are no pertinent German population based reference curves available enabling clinicians to easily convert preterm infants growth status into z–scores. **Objective:** Aim of the present study was to provide a new growth reference for preterm infants as z–scores.

Methods: Normalized growth standards were constructed by the LMS method (Cole TJ. J Clin Nutr 1990;44(1):45–60) from a cohort of 1.8 million German singleton newborns born from 1995 to 1997. Data were divided into distinct gestational age groups according to completed weeks of gestation. The power (L), mean (M) and coefficient of variation (S) were calculated for each week of gestation for the variables birth weight, length, head circumference, and weight for length. Finally smoothed L, M and S curves were computed by standard mathematical procedures.

Results: From 20 to 43 weeks of gestation the L, M and S values for the assessed variables will be presented together with corresponding smoothed curves. If A is the measured anthropometry for the preterm infant, then the z-score is calculated as: $z=((A/M)^{L}-1)/(LS)$. For example for the weight of boys at 25 weeks of postmenstrual age M=790g, L=0.23, and S=0.20. An actual body weight of 500g would correspond to a z–score of –2.2. The full set of data does not fit in this abstract and will be presented at the convention.

Conclusion: The presented data help to assess the growth of preterm infants. **Disclosure:** The biometrical evaluation was supported by Milupa, Germany.

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EFFECT OF *BIFIDOBACTERIUM LACTIS* ON THE INCIDENCE OF NOSOCOMIAL INFECTIONS IN PRETERM INFANTS

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Background: Nosocomial infections are frequent in preterm infants. **Objective:** To investigate whether *Bifidobacterium lactis* (*B. lactis*; C. Hansen, Danmark) reduces the incidence of nosocomial infections.

Methods: In a double-blind placebo controlled trial 128 preterm infants less than 30 weeks of gestation were stratified according to their gestational age (23–26 and 27–29 weeks) and randomly assigned to have their milk feedings (human milk or preterm formula) supplemented with *B. lactis* (6 x 10^9 cfu/kg/day) or placebo for the first six weeks of life. Early enteral nutrition following a standardized feeding protocol was performed. Primary outcome was the incidence density of nosocomial infections from day 7 after initiation of milk feedings until the 42nd day of life (number of nosocomial infections/total number of patient days). In case of suspected nosocomial infection both aerob and anaerob blood cultures were performed. Nosocomial infections were defined as periods of elevated CRP (C-reactive protein; >10 mg/dl). The sample size was calculated to proof a reduction in the incidence density of nosocomial infections of at least 25% (á=0.05, â=0.80). An adaptive interim analysis was scheduled to be performed after at least 50 infants in each group who were treated according to protocol. Data are presented as median and range where appropriate.

Results according to the intention to treat	*B. lactis*	Placebo
N	65	63
Birth weight (g)	830 (410–1530)	810 (370–1560)
Gestational age (weeks)	26.3(23–29.7)	26.4(23–29.7)
Individual study period (days)	31 (8–35)	31 (2–35)
Total number of nosocomial infections	41	28
Incidence density of nosocomial infections (p=0.09)	0.0217	0.0156

Results: The trial was stopped at the interim analysis for futility. There was no significant difference between the two groups with regard to clinical characteristics, patient days, total number of observed nosocomial infections and the incidence density of nosocomial infections (p = 0.9, Chi^2–test). *B. lactis* has not been detected in any of the blood cultures.

Conclusion: In the setting of the study treatment with *B. lactis* at a dosage of 6 x 10^9 cfu/kg/day appeared to be safe, however, there was no reduction in the incidence density of nosocomial infections.

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C-REACTIVE PROTEIN IN THE TRACHEOBRONCHIAL SECRETION OF A PRETERM INFANT

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Background: C reactive protein (CRP) is a major acute-phase plasma protein displaying rapid and pronounced rise of its serum concentration in response to infection or tissue injury. CRP is usually synthesized by hepatocytes and induced by cytokines. However, extrahepatic synthesis has been recently documented. In particular, CRP has been detected in adult human respiratory tract and it has been shown that its gene is expressed in epithelial cells.

Methods: Tracheobronchial secretions (TBS) were collected longitudinally in an infant delivered at 24+3 weeks of gestation who developed a middle right lobe pneumonia 5 weeks after delivery. Cultures of TBS were positive for Staphylococcus aureus. Antibiotic therapy with 100 mg/kg/day of amoxicillin/clavulanic acid and 7.5 mg/kg/day of amikacin was administered intravenously for 10 and 5 days, respectively. Nephelometry was used for the determination of CRP in neonatal serum, while a commercially available ELISA test was utilized for the measurement of both blood and TBS CRP concentrations. The sensitivity of the CRP assay was 0.39 ng/mL (Inter-assay coefficient of variation: 6.5%). To provide evidence that CRP is produced locally in the tracheobronchial system a ratio between CRP and IgG both in serum and in the TBS were calculated. The reason for this is twofold: first, IgG and CRP have a similar molecular size, and second, it is known that IgG are present in extremely low concentrations on the mucosal surface. To allow comparison, CRP and IgG concentrations in TBS were normalized to the total protein content.

Results: CRP was present in TBS. A marked increase of CRP in serum and in the TBS was noted during the course of pneumonia with a sharp decrease after antibiotic therapy. The highest CRP concentration in serum (160 mg/L) and TBS (345.9 ng/ml) was found 2 and 3 days after the diagnosis was made, respectively. The CRP – IgG ratio was 21340 times higher in the TBS than in serum. Serum CRP and TBS CRP decrease was observed 1 and 2 days after the initiation of antibiotic therapy, respectively.

Conclusion: CRP is detectable in the TBS of preterm infants during pneumonia. It can be speculated that CRP is not only involved in a systemic response against pathogens but also acts as a mediator in the local defense. It remains to be explored whether TBS CRP measurement is of value in clinical practice.

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NON-INVASIVE CEREBRAL PERFUSION MEASUREMENTS IN TERM NEONATES AND PREMATURE INFANTS USING ARTERIAL SPIN LABELLING

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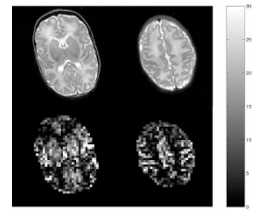
Background: Sick premature and term neonates have a vulnerable cerebral circulation. Studies of the cerebral circulation have been performed previously using either invasive methods, or non-invasive approaches that have not proven satisfactory. However, a non-invasive MR-method for measuring brain perfusion has recently been developed. MR Arterial spin-labelling (ASL) is an MR technique that enables accurate maps of regional cerebral perfusion to be acquired in a few minutes. The purpose of this study was to investigate the feasibility of ASL as a method for measuring cerebral perfusion in healthy premature infants at term equivalent age and in term neonates.

Methods: 20 infants were enrolled. Nine infants were born prematurely (group 1), median GA= 31 w, neonatal period uneventful. 11 infants were healthy term neonates (group 2). Both groups were MR scanned at term age. The local ethics committee accepted the study and informed parental consent was obtained. For the MR examination infants were unsedated, sleeping naturally after a feed. Silicone ear cups were used for noise protection. Images were acquired on a Siemens Magnetom Trio 3T scanner using a PICORE QUIPSS II sequence. Control and tag images acquired during motion-free periods were subtracted to give perfusion-weighted ASL images. Regions of interest (ROIs) were drawn on the control images in the basal ganglia (BG), cortical grey matter (GM) and white matter (WM). Mean perfusion values were calculated for each ROI and each subject.

Results: Results are shown in Table and an example in Figure. ASL was found to be a feasible method for measuring perfusion in neonates. Motion is a substantial problem that can be solved in most cases. Acquisition time is short (6 minutes). The calculated values correspond to values acquired using other methods. Perfusion is highest in BG and lowest in the WM. We found higher perfusion values in BG and GM for premature infants at term equivalent age as compared with term neonates. These differences were highly significant (p values .001).

Conclusion: ASL is feasible for measuring perfusion in neonates. Values are reliable. Perfusion values in BG are much higher as compared with GM and especially WM. Values in WM are low. Values of perfusion in premature infants at term equivalent age are significantly higher than in term neonates. ASL, allowing serial perfusion measurements, offers the possibility of better understanding pathogenetical mechanisms underlying brain damage in high-risk neonates.



	Median	Mean	SD
BG group 1	19.4	20.2	5.4
BG group 2	12.1	11.8	2.5
WM group 1	2.7	3.8	2.9
WM group 2	2.5	1.9	2.6
GM group 1	7.5	8.8	2.7
GM group 2	4.3	3.6	2.4
WM 1/ BG1	16%	18%	8%
WM2/ BG2	17%	14%	2.7%
GM1/ BG1	44%	44%	8%
GM2/ BG2	32%	29%	24%