

September 17th, 2021 15:00 - 17:00

## PARALLEL SESSION 28 - NUTRITION 4

## ID 25. EXPLORING THE ROLE OF BREAST MILK FORTIFIER IN THE DEVE-LOPMENT OF NECROTISING ENTEROCOLITIS IN PRETERM NEONATES, A 10 YEAR RETROSPECTIVE AUDIT

Doctor Kate Jordan<sup>1</sup>, Dr Laura De Rooy<sup>1</sup>, Dr Anay Kulkarni<sup>1</sup>

<sup>1</sup>St George's Hospital, London, United Kingdom

## Background

Breast milk fortifier (BMF) helps maintain adequate nutrition in preterm infants, which is crucial for physical and neurodevelopmental outcomes. However, conflicting reports linked BMF with the development of necrotising enterocolitis (NEC). We undertook a ten-year retrospective analysis in our tertiary neonatal centre in London, United Kingdom (UK) to evaluate if BMF use in preterm infants is associated with developing NEC.

### Methods

The audit cohort included babies inborn at St George's Hospital, London, between gestational ages 23+0 and 31+6 weeks, admitted to the NNU from January 2010 – September 2020, who had been discharged or were deceased (N = 952).

Data was collected from the electronic neonatal database system (Badgernet UK). BMF use and NEC were confirmed from clinical notes and NEC was stratified by severity; those with NEC, Bell's stage II and above were included.

Statistical analysis: odds ratios and risk ratios were calculated with corresponding confidence intervals and number needed to treat (where applicable).

## Results

BMF has been increasingly used in preterm infants on our NNU from 2010 – 2020 (10.5% of the 2010 cohort vs 45.8% in 2020). Contrastingly, NEC rates have remained stable (6.3% of the 2010 - 2014 cohort, 5.8% from 2015 to 2019) (Figure 1).

Use of BMF did not increase the odds or risk of developing NEC (OR 0.62, CI 0.30 to 1.29; RR 0.64, CI 0.32 to 1.28). BMF use in preterm infants was associated with a reduced risk of developing surgical/severe NEC (RR 0.24, CI 0.06 to 0.99, P 0.05, NNT (benefit) 18.04 – 344). Furthermore, BMF did not lead to an increased risk of all-cause mortality in preterm infants across the ten year audit (RR 0.31, CI 0.15 to 0.63, P 0.001, NNT (Benefit) 7.95 – 27.42).

Extremely premature infants, born <26 weeks gestation, had less risk of developing NEC if on BMF (RR 0.36, CI 0.16 to 0.90, P 0.01, NNT (Benefit) 4.97 – 30.3).

Conclusion









BMF use in preterm infants on our NNU from 2010-2020 was not associated with an increased risk of NEC development. Further work is being undertaken to examine the possible protective effect of BMF in some patients.



Figure 1 BMF and NEC Rates: BMF rates (% of preterm admissions) have increased since 2010 (red line), contrasting with stable rates of NEC (blue) and surgical/severe NEC (green).

None declared









# ID 199. BOVINE LACTOFERRIN AND FECAL CALPROTECTIN IN PREMATURE INFANTS

## Dmytro Dobryk<sup>1</sup>, Prof Dmytro Dobryanskyy<sup>1</sup>

<sup>1</sup>Danylo Halytsky Lviv National Medical University, Lviv, Ukraine

Background. The tendency of premature infants to develop an excessive inflammation in the intestines can lead to morbidities such as necrotizing enterocolitis (NEC) or sepsis. Lactoferrin theoretically can downregulate the intestinal inflammatory status of preterm newborns. In a randomized study, we investigated the effect of enteral bovine lactoferrin (bLF) supplementation on fecal calprotectin (FC) levels in premature infants.

Methods. The study included 26 preterm neonates with a gestational age of  $\leq$  32 weeks and a birthweight of  $\leq$  1500 g. All babies were aged less than 72 hours and tolerating minimal enteral feeds. Eleven infants were receiving bLF at a dose of 100 mg/day with enteral feeds until postmenstrual age (PMA) of 36 weeks (lactoferrin group), 15 infants were receiving standard medical care (control group). Stool samples were collected twice: during the first seven days of life (before administration of bLF) and at PMA of 36 weeks. FC measurements were done with an ELISA method.

Results. The baseline characteristics of the groups were not different. The initial median (IQR) FC level was lower in the lactoferrin group, but the difference was not statistically significant (264.9 (211.0-689.4)  $\mu$ g/g vs. 413.5 (274.2-800.0)  $\mu$ g/g, respectively, p>0.05). At PMA of 36 weeks, FC concentrations increased in the lactoferrin group (p>0.05) but were not different as compared to the control group (631.1 (232.0-800.0)  $\mu$ g/g vs 274.7 (144.8-599.6)  $\mu$ g/g, respectively, p>0.05). Initial FC concentrations were higher in infants with early-onset sepsis (EOS) (rS=0.44; p<0.05) but did not correlate with the incidence of NEC or late-onset sepsis (LOS). FC levels were not significantly different in patients with NEC or LOS compared to infants without these morbidities, both initially and at PMA of 36 weeks. Supplementation with bLF did not affect the incidence of either NEC or sepsis.

Conclusions. Daily enteral intake bLF at a dose of 100 mg until PMA of 36 weeks was associated with the increase of FC levels but this effect was not statistically significant. FC levels during the first week of life do not predict the development of NEC or LOS but might be an additional tool for diagnosing EOS.

None declared









## ID 328. CIRCADIAN VARIATION IN HUMAN MILK COMPOSITION, A SYSTE-MATIC REVIEW

Merel Italianer<sup>2</sup>, PhD Eva Naninck<sup>3</sup>, <u>MD PhD Jorine Roelants<sup>1</sup></u>, Prof Gijsbertus van der Horst<sup>4</sup>, Prof Irwin Reiss<sup>1</sup>, Prof Johannes van Goudoever<sup>5</sup>, Prof Koen Joosten<sup>6</sup>, PhD Ines Chaves<sup>4</sup>, MD PhD Marijn Vermeulen<sup>1</sup> <sup>1</sup>Department of Pediatrics - Division Neonatology, Erasmus MC - Sophia Children's Hospital, Rotterdam, The Netherlands, <sup>2</sup>Faculty of Health, Medicine & Life Sciences, University Maastricht, Maastricht, The Netherlands, <sup>3</sup>Department of Pediatrics, Amsterdam UMC, University of Amsterdam, Vrije Universiteit, Emma Children's Hospital, Amsterdam, The Netherlands, <sup>4</sup>Department of Genetics, Erasmus MC University, Rotterdam, The Netherlands, <sup>5</sup>Department of Pediatrics-Amsterdam UMC - Emma Children's Hospital, Amsterdam, The Netherlands, <sup>6</sup>Department of Pediatrics, Division Pediatric Intensive Care, Erasmus MC University - Sophia Children's Hospital, Rotterdam, The Netherlands

Background: Breastfeeding is considered the most optimal mode of feeding for neonates and their mothers. Composition of human milk changes over the course of lactation and throughout the day. Circadian (24-hour) fluctuations of certain bioactive components are suggested to transfer chronobiological information from mother to infant to assist the development of the infant's biological clock. This makes human milk a unique form of 'chrono-nutrition'. This review provides an overview of circadian rhythm ofhuman milk components.

Methods: We included studies assessing the concentration of human milk components more than once in 24 hours. Study characteristics, including gestational age, lactational stage, sampling strategy, analytical method, and outcome were extracted. Methodological quality was graded using a modified Newcastle-Ottawa Scale (NOS).

Results: Eighty-three reports were included, assessing the circadian variation of 71 human milk components. Heterogeneity among studies was high and the methodological quality varied widely. Strong evidence of circadian variation in human milk was found for tryptophan, fats, triacylglycerol, cholesterol, iron, melatonin, cortisol, and cortisone. No circadian variation was found in carbohydrate and total protein content of human milk. For other human milk components, the evidence was inconclusive or even contradictory due to limitations in experimental design.

Conclusion: The accumulated evidence indicates that several essential human milk components systematically vary over the day, thereby potentially playing an important role in development of the infant's biological clock, and thereby on growth and health.

None declared.









## ID 512. Preterm birth affects skeletal development in pigs

Mr Frank C Ko<sup>1</sup>, Ms Meghan M Moran<sup>1</sup>, Mr A Adra<sup>1</sup>, <u>Mr Martin Bo Rasmussen<sup>2</sup></u>, Mr Thomas Thymann<sup>2</sup>, Mr Per Torp Sangild<sup>2</sup>, Mr Dale Rick Sumner<sup>1</sup>

<sup>1</sup>Department of Cell & Molecular Medicine, Rush University Medical Center, Chicago, USA, <sup>2</sup>University Of Copenhagen, Department of Veterinary and Animal Sciences, Section of Comparative Pediatrics and Nutrition, Copenhagen, Denmark

### Background

Premature birth interrupts the critical period of bone development in late gestation. Consequently, metabolic bone disease of prematurity (MBDP) is common for preterm infants and may be associated with deficient skeletal development. A major barrier to understanding the skeletal consequences of prematurity and possible interventions is the lack of suitable animal models. We hypothesized that premature birth in piglets would be associated with skeletal growth deficiencies throughout the postnatal period.

### Methods

Premature pigs (cesarean delivery at 90% gestation) were reared for 1, 5 or 19 days (n=6-18, heated incubators and parenteral nutrition before transition to milk feeding) and compared with age-matched groups term pigs (n=7) reared by their mother (vaginal delivery at 117 d). We scanned the femurs by micro-computed tomography at 48.4  $\mu$ m voxel size to determine the distal femoral metaphyseal integral volumetric bone mineral density (vBMD) and midshaft cortical bone geometry. Statistical analyses examined the effects of birth status (preterm, term), age (1, 5 or 19 days) and their interaction, and adjusting for body weight and bone length. We also examined how the bone outcomes scaled with bone length.

#### Results

There were significant interactions between birth status and time for weight, (p<0.05), bone length (p<0.001), cortical area (p<0.05), total area (p<0.001) and medullary area (p<0.001). The increases in cortical and total area from day 1-19 were greater in full-term versus preterm animals (Figure). Integral vBMD was not affected by birth status. Cortical diameter and area, and total area, increased more rapidly in full-term pigs than in preterm pigs, as a function of bone length (p<0.01).

#### Conclusion

The femurs in preterm pigs were slender compared with those in term pigs because of suppressed periosteal expansion. This suggests that preterm long bones are poorly adapted to their mechanical environment. The lack of difference in integral vBMD as opposed to the differences in cross-sectional geometry suggests that bone diameter and length can be used to assess the skeletal consequences of prematurity if measured over time. The pig appears to be a useful model for studying the early skeletal consequences of premature birth.









Figure 1. (A-E) Cross-sectional geometry (scalebar = 5mm). (F) Histology showing formation at the periosteal surface and endocortical surface resorption (scalebar =  $100 \ \mu$ m). (G) Model of cortical expansion. Funding: Supported by University of Copenhagen, Denmark & Takeda, Cambridge, MA, USA, Rush University Cohn Research Fellowship, NIH 1T32AR073157



