Pediatric RESEARCH

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ABSTRACTS COLLECTION

4th Congress of Joint European Neonatal Societies: Nutrition

Pediatric Research (2021) 90:27–34; https://doi.org/10.1038/s41390-021-01762-6

Date: 14-18 September 2021

Location: Virtual Meeting

Sponsorship: Publication of this supplement was sponsored by MCA Events on behalf of the European Society of Paediatric Radiology (ESPR), Union of European Neonatal and Perinatal Societies (UENPS), European Foundation for the Care of Newborn Infants (EFCNI).

All content was reviewed and selected by the Scientific Committee and selected abstract reviewers, which held full responsibility for the abstract selections.

*Presenting author names have asterisks in the contributor lists.

ID 25. Exploring the role of breast milk fortifier in the development of necrotising enterocolitis in preterm neonates, a 10 year retrospective audit

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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 10-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 were 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.

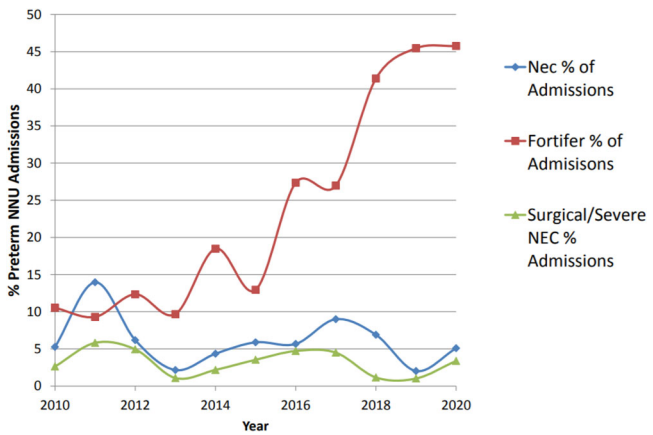
Statistical analysis: Odds ratios and risk ratios were calculated with corresponding confidence intervals and number needed to treat (where applicable).

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) (Fig. 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.



(ID 25) - Fig. 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 67. Prolonged oropharyngeal colostrum administration to very low birth weight infants

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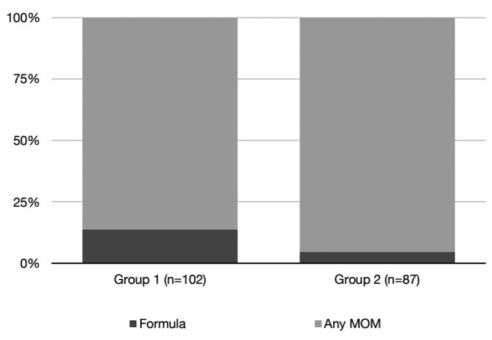
Background: Oropharyngeal colostrum (OPC) may be safely applied as immunological modulation therapy for very low birth weight (VLBW) infants. Most studies have described the safety of short-term application (5–7 days), with no differences in rates of necrotizing enterocolitis (NEC), infection, death or type of feeding. This study aims to investigate if the implementation of prolonged oral colostrum (POPC) administration protocol (from birth to oral transition) is associated with the reduction of morbidities or type of feeding at NICU discharge in VLBW infants.

Methods: We carried out a quasi-experimental study, with an intervention group using prolonged oropharyngeal colostrum (POPC) administration and historical control before the introduction of the practice. The intervention group received OPC as soon as available and continued until achieving oral transition of feedings. All VLBW infants admitted to the NICU and who had no contra-indications to human milk were included. The main outcome was survival without morbidities, including severe intraventricular haemorrhage (IVH), chronic lung disease at 33 weeks (CLD), necrotizing enterocolitis (NEC), any late infection or cystic periventricular leukomalacia (PVL). The secondary outcome was the administration of any volume of mother's own milk (MOM) at discharge.

Results: In total, 381 VLBW infants were included. Group 1 (control) had 200 patients and Group 2 (treatment) had 181 patients. Patients in the control group had lower birth weight (1081 ± 314 vs 1165 ± 280 g, p 0.01). There were no differences regarding gestational age, the number of multiples, antenatal steroids administration, and the number of extremely preterm (EPT) (<30 weeks) infants. In total, 348 (92.8%) infants survived hospitalization. At discharge, 324 (93.8%) were being breastfed at least once a day. POPC administration was associated with an increased chance of receiving any MOM volume at discharge in EPT infants (RR = 2.98, CI 95% 1.02–8.73; p = 0.04) (Fig.1). There were no differences in surviving without morbidities. There were no complications associated with the practice.

Conclusion: Prolonged oral colostrum administration is safe, feasible, and increased the frequency of receiving any volume of MOM at hospital discharge. Extreme preterm infants might be more benefitted by this practice.



(ID 67) - Any volume of MOM at discharge in <30 weeks preterm infants (n = 189)

None declared.

ID 167. Fortification of human milk with bovine colostrum in very preterm infants

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Background: Very preterm infants have high nutritional needs to support optimal growth and development. Accordingly, nutrient fortifiers are often added to mothers' own milk or donor human milk for such infants. However, there are concerns that such fortifiers, similar to infant formula products, may predispose to feeding intolerance, necrotizing enterocolitis (NEC) and late-onset sepsis (LOS). We hypothesized that intact bovine colostrum, rich in proteins, bioactive components and immunoglobulins, may be a good alternative to conventional fortifiers to stimulate growth without increasing NEC and LOS incidence.

Method: In a multicentre, open-label randomized pilot trial (NCT03537365), human milk for very preterm infants (26–31 weeks of gestation) was fortified with powdered bovine colostrum (BC, Biofiber Damino, Denmark, n = 115) or a powdered conventional fortifier (CF, PreNAN FM85, Nestlé, Switzerland, n = 117) when enteral feedings reached 100–140 mL/kg/day, and until 35 weeks post-menstrual age. Up to 1.4 g protein per 100 mL milk was added (e.g. 2.8 g BC, 4.0 g CF). Weight and head circumference (HC) were recorded at birth, weekly during the intervention, and at discharge. Plasma amino acids (AA) were analysed two weeks after start of fortification.

Results: Weight and gestational age at birth were similar between groups (1167 ± 327 g and 28.5±1.4 weeks, pooled means ± SD). *Z*-scores for weight and HC from birth until discharge did not differ between groups ($p = 0.16$ and $p = 0.72$, respectively), neither did delta z-scores for weight and HC in the same time period ($p = 0.87$ and $p = 0.22$, respectively). BC intake increased the mean levels of several AAs (Ser, Gly, Asn, Gln, His, Ala, Pro, Arg, Phe, Orn, Gln, +10–20%, all $p < 0.05$), with more pronounced increments of a few AAs (Val, Tyr, +40%, both $p < 0.001$). However, all AA values remained within reference levels. Fortification with BC did not affect the incidences of NEC (BC: 3/115 vs. CF: 5/117, $p = 0.49$) or LOS (BC: 24/115 vs. CF: 16/117, $p = 0.17$) (both unadjusted values).

Conclusion: Very preterm infants given human milk fortified with intact bovine colostrum showed similar short-term growth and moderate increases in AA levels, relative to infants given a conventional fortifier. Larger trials are required to verify effects on NEC, LOS and other health outcomes.

University of Copenhagen has filed a patent on BC for infants (PCT/DK2013/050184) together with Biofiber Damino. PTS has declined share of revenue and was not participating in NICU clinical work.

ID 188. Hyperglycemia and growth rate in very low birth weight infants—from birth until postmenstrual age 36 weeks

Johanna Karlsson[1], Johannes van Den Berg[1], Yonas Berhane[1], Elisabeth Stoltz Sjöström[1], Estelle Naumberg[1], Magnus Domellöf[1], Itay Zamir[1]*

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Background: Hyperglycemia is common in very low birth weight infants (VLBW, <1500 g) during the admission period at the neonatal intensive care unit. This might reflect underlying increased resistance for insulin, an important regulatory hormone that affects infant growth. Growth failure in early infancy is associated with neurodevelopmental abnormalities. The objective of this study was to investigate the associations between hyperglycemia and growth rate from birth until postmenstrual age (PMA) 36 weeks in VLBW infants.

Methods: The Very low birth weight infants—glucose and hormonal profiles over time (LIGHT) study is a prospective observational study that included 50 VLBW infants born during 2016–2019 and treated at Umeå University Hospital. Detailed data regarding glucose concentrations and growth parameters (weight, length and head circumference) were registered prospectively and Z-scores were calculated. A growth restriction phase was defined from birth until the day nadir weight z-score was reached and the entire period was defined from birth to PMA 36 weeks.

Results: Considering growth outcomes during growth restriction phase, for each day with hyperglycemia >10 mmol/L during this period there was a decrease of 0.14 (95% CI 0.06–0.22, $P = 0.001$) and 0.05 (95% CI 0.01–0.10, $P = 0.024$) in length and head circumference Z-scores, respectively. Considering growth during the entire study period, for each day with hyperglycemia >10 mmol/L during growth restriction phase there was a decrease of 0.10 (95% CI 0.03–0.18, $P = 0.005$) and 0.20 (95% CI 0.10–0.29, $P < 0.001$) in weight and length Z-scores, respectively. A decrease of head circumference Z-scores by 0.05 (95% CI 0.01–0.10, $P = 0.027$) during the entire study period was observed for each day with hyperglycemia >8 mmol/L during growth restriction phase.

Conclusion: Hyperglycemia during the first weeks of life is associated with reduced weight, length and head circumference growth rate during the admission period in VLBW infants. Such changes might influence growth and neurodevelopment later in life. Further studies are needed to elucidate possible mechanisms and treatment modalities for this common and modifiable clinical condition.

None declared.

ID 196. Ultra-high temperature (UHT) treatment and prolonged storage of liquid infant formula induces protein modifications, gut dysfunction and inflammation in preterm pigs

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Background: Ultra-high temperature (UHT)-treated infant formula (IF) is increasingly being used for hospitalized infants when human milk is unavailable. UHT treatment eliminates pathogens and extends shelf life, but heating and storage may negatively affect the quality by reducing bioactivity and increasing the formation of Maillard reaction products (MRPs). We hypothesized that stored UHT-treated IF negatively affect gut health in sensitive newborns.

Methods: Using preterm pigs as a model for sensitive newborn infants, we fed liquid IFs subjected to indirect UHT (UHT), UHT with storage at 40 °C for 60 days (SUHT) or just pasteurized (PAST). Diet bioactivity and MRP levels were determined together with markers of gut maturation and health.

Results: Relative to PAST, the UHT-IFs contained reduced levels of bioactive proteins (IgG, lactoferrin). Storage increased MRP levels (up to 13-fold) and non-reducible protein aggregates (SUHT vs. UHT). Furthermore, SUHT had lower antimicrobial capacity (versus *E. faecalis*, *S. epidermidis*) than PAST. Following 5 days of feeding, pigs fed SUHT had more diarrhea than pigs fed PAST and more signs of intestinal inflammation (necrotizing enterocolitis) than PAST and UHT pigs. UHT and particularly SUHT pigs showed lower intestinal villus heights and higher crypt depths and an increase in MPO-positive cells (monocytes and neutrophils), relative to PAST. Additionally, digestive enzyme activities (lactase, aminopeptidase N) were reduced in SUHT vs. PAST pigs, with intermediate values in pigs fed UHT. In SUHT pigs, this was accompanied by gut accumulation of MRPs (furosine and advanced glycation endproducts (AGEs), including N-ε-carboxymethyllysine (CML)) as well as the protein-cross-links lysinoalanine (LAL) and lanthionine (LAN) and RAGE-mediated inflammatory responses involved upregulation of genes involved in acute inflammatory responses and cell turnover (e.g. C3, TNFA, TNFAIP3, IL6, MCP1, CD62L, CASP3, PCNA, OLFM4, TGFB1).

Conclusion: Indirect UHT treatment followed by prolonged storage of IF reduced protein bioactivity and increased MRP and protein cross-link accumulation. This was associated with impaired gut maturation and function in preterm pigs in the first days of life. UHT-treatment and storage may negatively affect the quality of liquid IFs and may thereby negatively affect organ development in newborn infants, particularly those that are very diet-sensitive or immature.

This work was partly financed by Arla Foods Ingredients, Viby J, Denmark.

ID 199. Bovine lactoferrin and fecal calprotectin in premature infants

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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 ≤ 32 weeks and a birthweight of ≤1500 g. All babies were aged less than 72 h 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 7 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) vs. 413.5 (274.2–800.0) µg/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) vs 274.7 (144.8-599.6) µg/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 200. Both hyperglycemia and hypoglycemia are common nearing term age in very low birth weight infants - results: from the light study

Itay Zamir[1], Elisabeth Stoltz Sjöström[1], Johannes van Den Berg[1], Estelle Naumburg[1], Yonas Berhane[1], Magnus Domellöf[1]*

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Background: Hyperglycemia as well as hypoglycemia are common during the first weeks of life in very low birth weight infants (VLBW; <1500 g). These disturbances have been associated with adverse outcomes such as mortality and neurodevelopmental disabilities. However, glucose concentrations are seldom controlled for at later stages of the admission period, nearing term age. This study aimed to assess the prevalence of and risk factors for glucose disturbances in VLBW infants at PMA 36 weeks.

Methods: The Very Low birth weight infants - glucose and hormonal profiles over time (LIGHT) study is a prospective observational cohort study that included 50 VLBW infants born during 2016–2019 and admitted to the tertiary neonatal intensive care unit at Umeå University hospital, Sweden. Perinatal and glucose data were registered prospectively during the admission period. Continuous glucose monitoring (CGM) was performed in 35 (70%) of the infants during a period of 48 h at PMA 36 weeks. Protracted hyperglycemia and hypoglycemia episodes in the CGM registration were defined as glucose values >8 and <2.6 mmol/L, respectively, lasting for at least 30 min.

Results: Analyzing a total of 19907 glucose measurements registered at PMA 36 weeks, 54% of the infants experienced protracted hyperglycemia, 29% experienced protracted hypoglycemia, and 37% experienced no protracted episodes of glucose disturbances. Infants who had protracted hyperglycemia at PMA 36 weeks were more likely to have had amnionitis and prior hyperglycemia and hypoglycemia during the admission period. Longer hyperglycemia episodes were registered at PMA 36 weeks in male infants compared to females. Lower Apgar scores at 10 min and prior hyperglycemia during the admission period were significantly associated with more time spent in hypoglycemia at PMA 36 weeks.

Conclusion: Glucose disturbances were registered in nearly two thirds of VLBW infants nearing term age. Low apgar scores and hyperglycemia during the admission period are risk factors for hypoglycemia nearing term age. Male sex, amnionitis and glucose disturbances during the admission period are risk factors for hyperglycemia nearing term age. Screening for glucose concentrations during the entire admission period might be advised even in clinically stable infants.

None declared.

ID 205. Insulin resistance and hyperglycemia in very low birth weight infants—results: from the light study

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[1]Umeå University, Umeå, Sweden

Background: Hyperglycemia is a common condition in very low birth weight infants (VLBW; <1500 g) which has been associated with adverse outcomes such as mortality and neurodevelopmental disabilities. Both insulin resistance and relative insulin deficiency were suggested as possible mechanisms but description of relevant metabolic markers of insulin resistance in preterm infants during the admission period is scarce. This study aimed to analyze blood markers for insulin resistance in VLBW infants at 7 days of age and at postmenstrual age (PMA) 36 weeks.

Methods: The very low birth weight infants - glucose and hormonal profiles over time (LIGHT) study is a prospective observational cohort study that included 50 VLBW infants born during 2016–2019 and admitted to the tertiary neonatal intensive care unit at Umeå University hospital, Sweden. Perinatal and glucose data were registered prospectively during the admission period. Blood samples were obtained at 7 days of age and at PMA 36 weeks, mostly just before feedings. Samples were analyzed for plasma C-peptide, insulin, proinsulin and leptin levels. Hyperglycemia was defined as a single glucose value >8 mmol/L at any time during the admission period.

Results: Lower gestational age was associated with higher plasma C-peptide levels at 7 days of age, and with higher plasma C-peptide, insulin and leptin levels at PMA 36 weeks (all $P < 0.05$). Extremely low birth weight (ELBW; <1000 g) was associated with higher plasma proinsulin levels at 7 days of age compared to infants with birth weight 1000–1500 g ($P < 0.01$). At PMA 36 weeks, ELBW was associated with higher plasma C-peptide, insulin, proinsulin and leptin levels (all $P < 0.05$). Hyperglycemic infants had higher plasma proinsulin levels at 7 days of age, and higher plasma C-peptide, insulin, proinsulin and leptin levels at PMA 36 weeks ($P < 0.005$). Proinsulin/insulin ratio did not differ between hyperglycemic and normoglycemic infants.

Conclusion: Lower gestational age and birth weight are associated with increased insulin resistance in preterm infants nearing term age. Hyperglycemia in VLBW infants is associated with increased insulin resistance and intact insulin secretion. Further studies are needed to explore possible treatment modalities.

None declared.

ID 225. A novel high temperature short time pasteurisation treatment for human milk

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Background: Holder pasteurisation (HoP) of human milk (HM) allows a 5-log10-reduction in bacterial content but also destroys heat-labile bioactive components, hence the need of alternative treatment methods. We redesigned a high-temperature short-time (HTST) pasteurisation device and compared it to HoP in its ability to inactivate artificially inoculated bacteria.

Methods: HoP pasteurised (62.5 ± 0.5 °C/30 min) HM aliquots were inoculated with 10^5 colony forming units (CFU)/mL of *E. faecalis* (ATCC29212) and two isolates each of *L. monocytogenes* (218, 15) and *C. sakazakii* (RV5-I-92, RV00078). Inoculated aliquots underwent HoP (S90, Sterifeed, UK) or HTST at 62 or 81 °C for 5 s in a modified bulk device that was originally designed for Cytomegalovirus inactivation (Virex, Lauf, Germany) by rapidly heating a thin milk layer within a rotating flask with hot air. We inoculated Columbia blood agar with 100 µl of each treated and various control samples and determined CFU/mL by MALDI-TOF-spectroscopy, after culturing the samples for 24 and 48 h, lower limit of detection was <10 CFU/mL. Bacterial counts were analysed by using a one-sample T-test (GraphPadPrism), $p < 0.05$ was considered significant.

Results: Post-incubation colony counts were 5.8×10^4 for *E. faecalis*; 1.4×10^5 for *C. sakazakii* RV00078, 2.1×10^5 for *C. sakazakii* RV5-I-92; 1.8×10^5 for *L. monocytogenes* 218 and 1.1×10^5 for *L. monocytogenes* 15. HoP yielded no growth (>4.76 log10-reduction) for all cultures. HTST at 62 °C/5 s achieved a reduction of max. 1.93 log10 (HTST 62 °C vs. HOP, $p = 0.0076$). HTST at 81 °C/5 s allowed a 3.32–5.32 log10-reduction of all inoculated bacteria. There was no significant difference in bacterial count reduction between HoP and HTST at 81 °C s for all tested strains ($p = 0.29$). Only *E. faecalis* could be cultured after 81 °C/5 s (log10-reduction 3.32).

Conclusion: We previously demonstrated the retention of bioactive HM components after HTST at 62 °C/5 s but were unable to achieve a 5-log10-reduction of bacteria. This study aimed at defining an appropriate HTST time–temperature curve to obtain reliable bacterial count reductions. HTST at 81 °C/5 s is a promising alternative to HoP in its ability to destroy bacteria across a range of heat tolerance spectra. The retention of bioactive HM components after HTST is currently being investigated.

None declared.

ID 226. Improved preservation of human milk proteins by automated water bath pasteurisation compared to dry tempering

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Background: Pasteurisation of human milk at 62.5 ± 0.5 °C for 30 min (Holder pasteurisation, HoP) leads to an exposure-dependent reduction of protective and nutritive human milk (HM) proteins. Recently, aluminium block thermostats (dry tempering, DT) were introduced for HoP replacing traditional water baths (WB). However, since heating profiles differ between DT and WB pasteurisation and prolong the pasteurisation process, we hypothesised that DT.

Results: in even lower protein retention rates compared to WB pasteurisation.

Methods: HM of 15 donors was aliquoted to 60 mL samples each. Samples were either left untreated or Holder pasteurised using a WB (S90, Sterifeed, UK) or a DT device (clinitherm pasteur, Barkey, Germany). All samples were then appropriately prepared using repeated steps of centrifugation and filtration. We determined concentrations of secretory immunoglobulin A (sIgA) and lactoferrin in the resulting milk whey (SimpleStep ELISA-Kit, Abcam, UK). Samples were handled and tests were performed in a thermo-controlled and digitally recorded environment. All pasteurisation procedures were carried out in triplicates, protein determinations in duplicates resulting in 6 × 15 (sIgA) and 6 × 8 (lactoferrin) values per protein and procedure for statistical evaluation (ANOVA and T- or rank-sum test where appropriate (GraphPadPrism V8)).

Results: in the untreated human milk Mean (SD) concentration of sIGA was 0.29 (0.18) g/L (100%) and mean (SD) concentration of lactoferrin was 21.1 (7.21) g/L (100%). Mean (SD) sIgA retention rates after WB pasteurisation were 73.2 ± 1% and mean (SD) sIgA retention rates after DT pasteurisation were 57 ± 1% ($p = 0.002$). Mean (SD) lactoferrin retention rates after WB pasteurisation were 45.2 ± 2% and mean (SD) lactoferrin retention rates after DT were 23.4 ± 8% ($p = 0.06$).

Conclusion: WB pasteurisation displays an increased protein preservation of IgA and lactoferrin compared to DT pasteurisation. We attribute this to the shortened heating phase due to more efficient heat conduction in WB compared to DT. For hygienic aspects and reasons of practicability, dry temperation devices are sometimes preferred over water containing devices. However, our data show that DT devices may be inferior to WB pasteurisation in terms of HM quality. We are currently investigating the retention of further HM proteins.

None declared.

ID 241. Questioning the adequacy of standardized vitamin D supplementation protocol in very low birth weight infants: a prospective cohort study

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Background: Preterm infants are at increased risk for vitamin D insufficiency or deficiency. The vitamin D status of preterm infants at birth depends entirely on the vitamin D status of their mothers. Although intensity of the researches on vitamin D accelerated in the last decade, the amount of vitamin D intake required to maintain vitamin D status in preterm infants remains still controversial. We aimed to assess the adequacy of standardized vitamin D supplementation protocol in very low birth weight (VLBW) infants. In addition, to determine vitamin D status of mother/infant couples and to investigate the associations between vitamin D status at birth and morbidities of the infants.

Methods: In this single-center, prospective cohort study blood samples were collected from 55 mothers just before delivery and from their infants at birth and on the 30th day of life (DOL) for 25-hydroxy vitamin D (25OHD) measurements. According to standardized supplementation protocol vitamin D was initiated in dose of 160 IU/kg by parenteral nutrition on the first DOL and oral vitamin D supplementation (400 IU/day) was administered when enteral feedings reached 50% of the total intake or on the 15th DOL, whichever was earlier.

Results: The median 25OHD levels of the infants were 16.12 (9.14–20.50) in cord blood and 36.32 (31.10–44.44) in venous blood on the 30th DOL ($p < 0.01$). In 98% of the VLBW infants 25OHD reached sufficient levels on the 30th DOL. None of the mothers had sufficient vitamin D levels (25OHD>30 ng/ml). Maternal 25OHD levels were correlated with the 25OHD levels of the infants in cord blood ($r = 0.665$, $p < 0.001$). There was a significant difference in mean cord 25OHD levels between winter (13.65 ± 5.69 ng/ml) and summer seasons (19.58 ± 11.67 ng/ml)
($p = 0.021$). No association was found between neonatal morbidity and vitamin D status.

Conclusion: With the current supplementation protocol the majority of the VLBW infants with deficient/insufficient serum 25OHD levels reached sufficient levels on the 30th DOL.

None declared.

ID 268. Necrotizing enterocolitis in neonates: early genetic markers

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Background: The most widely used tests for early necrotizing enterocolitis (NEC) detection are still non-specific. Investigating gene expression and pathophysiological pathways would allow us to find gut-associated specific biomarkers. This study aimed to reveal potential genetic predictors of NEC in neonates.

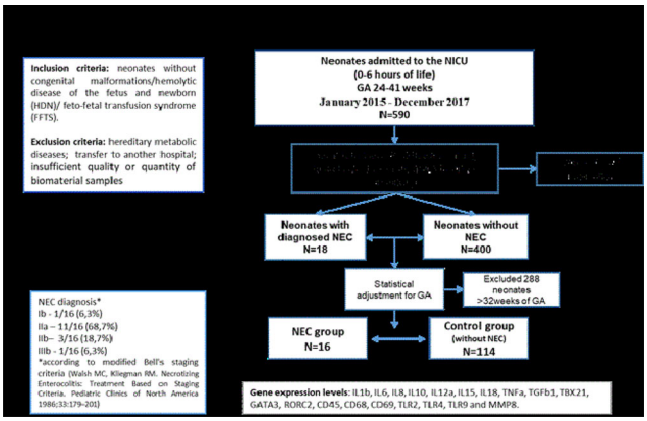
Methods: The study included 590 neonates (gestational age (GA) 24–41 weeks) admitted to the NICU during the first hours of life from January 2015 to December 2017. All neonates underwent sampling of biological material (venous blood (VB) and buccal swabs (BS) before the start of medical treatment and enteral feeding. The reverse transcription method was used to measure gene expression levels: IL1b, IL6, IL8, IL10, IL12a, IL15, IL18, TNFa, TGFb1, TBX21, GATA3, RORC2, CD45, CD68, CD69, TLR2, TLR4, TLR9 and MMP8. We compared gene expression in VB and BS of neonates who developed NEC and those without NEC.

Results: The development of NEC was noted in 25 out of 590 newborns initially included in the study (4,2%). After the technical assessment of biomaterial and exclusion of 172 newborns, there were remaining 418 patients with 18 cases of NEC. After statistical adjustment according to GA, 130 patients were remaining: 16 Neonates with NEC and 114 patients in the control group (without NEC).

In premature infants, a statistically significant increase in the level of TLR4 expression in VB was associated with the development of NEC. Also, a downward trend in GATA3 was noted in neonates with NEC compared to the control. The decimal Lg (TLR4/GATA3) then was calculated and ROC analysis showed a decent prognostic value of this criterion: threshold value of 0.74, the sensitivity −88%, and the specificity −77%; positive predictive value (PPV) −39%, negative predictive value (NPV) −97%.

The same analysis in the buccal epithelium didn't show significant differences between the groups. The expression level of other genes did not differ statistically significantly between groups.

Conclusion: TLR4 gene expression measured in the first hours of life as well as Lg (TLR4/GATA3) could be considered as potential early biomarkers of subsequent NEC development; future research is needed to approve obtained data.



(ID 268)

None declared.

ID 271. Two types of third-generation lipid emulsions for parenteral nutrition in neonates: a randomized pilot study of short-term neonatal outcomes

Anna Lenyushkina[1], Olga Krogh-Jensen[2], Anna Pupysheva[1], Ksenia Titova[2], Irina Nikitina[1]*

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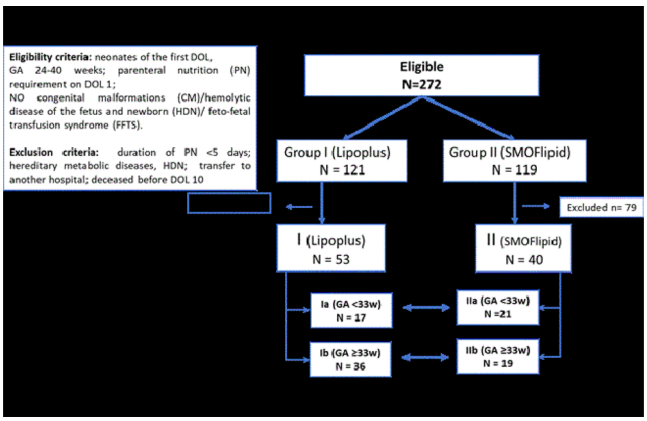
Background: It is assumed that lower content hepatotoxic phytosterols from soybean oil and a higher content of anti-inflammatory components (fish oil (FO) ω-3 PUFA, α-tocopherol form olive oil) in the intravenous lipid emulsions (IVLE) will contribute to a decrease in the incidence of neonatal cholestasis (NC), bronchopulmonary dysplasia (BPD) and retinopathy of prematurity (ROP). However, this hypothesis hasn't been confirmed by studies in neonates. Our study aimed to assess the frequency of NC, BPD, and ROP in newborns receiving 2 types of 3rd generation IVLE: the 1st—10% FO, 40% soybean oil, and 50% coconut oil (LipoPlus), vs the 2nd—15% FO, 30% soybean oil and 25% olive oil (SMOFlipid).

Methods: 272 newborns GA 24–40 weeks were randomly assigned to Group I (Lipoplus) and II (SMOFlipid). 125 neonates met the exclusion criteria. Subgroups according to GA were compared: Ia (<33 weeks, n = 17) vs IIa (<33 weeks, n = 21); Ib (GA ≥33 weeks, n = 36) vs IIb (GA ≥33 weeks, n = 19). Assessed parameters: total bilirubin (Bil), direct Bil, alkaline phosphatase (ALP), P, Ca on DOL 10, 20, and 30, the frequency and severity of NC, BPD, and ROP.

Results: The groups were comparable (BW, GA, Apgar score, gender, frequency of CS, antenatal RDS prophylaxis, PN, and MV duration). The incidence of NC and ROP didn't differ. BPD was noted in 1/17 vs 4/21 in subgroups Ia and IIa, which didn't reach statistical significance (p = 0.63). The level of ALP was higher in patients receiving SMOFlipid: on DOL 10 (Ia - Me = 324 vs IIa - Me = 484 U/L, p = 0.016), and on DOL 30 (Ib - Me = 286 vs IIb - Me = 480 U/L). The other assessed biochemical parameters did not differ.

Conclusion: Comparative analysis of the two types of IVLE didn't reveal a statistically significant difference in the incidence of NC, BPD, and ROP. The revealed increase in ALP and a tendency to an increased BPD incidence in neonates on SMOFlipid require further investigation with lipid blood profile on a larger sample of patients with long-term PN.



(ID 271)

None declared.

ID 284. Neonatal admissions for hypoglycaemia: balancing risks and benefits through the use of a lower treatment threshold fro hypoglycemia

Ibrahim Dafalla[1], Sarah Kasha[1], Avril Kearney[1], Shirley Moore[1], Hilda Wall[1], Anna Curley[1]*

[1]National maternity Hospital, Dublin, Ireland

Background: Early identification of hypoglycaemia in at risk babies can reduce risk of persistent brain injury. There is no consensus internationally, however, on a treatment threshold that is safe but also minimises over medicalization of at risk babies. In 2020 the hypoEXIT study demonstrated treatment at a blood sugar threshold of 2 mmol/L was non-inferior to a traditional threshold (2.6 millimol/L) with regard to psychomotor development at 18 months. We implemented this new threshold for treatment of hypoglycaemia in May compared admissions for neonatal hypoglycaemia to our neonatal unit, before and after implementation of the new protocol.

Methods: Setting: tertiary neonatal unit in a maternity hospital with c9000 deliveries annually. Retrospective study, of all newborn babies >35 weeks admitted with hypoglycaemia as primary reason for admission, data were collected from electronic patient's charts; from 16/09/19 to 15/03/20 and 01/06/20 to 15/11/20 and compared. We assessed overall number of admissions for hypoglycaemia, demographic data of those admitted including background risk factors, medical management, length of stay and discharge destination.

Results: There was no significant difference in baseline characteristics. There was a reduction in the admission rate of patients with hypoglycaemia from 118 (3% neonatal unit admissions) to 34 patients (0.9% neonatal admissions) between the two time periods. Additional treatment with boluses or intravenous (IV) fluids also reduced with the new protocol threshold. A bolus of dextrose was required in 25% vs 6& (<2.6 group vs <2.0 mmol/L). 38% of patients required IV fluids in <2mmol group compared to 45% in the <2.6 mmol group (see Table). No babies suffered adverse effects of hypoglycaemia such as seizures in either timeframe.

Conclusion: we demonstrated a greater than two thirds reduction in admission rate with no increase in adverse events for babies with hypoglycaemia following a reduction in treatment threshold from 2.6 mmol to 2 mmol/L. This resulted in reduced workload for the neonatal unit, and decreased separation of newborn babies from their mothers. The lessons we learned can be applied to other maternity hospitals and we hope will reduce mother and baby separation and enhance bonding and breastfeeding improving maternity and newborn care.

Table 1 shows comparison between different variables before and after implementing of hypoglycaemia protocol.

Demographic data	Hypoglycaemia threshold 2.6 mmol/L Sept. 2019–March 2020	Hypoglycaemia threshold 2.6 mmol/L June to December 2020
Total number of deliveries	3883	3806
Admission with hypoglycaemia	118 (3%)	34 (0.9%)
Median gestational age	39^{+1} (IQR: 38-40^{+1}week)	38^{+5} (IQR: 37^{+5}– 40 weeks)
Median birth weight (kg)	3.45 kg(IQR: 3-3.9)	3.7 kg(IQR: 3–4.5)
Symptoms on admission	**Symptomatic (46%) A (54%)**	**Symptomatic (30%) A (70%)**
Sugar on admission (mmol/l)	1.4 (IQR: 1.2–1.5)	1.5 (IQR: 1–1.8)
Repeated blood sugar mmol/l	2 (IQR 1.6–2.5)	2.3 (IQR: 1.8–3)
Glucogel alone/without IV fluids	55% (66/1 18)	62% (21/34)
IV glucose boluses %	25% (29/1 18)	6% (2/34)
IV glucose and Glucogel %	45% (521118)	38% (13/34)
IV glucose duration (hours)	18 (IQR: 12–30)	17 (IQR: 15–62)
Length of stay (days)	1.75 (IQR 1–3)	2 (IQR 2–3)
Discharge destination	Home: 27%, PN ward 73%	Home: 24%, PN ward 76%
Risk factors	**Before**	**After**
Maternal diabetes mellitus	42 (35%)	10 (29%)
Low birth weight	4 (3%)	1 (3%)
No risk factor	72 (62%)	23 (68%)

(ID 284) - Table 1 shows comparison between different variables before and after implementing of hypoglycaemia protocol.

None.

ID 302. Insights into patterns of breastfeeding in preterm babies up to six months of actual age from the last UK National Infant Feeding Survey

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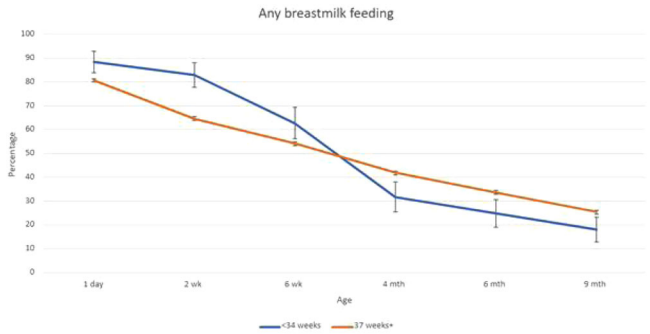
Background: There is minimal representative data available on long-term breastfeeding outcomes of preterm babies in the UK, particularly those born <34 weeks' gestation. The last national Infant Feeding Survey is an unexplored source of data.

Method: A series of questionnaires were sent to a representative sample of those giving birth in Aug/Sept 2010; the final questionnaire was sent at 7–9 months of actual age. The dataset is freely available for academic purposes in the UK Data Archive and this is covered by the original ethical approvals. Data are presented as means and standard deviation. Error bars were constructed using binomial proportion confidence intervals. Categorical data were analysed using chi squared tests.

Results: Final data were available for 10,064 term babies, 429 late preterm (mean gestation 35.3 ±0.8 weeks) and 148 babies born <34 weeks' (mean gestation 30.9±2.1 weeks). Breastmilk initiation was highest in babies born <34 weeks' (89% compared to 81% for term babies, p = 0.02) but any & exclusive breastmilk rates drop below those for term babies by around 2 months actual age (near

term corrected age; Fig. 1). 25% receive any breastmilk at 6 months actual age, compared to 34% of term babies (p = 0.02). In contrast, babies born at 34–36 weeks' gestation have the worst breastmilk feeding outcomes throughout, with initiation of 77%, exclusive breastmilk on day one of only 48% and an absolute difference of up to 29% in exclusive breastmilk rate between gestation categories (p < 0.00001 at all timepoints up to 4 months of age).

Conclusion: Despite limited power, useful relationships were seen in this previously unexplored data. Babies born <34 weeks' have the highest breastmilk initiation rate of all groups, likely due to an understanding of the value of breastmilk in this setting. By around term corrected age they receive less breastmilk than term babies, showing the challenges of establishing and maintaining a sustainable milk supply. The data support that of Bonnet et al. (2018) showing that the UK is one of the worst in Europe in breastmilk outcomes for very preterm babies at 6 months. Late preterm babies have the worst outcomes of all, emphasising their need for tailored feeding support.



(ID 302) - Fig. 1: Rate of any breastmilk feeding over time in babies born <34 weeks' gestation, compared to term babies.

Co-chair of a national knowledge sharing and advocacy group in the UK (the Hospital Infant Feeding Network). Receives funding from the National Institute for Health Research (Clinical Doctoral Fellowship)

ID 344. Controlled trial of two timepoints for introduction of standardized complementary food in preterm infants

Nadja Haiden[1], Margarita Thanhaeuser[1], Mercedes Huber- Dangl[1], Melanie Gsoellpointner[1], Robin Ristl[1], Sophia Brandstetter[1], Renate Fuiko[1], Fabian Eibensteiner[1], Margit Kornsteiner-Krenn[1], Christoph Binder[1], Angelika Berger[1], Bernd Jilma[1]*

[1]Medical University Of Vienna, Vienna, Austria

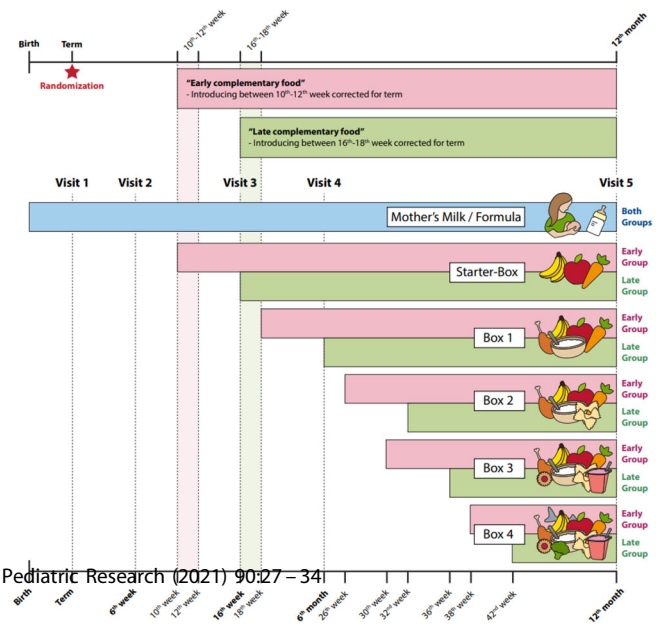
Background: In term infants it is recommended to introduce solids between the 17th and 26th week of life, whereas data for preterm infants are missing. Aim of the study was to investigate the impact of timepoint for introduction of standardized solid foods on growth of VLBW (very low birth weight)-infants.

Methods: In a prospective, two arm intervention study we investigated longitudinal growth of VLBW-infants after early (10–12th) or late (16–18th week of life) introduction of standardized complementary food (Fig. 1). Primary objective was length at one year of age, secondary objectives were other parameters of growth such as weight, head-circumference, BMI, and z-scores.

Results: Among 177 infants who underwent randomization primary outcome could be assessed in 80 (90%) assigned to the early and 75 (85%) to the late group. Mean birthweight was 940 g (±253 g) in the early and 932 g (±256 g) in the late group, mean gestational age at birth was 27+1 weeks in both groups.

At 1 year of age corrected for prematurity length was 74.7 cm (=mean; SD ± 2.7 cm) in the early and 74.4 cm (=mean; SD ± 2.8 cm; n.s.) in the late group. There were no differences in other anthropometric parameters between the study groups except for weight z-score at 6 months corrected for age (early group −0.49; SD ± 1.2, late group −0.56; SD ± 1.04; p = 0.04).

Conclusions: There was no significant difference in anthropometric parameters at one year of age in VLBW-infants with a strategy of early introduction of standardized solids between 10–12 weeks as compared to late introduction between 16–18 weeks. Starting solids should be rather related to neurological ability of the infant than to considerations of nutritional intake and growth.



(ID 344) - Studyflowchart, timing and type of standardised diet.
The study was sponsored by a national grant: Nationalbank Jubiläumsfondsprojekt 15378.

ID 356. The in-hospital growth pattern of preterm infants identifies the true growth faltering better than EUGR cut-off

Nadia Liotto[1], Camilla Menis[1,2], Orsola Amato[1], Anna Orsi[1], Pasqua Piemontese[1], Michela Perrone[1], Fabio Mosca[1,2], Paola Roggero[1,2]*

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Background: Extrauterine growth restriction (EUGR) is often reported in VLBW preterm infants, and is not necessarily predictive of adverse outcomes. The growth pattern and not a one-time size value at discharge could improved the identification of true growth faltering and optimized the outcomes.

The aim was to describe the growth pattern of VLBW preterm infants according to the occurrence of EUGR during the hospitalization with or without morbidities.

Methods: We analyzed the clinical records of VLBW infants admitted in our NICU between 2015 tand 2020. We computed the weight z-scores (WZS) at birth, at first week of life (W1), at the day of achieving full enteral feeding (FEF day) and at discharge according to Intergrowth-21st Growth Charts. EUGR was defined as a delta-WZS between birth and discharge >1. The infants were categorized in EUGR+ with morbidities (BPD, NEC, sepsis) or without morbidities and EUGR-. We performed a paired T-test between the WZS at the different periods and an ANOVA test with Bonferroni post hoc analysis.

Results: We included 414 VLBW infants. Their characteristic and WZS are described in the table. The birth weight of EUGR+ infants without morbidities was significantly higher (p = 0.02) than that of EUGR+ with morbidities and EUGR− infants. The EUGR+ infants without morbidities showed the main loss in WZS during the first week, similar to that observed in infants EUGR− (48% of total lost). However, the delta-weight loss between birth and W1 was higher in EUGR+ infants without morbidities compared to EUGR− infants (p = 0.001). EUGR+ infants with morbidities showed a continuous decline after the first week of life until discharge.

Conclusions: EUGR+ infants who developed morbidities are a category that need a multidisciplinary approach that include the neonatologist and the nutritionist, in order to limit their true growth faltering. In EUGR+ infants without morbidities, the main weight loss was observed during the first week of life. The early discharge with the growth assessment prior the growth slowing of the reference healthy preterm infants, that occurs around 40 weeks, could explain the inclusion in EUGR+ category of theses infants.

	Infants EUGR+ without morbidities (n=32)	Infants EUGR+ with morbidities (n=63)	Infants EUGR- (n=319)
GA (weeks)	30.4±2.0	27.9±2.2*	28.7±2.5
Birth weight (g)	1317±172	1013.0±256*	1194.0±253^
GA at discharge (g)	37.5±1.2	41.6±5.0*	38.8±3.5
Weight loss %	11.0±4.4	11.3±4.7	9.2±4.4
WZS at birth	-0.21±1.18	-0.22±1.01	-0.91±1.08§
WZS at W1	-1.08±1.38	-0.59±1.05	-1.09±1.27^
WZS at the FEF day	-1.18±1.18	-1.31±1.2	-1.13±1.19
WZS at discharge	-1.73±0.98	-1.89±0.9	-1.06±1.06§
Delta-WZS from birth to W1	0.72±0.54	0.38±0.77	0.19±0.69*
Delta-WZS from W1 to FEF day	0.17±0.47	0.81±0.89*	0.06±0.95
Delta-WZS from FEF day to discharge	0.54±0.64	0.55±0.85	-0.06±0.71§
Delta-WZS from birth to discharge	1.51±0.60	1.66±0.61	0.14±0.57§

(ID 356) –
*EUGR+ with vs EUGR+ without morbidities and EUGR−; p < 0.001.
§EUGR− vs EUGR+ with and without morbidities: p < 0.001.
^EUGR− vs EUGR+ with morbidities: p = 0.02.
+EUGR− vs EUGR+ without morbidities: p = 0.001.
*EUGR+ with vs EUGR+ without morbidities and EUGR−; p < 0.001.
§EUGR− vs EUGR+ with and without morbidities: p < 0.001.
^EUGR− vs EUGR+ with morbidities: p = 0.02.
+EUGR− vs EUGR+ without morbidities: p = 0.001.
None declared.

ID 361. Splanchnic oxygenation below 30% as predictor for NEC in extremely preterm neonates

Elena Palleri[1,3], Martin van der Heide[2], Jan BF Hulscher[2], Elisabeth MV Kooi[2], Marco Bartocci[1,3], Tomas Wester[1,3]*

[1]Karolinska University Hospital, Stockholm, Sweden, [2]University of Groningen, University Medical Center Groningen, Beatrix Children's Hospital, Groningen, Netherlands, [3]Karolinska Institutet, Stockholm, Sweden

Background: Impaired splanchnic microcirculation seems to play an important role in the pathogenesis of NEC in extremely preterm neonates. A previous study showed that a mean splanchnic oxygenation <30% is associated with increased risk to develop NEC. The aim of this study was to assess the sensitivity and specificity of 30% as cut off for splanchnic oxygenation (SrSO2) at day 2–6 of life to predict NEC in a pooled cohort of extremely preterm infants.

Methods: Two cohorts of extremely preterm neonates (<28 weeks GA) from two university hospitals were pooled together in a mixed cohort study. Splanchnic oxygenation was measured for 1–2 h in extremely preterm infants at 2–6 days of life, after enteral nutrition had been introduced. Both centers used the INVOS 5100c with neonatal somasensor to perform NIRS monitoring. The primary outcome was NEC (Bell's stage >2a). Odds ratio to develop NEC was assessed with generalized linear model analysis, adjusting for center. We calculated sensitivity, specificity, positive and negative predictive values, for the SrSO2 cut-off 30%.

Results: We included 89 extremely preterm infants, 55 (61.8%) boys, median gestational age 26.2 (range 23.0–27.9). Seventeen (19%) developed NEC, 8 (18%) in center A and 9 (20%) in center B. In cohort A all infants were continuously fed (n = 44) while in cohort B infants were bolus-fed (n = 45). There was no difference in mean SrSO2 between the two centers (40.1 SD (18.5) vs 38.2 SD (20.3), p = 0.65. Mean SrSO2 < 30% was found in 33.3% of infants who did not develop NEC compared to 70.5% of those who did develop NEC (p = 0.07). The odds ratio to develop NEC, adjusted for center, with mean SrSO2 < 30% was 4.8 (CI (1.51–15.3), P = 0.008). Specificity and sensitivity of the SrSO2 cut-off

30% are shown in the table. Sensitivity, specificity, positive and negative predictive values were similar in the two centers despite the different feeding strategies.

Conclusions: Mean SrSO2<30% in extremely preterm infants between day 2–6 of life may be useful to predict who is going to develop NEC or not. The negative predictive value of mean SrSO2 < 30% provides further proof for the importance of impaired splanchnic microcirculation in NEC pathogenesis.

Center	Both cohorts (n = 89)	Center A (n = 44)	Center B (n = 45)
AUC (95% CI)	0.63 (047–0.78)	0.67 (0.41–0.89)	0.61(0.4–0.79)
Sensitivity (95% CI)	0.71 (0.47–0.88)	0.75 (0.38–1)	0.67 (0.33–1)
Specificity (95% CI)	0.67 (0.56–0.78)	0.72 (0.58–0.86)	0.61 (0.44–0.78)
PPV (95% CI)	0.33 (0.24–0.45)	0.38 (0.23–0.56)	0.30 (0.17–0.44)
NPV(95% CI)	0.91 (0.84–0.97)	0.93 (0.84–1)	0.88 (0.78–1)

(ID 361) - Table: Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). Area under the curve (AUC) 95% confidence interval.

None declared.

ID 396. Mild therapeutic hypothermia is safe for preterm infants with NEC stage II

Lara Malosso Sgarbi Albuquerque[1], Cristina Calixto[1], Gerson Claudio Crott[1], Julia Belcavelo Contin Silva[1], Mariel Versiane Caixeta[1], Cristina Helena Faleiros Ferreira[1], Thayane de Castro Peres[1], Lisianne Virginia Pereira Monte Costa[1], Davi Aragon[1], Walusa Assad Gonçalves-Ferri[1]*

[1]Hospital das Clinicas da Faculdade de Medicina de Ribeirão Preto, Ribeirão Preto, Brazil

Background: Therapeutic hypothermia to premature infants is not considered safe; however, it can be helpful to diseases treatment. Mild therapeutic hypothermia has beneficial effects on adults and pediatric patients. We evaluated the safety of mild therapeutic hypothermia for premature infants with necrotizing enterocolitis stage II.

Methods: A Quality study was performed from January 2015 to March 2021. The NEC diagnosis (established by the modified Bell criteria) was made by the neonatology team and two independent neonatologists. The SQUIRE checklist was followed. The patients were divided into two groups: the control group (antibiotics and fasting) and the hypothermia group (conventional treatment and passive hypothermia for 48 h after diagnosis). Hypothermia was induced by turning off the incubators' heating mechanisms, with a room temperature of 23–25 °C. The target temperature was 35 °C (0.5°± C). The cooling speed was 0.5 °C per hour; the vital signs and esophageal temperature were monitored every 15 min. Clinical and laboratory outcomes were assessed for 72 h (before hypothermia, during 48 h of hypothermia, and 24 h after rewarming). Multiple log-binomial regression models were adjusted to estimate the relative risks; N-Sofa and IG were covariates. The linear model of mixed Bayesian effects was adjusted to compare means (CI 95%).

Results: 83 newborns were included, 53 underwent therapeutic hypothermia, and 30 remained received the conventional treatment. Normothermia group versus hypothermia group: Gestational age mean was 30.3 (±8.7) versus 32.4 (±3.3) weeks, mean weight at NEC onset was 1063 (±654.8) versus 1221.6 (±633.5) g. Hypothermia group presented a significant mean difference: higher hemoglobin level 2.05 (IL: −3.49; UL: −0.49); higher sodium level 3.97 (IL: −6.92; UL: −1.1); higher PO2/FiO2 0.69 (IL: −1.3; UL: −0.07), lower potassium level −1.04 (IL: 0.6; UL: 1.5), lower creatinine level −0.38 (IL: 0.1; UL: 0.67) and lower lactate level −1.2 (IL: 0.13; UL: 2.3). Hypothermia did not cause hemodynamic or thermal instability, coagulation, ventilatory or metabolic disorders. Hypothermia decreased the mortality (RR = 0.11 (0.02; 0.53). (Table 1)

Conclusion: Mild hypothermia is feasible, safe, and unrelated to adverse effects, in addition to protecting death in preterm infants with NEC.

Variables	Hipothermia (n = 53)	Control (n = 30)	RRaj (95% CI)
Dystermias*	48 (90.6%)	27 (90%)	1.01 (0.61; 1.9)
Desaturation (<90%)	29 (54.7%)	23 (76.7%)	0.72 (0.40; 1.30)
Apnea	20 (37.7%)	9 (32.1%)	1.31 (0.56; 3.03)
Bradycardia (<100 bpm)	19 (35.9%)	6 (20%)	1.86 (0.71; 4.92)
Tachycardia (>160 pbm)	34 (64.2%)	22 (73.3%)	0,95 (0.53; 1.70)
Seizures	5 (9.4%)	4 (13.8%)	0.62 (0.15; 2.56)
Coagulopathy	1 (3.3%)	1 (10%)	0.15 (0.004; 5.16)
Thrombocytopenia	16 (30.8%)	14 (48.3%)	0.76 (0.35; 1.65)
Arterial hypotension	23 (43.4%)	19 (65.5%)	0.82 (0.43; 1.58)
Metabolic acidosis	17 (34%)	20 (66.7%)	0.56 (0.28; 1.14)
Hyperkalemia	13 (28.9%)	14 (46.7%)	0.70 (0.31; 1.56)
Hypocalcemia	5 (9.4%)	3 (10%)	1.08 (0.23; 4.99)
Anuria (< 1ml/kg/h)	3 (5.7%)	1 (3.3%)	3.00 (0.29; 30.90)
Bleeding (anywhere)	18 (34.0%)	11 (36.7%)	1.23 (0.55; 2.77)
IVH	3 (6.0%)	3 (10.3%)	0.95 (0.17; 5.07)
Sepsis during NEC	39 (73.6%)	29 (96.7%)	0.83 (0.5; 1.40)
Death related to NEC	2 (3.8%)	11 (36.7)	0.11 (0.02; 0.53)

(ID 396) - Multiple log-binomial regression of laboratory values and clinical parameters of the groups during 48 h after diagnosis of NEC.
Dystermias: Variations outside the recommended range:hypothermia group 35.5 and normothermia group 36.5.

None declared.

ID 399. Evaluation of late outcomes in premature patients undergoing mild therapeutic hypothermia as a treatment for necrotizing enterocolitis

Mariel Versiane Caixeta[1], Júlia Belcavelo Contin Silva[1], Lara Malosso Sgarbi Albuquerque[1], Lisianne Virgínia Pereira Monte Costa[1], Davi Casale Aragon[1], Cristina Calixto[1], Thayanne de Castro Peres[1], Cristina Helena Faleiros Ferreira[1], Walusa Assad Gonçalves Ferri[1]*

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Background: Necrotizing enterocolitis (NEC) leads to prolonged use of parenteral nutrition, generating malnutrition, and increased risk of infection through long-term venous access duration. NEC treatment with mild and controlled hypothermia is performed in our service as an additional treatment for stage 2 NEC since 2018. This study evaluated the outcomes related to the morbidity of premature infants who underwent mild therapeutic hypothermia.

Methods: A quality study was performed from January 2015 to March 2021. The NEC diagnosis (established by the modified Bell criteria) was made by the neonatology team and two independent neonatologists. The SQUIRE checklist was followed. The patients were divided into two groups: the control group (antibiotics and fasting) and the hypothermia group (conventional treatment and passive hypothermia for 48 h after diagnosis). The variables studied were days of parenteral nutrition, time for the reintroduction of the milk, days of gastric residuals, time for normalization of the abdominal physical examination. Severe neurological outcome was also assessed, considered delayed neurodevelopmental impairment and/or epilepsy and/or grade II/III intraventricular hemorrhage (Volpe classification) and/or leukomalacia at 6 months.

Results: 83 children were diagnosed with necrotizing enterocolitis; 53 babies underwent mild therapeutic hypothermia, in addition to conventional treatment and 30 babies received only conventional treatment. The group submitted to therapeutic hypothermia presented significant differences ($p < 0.01$) in the digestive aspects: parenteral nutrition (TPN) for less time 27.4 days (SD: 30.3) versus control group 58.2 days (SD: 86.7); the reintroduction of enteral feeding earlier (13.3 ± 7.9 days) versus the control group patients (19.9 ± 14.9 days), normalization of the abdominal examination 10.9 days (SD: 5.0) versus 18.8 (SD: 11.0) and decreased gastric waste earlier 8.3 days (SD: 7.2) versus 13 days (SD 7.5). The hypothermia group had a lower risk of severe neurological outcomes (RR = 0.91 (0.55; 1.49)) and a lower occurrence of death associated with NEC (36.6% vs 3.7% $p < 0.01$).

Conclusion: Preterm infants with NEC who underwent mild and controlled hypothermia had better late outcomes related to digestive and neurological outcomes when compared to patients who only received conventional therapy for NEC.

OUTCOMES	HYPOTERMIA GROUP (n=53)	CONTROL GROUP (n=30)	p VALUE
Time to reintroduce the diet (days)*	13.3 (±7.9)	19.9 (±14.9)	p < 0.01
Duration of gastric residuals (days)*	10.9 (±5.0)	18.8 (±11.0)	p< 0.01
Time for normal abdominal examination (days)*	8.3 (±7.2)	13 (±7.5)	p < 0.01
Duration of use parenteral nutrition (days)*	27.4 (±30.3)	58.2 (±86.7)	p < 0.01

(ID 399) - *Mean (standard deviation).

None declared.

ID 444. Xpres QI initiative: reducing the time to first colostrum on a neonatal intensive care unit (NICU)

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Background: Human colostrum obtained in the first few days following delivery is rich in essential immunological components. Early administration of colostrum reduces the risk of severe necrotising enterocolitis and increases the breast feeding rate at discharge. British Association of Perinatal Medicine (BAPM) recommends that buccal colostrum should be administered within 6 hours of birth.

Our aim was to reduce the time to first colostrum administration in a Neonatal Intensive Care Unit (NICU) in the United Kingdom by 20%.

Methods: XPRES, a multi-professional quality improvement group, was formed to identify the key drivers for change. These included staff education as well as better provision of equipment. Process mapping highlighted the importance of a multi-disciplinary team approach.

We have completed three PDSA cycles:

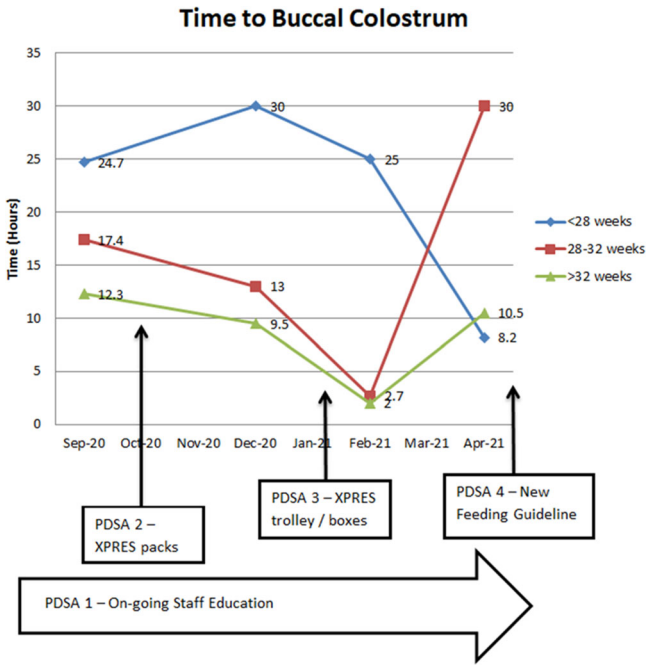
PDSA 1: September 2020—On going staff education via road shows was introduced for the neonatal and midwifery teams.

PDSA 2: October 2020—XPRES packs were introduced containing colostrum syringes and parental information. These were delivered during antenatal counselling or during the parental first visit.

PDSA 3: January 2021—A 'XPRES trolley' was introduced which can be wheeled to the patient's cot side and contains expressing equipment and parent information. 'XPRES boxes' were introduced on delivery suite and the postnatal wards containing the same tools. Prospective data collection was carried out to monitor the impact of our change ideas.

Results: In September 2020 the mean time to colostrum administration was 18 h for all infants <34 (for <28 weeks gestation, 24.7 h; 28–32 weeks gestation, 17.4 h; 32–34 weeks gestation 12.3 h). Since completing our three PDSA cycles we have seen an improving trend in time to administration (Fig. 1). This has been especially evident in our extreme preterm population (<28 weeks), showing a 67% improvement (24.7 to 8.2 h).

Conclusion: Increased awareness and education of multidisciplinary stakeholders, as well as better provision of expression equipment has improved the time to first colostrum administration on the NICU. Although extreme preterm babies are receiving colostrum earlier, there is still work to be done and hence a new feeding guideline with more focussed staff/parent education has been planned.



(ID 444) - Time to buccal colostrum and PDSA cycles

None declared.

ID 489. Cytomegalovirus and neonatal cholestasis in preterm infants

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Background: Human cytomegalovirus (CMV) is one of the most common viral infections in the neonatal period and is known to affect the liver. The objective of this study was to evaluate the prevalence of CMV in preterm infants with cholestasis.

Methods: Preterm (<37 weeks) cholestatic infants in neonatal wards at Karolinska University Hospital were included and sampled in peripheral mononuclear blood cells (PBMC), plasma and urine for CMV DNA using quantitative PCR. Any missing samples were assumed to be negative, and the infants were regarded as positive for CMV if any sample tested positive. Their mothers were tested for CMV serostatus simultaneously. Later, a reference group of preterm infants (and their mothers) without cholestasis were included and tested in the same manner when at least 3 weeks old (but less than 6 weeks). Cholestatic infants were compared to the reference group regarding CMV DNA prevalence, and cholestatic CMV positive infants were compared to cholestatic CMV negative infants.

Results: 45 cholestatic preterm infants and 24 non-cholestatic were included. 69% (31/45) of the cholestatic infants were CMV positive versus 13% (3/24) of the non-cholestatic ($p < 0.00001$). Cholestatic infants had similar gestational age but were generally sicker with more cases of necrotizing enterocolitis, need for mechanical ventilation and parenteral nutrition. After adjusting for necrotizing enterocolitis, parenteral nutrition and gestational age using logistic regression, being CMV positive remained significantly associated with cholestasis. Among the cholestatic infants, the CMV positive and negative did not differ regarding baseline characteristics or neonatal morbidity, except for necrotizing enterocolitis, occurring in 55% (17/31) of CMV positive and in 21% (3/14) of CMV negative, bordering on significance ($p = 0.054$). Eight CMV positive infants died versus none of the CMV negative ($p = 0.044$).

Conclusion: CMV DNA was detected in two out of three cholestatic preterm infants, by far more often than in age-matched controls. Samples from several locations may be needed to test to detect viral DNA. Cholestasis with simultaneous detection of CMV DNA may be associated with a more severe outcome.

Characteristics and CMV status of cholestatic and non-cholestatic infants.

	Cholestatic (n = 45)[a]	Non-cholestatic (n = 24)[a]	p[b]
Mother and pregnancy			
Maternal age, years	31 (27, 35)	33 (29.5, 35)	0.32
Singleton	36/45 (80.0)	20/24 (83.3)	1.00
Steroids, antenatal	39/45 (86.7)	23/24 (95.8)	0.41
Caesarian incision	33/45 (73.3)	16/24 (66.7)	0.59
Neonatal characteristics			
Gestational age, week + days	26+5 (25+4, 29 + 1)	26+4 (24+6, 27+3)	0.31
Birth weight, kg	0.963 (0.738, 1.194), n = 44	0.777 (0.606, 1.002)	0.053
Small for gestational age	15/44 (34.1)	8/24 (33.3)	1.00
Female gender	21/45 (46.7)	10/24 (41.7)	0.80
Neonatal course			
Mechanical ventilation, days	23 (12, 36)	5.5 (0, 11)	<0.0001*
Erythrocyte transfusions	14 (11, 21)	6 (3.5, 8)	<0.000001*
Sepsis	28/45 (62.2)	8/24 (33.3)	0.026*
Patent ductus arteriosus	29/45 (64.4)	9/24 (37.5)	0.043*
NEC, ≥stage 2	20/45 (44.4)	1/24 (4.2)	<0.001*
Nutrition and growth			
Parenteral nutrition, ≥2 weeks	42/45 (93.3)	11/24 (45.8)	<0.0001*
Maternal breast milk, fed at any time	86.7 (36/45)	95.8 (23/24)	0.408
Donor breast milk, fed at any time	72.7 (32/44)	95.2 (20/21)	0.046*
Outcomes			
BPD grade 2 or higher	24/40 (60.0)	8/24 (33.3)	0.070
ROP stage 3 or higher	12/42 (28.6)	4/24 (16.7)	0.375
Deceased	8/45 (17.8)	1/24 (4.2)	0.15
Infant CMV DNA PCR			
PBMC+	12/45 (26.7)	3/24 (12.5)	0.23
Urine+	6/30 (20)	0/21 (0.0)	0.036*
Plasma+	27/45 (60)	0/18 (0.0)	0.000007*
Positive in any sample	31/45 (68.9)	3/24 (12.5)	<0.000009*
Age at blood sampling (PBMC, plasma), days	32 (19, 41), n = 41	29 (27, 38), n = 22	0.53

(ID 489) - [a]n/N (%) for proportions, median ([IQR]: 25th percentile, 75th percentile) for continuous variables.
[b]Fisher exact test for proportions, Mann-Whitney U-test for continuous variables.
*Statistical significance.

None declared.

ID 494. Comparative clinical effectiveness of two methods: of hyperglycemia correction in very low birth weight preterm infants

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Background: Management of early neonatal hyperglycaemia in preterm newborns remains controversial. The aim of this study was to compare clinical effectiveness of two.

Methods: of hyperglycaemia correction (insulin therapy and reduction of glucose infusion rate) in VLBW infants with respiratory distress syndrome (RDS).

Methods: Sixty VLBW newborns (gestational age <32 weeks) with hyperglycaemia and RDS were enrolled in the study on the first day of life and were followed until discharge or death. Criteria of hyperglycaemia were blood glucose concentration (BGC) >8.3 mmol/L with glucosuria (GU) or BGC ≥10 mmol/L regardless of GU. The neonates were randomly divided into two groups. Newborns in the insulin group (n = 30) were treated with insulin (0.1 U/kg) and control babies (n = 30) were managed with reduction of glucose infusion rate by 25%. Normal saline was infused for 1 h if above mentioned measures were ineffective and hyperglycaemia persisted with BGC >10 mmol/l.

Results: The groups were not different in terms of gestational age and birth weight (28.07 ± 2.38 weeks and 1016.33 ± 245.25 g in the insulin group vs. 28.23 ± 2.31 weeks and 1058.33 ±258.95 g in the control group; $p > 0.05$). The median age at the first episode of hyperglycaemia and median time to normalization of glycaemia were the same in both groups—1 day and 1 h respectively. The duration and number of episodes of hyperglycaemia recurrence didn't differ

either. The incidence of postnatal growth retardation at the postmenstrual age of 36 weeks was higher in the group of glucose reduction (27%) versus 15% in the insulin group, but the difference was not significant ($p > 0.05$). Reactive hypoglycemia occurred in 6.7% neonates from glucose reduction group and in 20% from insulin group ($p > 0.05$). There was no statistical difference in the frequency of adverse outcomes, such as mortality, intraventricular haemorrhage, sepsis, necrotizing enterocolitis, and retinopathy of prematurity.

Conclusion: Both reduction of glucose infusion rate and insulin therapy are clinically equivalent methods of hyperglycaemia treatment in VLBW infants but reduction of glucose infusion rate can be associated with suboptimal postnatal growth.

None declared.

ID 512. Preterm birth affects skeletal development in pigs

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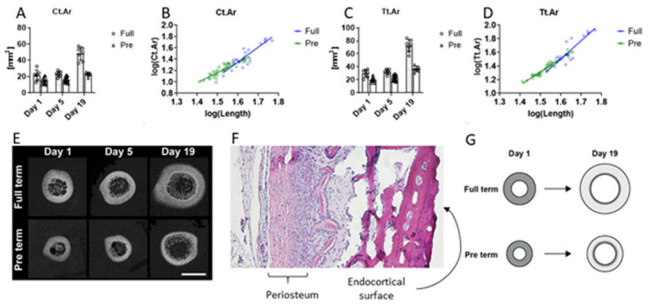
Background: Premature birth interrupts the critical period of bone development in late gestation. Consequently, metabolic bone disease of prematurity (MBDP) is common for preterm infants and may be associated with deficient skeletal development. A major barrier to understanding the skeletal consequences 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 days). We scanned the femurs by micro-computed tomography at 48.4 µm 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.



(ID 512) - Fig. 1. **a**–**e** Cross-sectional geometry (scalebar = 5 mm). **f** Histology showing formation at the periosteal surface and endocortical surface resorption (scalebar = 100 µm). **g** Model of cortical expansion.

Funding: Supported by University of Copenhagen, Denmark & Takeda, Cambridge, MA, USA, Rush University Cohn Research Fellowship, NIH 1T32AR073157.

ID 519. OroPharyngeal therapy with mother's own milk (OPT-MOM) improves feeding and reduces length of stay in premature infants

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Background: OroPharyngeal Therapy with Mother's Own Milk (OPT-MOM) can serve as substitute for biofactor-rich amniotic fluid, providing oropharyngeal immunostimulation until per-oral feeds can be provided to preterm infants (PT). We hypothesized that OPT-MOM improves immune function and intestinal health, thereby improving feeding tolerance and reducing length of stay.

Objectives: To measure effects of OPT-MOM on reducing length of stay, time to full enteral feedings and to full oral feedings and reducing NEC incidence, late-onset sepsis (L-OS), and death in PT <1250 g.

Methods: A double-blind, placebo-controlled, randomized safety and efficacy trial of OPT-MOM among PT infants in 5 NICUs (Group A, OPT-MOM, $n = 105$ v. Group B, placebo, $n = 101$). Infants were randomized to receive 0.2 mL of 'study substance' every 2 for 48 h (beginning <96 h of life), then every 3h until 32 weeks CGA.

Results: There were no differences in birthweight, GA, or Snappe Score for groups A and B. Compared to B, A had shorter length of stay (mean ± SD: 77 ± 33 vs. 86 ± 38 days, $d = 0.25$, $p = 0.23$), shorter time to reach full enteral feedings (21 ± 15 vs. 28±35 days, $d = 0.26$, $p = 0.40$), and reduced time to reach full PO feedings (23 ± 16 vs. 29 ± 31 days, $d = 0.24$, $p = 0.18$). L-OS was similar (15.1% vs. 15.6%), as it was mortality (1.2% vs 1.1%), but there was a trend towards less NEC (1.2% vs. 3.4%, $p=0.37$) in A vs. B, respectively. Sample size using PASS 14.0 software (NCSS, LLC. Kaysville, UT), with a two-tailed alpha of 0.05 and a 20% attrition rate was estimated at 548 infants ($n = 274$ in each group), to detect a minimum effect size of 0.24 with 80% power, suggesting that the findings are relevant and that results may have reached statistical significance with a larger sample size.

Conclusion: In this pilot study, we found a 9-day reduction in length of stay, 7-day reduction in time to full enteral feedings, a 6-day reduction in time to full PO feedings, as well as lower NEC in OPT-MOM-treated infants, compared to controls. We speculate that less inflammation and improved commensal microbiome contributed to these improved outcomes. A 9-day reduction in stay for PT infants is a potential savings of 1.8 billion in USD yearly.

None declared.