ESPGHAN 2013 - Abstract Submission

CLINICAL NUTRITION

ESPGHAN13-1744

UNDERNUTRITION CAUSES CARDIAC DYSFUNCTION IN A PIGLET MODEL

C. Fabiansen [1], M. Lykke [1], A.-L. Hother [1], I. Hunter [2], J. Koch [2], J. P. Gøtze [3], O. B. Nielsen [4], H. Friis [1], P. T. Sangild [5], T. Thymann [6,*]

[1]Department of Nutrition, Exercise and Sports, Faculty of Science, [2]Department of Veterinary Clinical and Animal Sciences, University of Copenhagen, Frederiksberg C, [3]Department of Clinical Biochemistry, Copenhagen University Hospital, Copenhagen, [4]Department of Biomedicine, Aarhus University, Aarhus, [5]Department of Nutrition, Exercise and Sports, Faculty of Science, Copenhagen University Hospital, Frederiksberg C, [6]Department of Nutrition, Exercise and Sports, Faculty of Science, University of Copenhagen, Copenhagen, Denmark

Please select your preferred presentation type: Oral or Poster
Has this abstract previously been presented?: No
Has this abstract previously been published?: No

Objectives and Study: The association between undernutrition and cardiac function in pediatric patients is still poorly understood. A possible link is important for an estimated 60 million children up to 5 years of age that are suffering from undernutrition. The objective of this study was to investigate cardiac function with respect to undernutrition, using an experimental piglet model.

Methods: Four-week old piglets were given *ad libitum* access to either a low-nutrient diet consisting of pure maize flour (MAIZE, n=12) or a control diet (CON, n=12) for 7 weeks. Temporal changes in plasma levels of pro-atrial natriuretic peptide (proANP) and troponin T (TNT) were measured as markers for cardiovascular disease. Echocardiography was performed at 7 weeks when cardiac tissue was collected for analysis of Na/K ATPase density. For comparison, echocardiography was also performed on a reference control group consisting of pigs with a body weight similar to maize-fed pigs without undernutrition.

Results: Body weight was lower in MAIZE relative to CON pigs (-72%, $P<0.001$). There was an initial decline in proANP for both MAIZE and CON pigs during the first 3-4 weeks, then a marked increase in MAIZE pigs at 5-7 weeks, relative to CON pigs ($P<0.05$). Likewise, mean TNT tended to be higher in MAIZE ($P=0.07$) suggesting myocardial damage. Echocardiography, as indicated by the myocardial performance index, showed left ventricle dysfunction in MAIZE relative to both weight- and age-matched control pigs. Heart to body weight ratio was similar between groups but the heart had a flabby appearance in the MAIZE group. Myocardial Na/K ATPase levels were 50% higher in MAIZE vs. age-matched control pigs ($P<0.01$).

Conclusion: Undernutrition in a piglet model causes adverse cardiac remodeling and dysfunction. The results suggest that assessment of cardiac function is important in undernourished patients and that proANP may be a relevant plasma biomarker of cardiac dysfunction.

Disclosure of Interest: None Declared

ESPGHAN 2013 - Abstract Submission

NUTRITION, METABOLISM AND EXPERIMENTAL APPROACHES

ESPGHAN13-1167

HEAT TREATMENT OF MILK REDUCES INTESTINAL FUNCTION AND RESISTANCE TO NECROTIZING ENTEROCOLITIS IN PRETERM PIGS

Y. Li [1, 2,*], T. Thymann [1], A. S. Kvistgaard [2], D. E. W. Chatterton [3], P. T. Sangild [1]

[1]Department of Nutrition, Exercise and Sports, Faculty of Science, University of Copenhagen, Frederiksberg, [2]Arla Foods Ingredients Group P/S, Viby J. , [3]Department of Food Science, Faculty of Science, University of Copenhagen, Frederiksberg, Denmark

Please select your preferred presentation type: Oral or Poster
Has this abstract previously been presented?: No
Has this abstract previously been published?: No

Objectives and Study: In preterm infants, exclusive feeding with mother's own milk improves intestinal health and resistance to necrotizing enterocolitis (NEC) relative to infant formula. Donor milk may be less effective because it is obtained at a relatively late stage of lactation, and pasteurization couldreduce its bioactivity. We have previously shown, using a preterm pig model that fresh unpasteurizedbovine colostrum may support gut function and protect against NEC. Part of this beneficial effect may be explained by lack of heat treatment. Hence, we hypothesized that freeze-dried bovine milk powder would show improved bioactivity in preterm pigs, relative to a milk powder produced by pasteurization and spray-drying of bovine milk.

Methods: Seventy-four caesarean-delivered preterm pigs were given parenteral nutrition plus minimal enteral nutrition for two days followed by two days of total enteral nutrition. In experiment 1 (Expt1), freeze-dried bovine mature milk (BM, *n*=13) was compared with fresh bovine colostrum (BC, n=14) and powdered infant formula (IF, *n*=13). In experiment 2 (Expt2), heat-treated whole milk powder (WMP, *n*=15) was compared with freeze-dried BM (n=9) and IF (n=10). The four diets were iso-energetic.

Results: In Expt 1, BM decreased NEC incidence and NEC severity in the small intestine relative to infant formula ($P < 0.05$). Similar to BC, BM significantly improved gut structure (mucosal weight, villus height) and functions (barrier function, nutrient absorption, digestive enzyme activities, colon fermentation), relative to the IF group. Compared with BC, BM was less effective in increasing lactose digestion and absorption, lactase activity and decreasing colon fermentation and tissue IL-8 concentrations. In Expt 2, the processed milk (WMP) showed reduced intestinal NEC resistance, mucosal weight, lactose digestion and lactase activity, relative to BM.

Conclusion: Avoiding heat-treatment of bovine mature milk improves NEC resistance and intestinal structure and functions in preterm pigs, relative to infant formula and whole milk powder. The effects were in most cases similar to those of fresh bovine colostrum although differences were observed with some parameters. Processing of bovine milk (e.g. pasteurization, spray-drying) may significantly reduce the milk bioactivity and this could be particularly detrimental for sensitive newborns, such as preterm infants. Based on these results, we suggest that future efforts should be focused on optimizing thermal treatments of milk to retain beneficial effects.

Disclosure of Interest: Y. Li Industry of: Arla Foods Ingredients Group P/S, T. Thymann: None Declared, A. Kvistgaard Employee of: Arla Foods Ingredients Group P/S, D. Chatterton: None Declared, P. Sangild Grant / Resarch Support from: Arla Foods Ingredients Group P/S

ESPGHAN 2013 - Abstract Submission

NUTRITION, METABOLISM AND EXPERIMENTAL APPROACHES

ESPGHAN13-1301

POSTNATAL AMNIOTIC FLUID FOR NEC PREVENTION: EXPERIENCE FROM PRETERM PIGS

M. V. Østergaard [1,*], J. Siggers [1], R. H. Siggers [1], T. Thymann [1], M. Schmidt [2], S. Purup [3], P. T. Sangild [1], S. B. Bering [1]
[1]Department of Nutrition, Exercise and Sports, Faculty of Science, University of Copenhagen, Frederiksberg, [2] Department of Large Animal Sciences, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, [3]Department of Animal Science, Aarhus University, Tjele, Denmark

Please select your preferred presentation type: Oral or Poster
Has this abstract previously been presented?: No
Has this abstract previously been published?: No

Objectives and Study: Opposite to infant formula, maternal colostrum and milk are rich in bioactive components and protect against necrotizing enterocolitis (NEC) in preterm neonates. Amniotic fluid (AF) contains similar bioactive components including growth, immunomodulatory and antimicrobial factors that stimulate prenatal intestinal development and maturation. We hypothesized that postnatal AF feeding would protect against NEC. We tested the effects of minimal enteral nutrition (MEN) with AF during parenteral nutrition, AF supplementation during full enteral formula feeding or both in our preterm pig model of formula-induced NEC.
Methods: In 3 experiments, a total of 76 preterm pigs were delivered by cesarean section on day 105 of gestation (term day 115) and allocated to 5 treatment groups to test the effects of porcine AF (pAF) and human AF (hAF) as MEN in the parenteral nutrition period (2 d) and in the following enteral formula feeding period (2 d): -/-, -/pAF, pAF/-, hAF/-, pAF/pAF. In an additional experiment, a group of pigs (n=27) received AF as MEN and was euthanized already after the parenteral period: -/0, pAF/0, hAF/0. After euthanasia, the gastrointestinal tracts were evaluated for macroscopic NEC lesions, and mucosal morphology, nutrient uptake capacity and brush-border enzyme activities were analyzed. The effects of pAF and hAF on intestinal epithelial proliferation and migration were tested *in vitro* in IEC-6 cells.
Results: NEC incidence was decreased in pAF/pAF (2/10) compared with -/- pigs (18/40), whereas no effects were observed in -/pAF (7/14) and pAF/- (6/12) pigs. Body weight was increased in pigs receiving AF (pAF or hAF) in the MEN period (pAF/pAF, pAF/-, hAF/-, pAF/0, hAF/0) compared with -/- (P<0.05), whereas -/pAF did not affect body weight. No clear effects of postnatal AF supplementation compared with -/- were identified on mucosal morphology, galactose absorption or brush-border enzyme activities. *In vitro*, pAF and hAF increased proliferation up to 20% and migration up to 150% at a concentration of 15% AF (P<0.01) in IEC-6 cells.
Conclusion: Postnatal feeding with AF reduced NEC susceptibility in preterm pigs when given as MEN and during subsequent enteral formula feeding, but not when given solely as MEN or during enteral formula feeding. The structure and function of the intestine were not improved by postnatal AF feeding, which indicates other mechanisms of function, possibly via inflammatory pathways or the gut microbiota. To fully elucidate the potential of postnatal AF feeding in NEC prevention further studies are needed.

Disclosure of Interest: None Declared

ESPGHAN 2013 - Abstract Submission

NUTRITION, METABOLISM AND EXPERIMENTAL APPROACHES

ESPGHAN13-1312

MILD HEAT TREATMENT DOES NOT REDUCE THE COLITIS-PROTECTIVE EFFECTS OF BOVINE COLOSTRUM IN PRETERM PIGS

A. C. Støy [1,*], P. Sangild [2], K. Skovgaard [1], T. Thymann [2], M. Bjerre [3], D. Chatterton [2], S. Purup [4], M. Boye [1], M. Schmidt [2], P. Heegaard [1]

[1]Technical University of Denmark, [2]University of Copenhagen, Frederiksberg, [3]Aarhus University, Aarhus, [4]Aarhus University, Tjele, Denmark

Please select your preferred presentation type: Poster only
Has this abstract previously been presented?: No
Has this abstract previously been published?: No

Objectives and Study: Fresh bovine colostrum (BC) prevents development of necrotizing enterocolitis (NEC) in preterm pigs. Spray drying and pasteurization are required to use BC in clinical settings but this may also reduce its bioactivity. In studies on preterm pigs, we compared raw BC with spray dried and pasteurized BC.

Methods: Preterm pigs were fed total parenteral nutrition for 2 days, followed by two boluses of milk formula (15 mL/kg/3h) and continued enteral feeding with milk formula (FORM, n = 14), fresh BC (COLOS, n = 14), spray dried, powdered BC (POW, n = 8), or spray dried, pasteurized BC (POWPAS, n = 9). Pigs were euthanized after two days of enteral feeding and NEC lesions, intestinal structure, digestive and absorptive functions, microbiota, and tissue protein and mRNA levels of immune factors were analyzed. Finally, we determined the concentrations of some bioactive proteins in the colostrum products and studied treatment-related aggregation of proteins.
Results: POW and POWPAS pigs showed lowered gut NEC severity, IL-1β and IL-8 levels and lactic acid levels, and higher intestinal villus heights, hexose absorption, hydrolase activities (lactase, maltase, peptidases) than FORM pigs (all $P < 0.05$). These values in POW and POWPAS groups were similar to those in the COLOS group. Intestinal expression of *IL1B*, *IL6* and *IL8* and bacterial abundance score were positively correlated with NEC severity ($P < 0.05$). Spray drying, and especially pasteurization, increased the breakdown of growth factors (TGF-β1 and -β2) and aggregation of milk proteins.
Conclusion: Spray drying and pasteurization affect BC proteins but such treatments do not necessarily decrease its trophic and anti-inflammatory effects on the immature intestine. It remains to be studied if such colostrum products also improve gut maturation in preterm infants.

Disclosure of Interest: A. C. Støy: None Declared, P. Sangild Grant / Resarch Support from: Biofiber-Damino, Gesten, Denmark, K. Skovgaard: None Declared, T. Thymann: None Declared, M. Bjerre: None Declared, D. Chatterton: None Declared, S. Purup: None Declared, M. Boye: None Declared, M. Schmidt: None Declared, P. Heegaard: None Declared

ESPGHAN 2013 - Abstract Submission

CLINICAL NUTRITION

ESPGHAN13-1492

CHEMOTHERAPY-INDUCED GASTROINTESTINAL TOXICITY IN MILK-FED PIGLETS

R. L. Shen [1,*], P. E. L. Pontoppidan [1], P. Jiang [1], T. Thymann [1], R. K. Buddington [2], K. Müller [3, 4], P. T. Sangild [1]
[1]Department of Nutrition, Exercise and Sports, University of Copenhagen, Copenhagen, Denmark, [2]Department of Health and Sports Sciences, University of Memphis, Memphis, United States, [3]Department of Pediatrics, [4]Institute for Inflammation Research, Rigshospitalet Copenhagen University Hospital, Copenhagen, Denmark

Please select your preferred presentation type: Oral or Poster
Has this abstract previously been presented?: No
Has this abstract previously been published?: No

Objectives and Study: Gastrointestinal toxicity remains a clinical problem for patients subjected to chemotherapy. Little is known about gut structure and function in such patients, and the relations to clinical outcomes. The objective of this study was to develop a piglet model for chemotherapy-induced gut toxicity and the responses to different diets.
Methods: Experiment 1. Nine-day-old piglets were given doxorubicin (single dose, i.v., 75 mg/m^2, DOX1, n=9) or saline (Control, n=8). The piglets were fed a milk-replacer for 9 days before being euthanized for tissue collection. Experiment 2. Seven-day-old piglets were given doxorubicin (single dose, i.v., 100 mg/m^2, DOX2, n=18) or saline (Control, n=14) and euthanized 6 days later for tissue collection. The piglets were distributed into groups fed bovine colostrum (DOX2-COL and Control-COL, both n=9) or a bovine milk formula (DOX2-FORM and Control-FORM, both n=7). For all pigs, diarrhea scores and body weight were recorded before and after treatment. Intestinal dimensions and digestive enzyme activities were measured by the end of the experiments as markers of intestinal damage.
Results: Experiment 1. During the study, diarrhea was more frequent in DOX1 pigs vs. controls (100 vs. 33%, $p<0.05$). Relative to Controls, the DOX1 pigs showed reduced growth rate (7 vs. 37 g/kg/d), reduced weight of the intestine (40.4 vs. 48.4 g/kg) and colon (9.6 vs. 13.4 g/kg) (all $p<0.05$). DOX1 reduced activity of dipeptidyl peptidase IV (DPPIV) and lactase, and increased sucrase activity in the distal intestine (all $p<0.05$). Villus heights and amount of mucosa were not affected. Experiment 2. Diarrhea was more frequent in DOX2 pigs vs. controls (67 vs. 22%, $p<0.05$), and DOX2 pigs had lower growth rate (20 vs. 35 g/kg/d, $p<0.05$), weight of the intestine (31.7 vs. 40.6 g/kg $p<0.05$) and colon (11.5 vs. 13.5 g/kg, $p=0.09$), with no consistent effects of diet. However, DOX2-COL pigs showed increased villus heights, increased activity of sucrase, maltase, and lactase in the proximal intestine, and increased DPPIV activity in the distal intestine (all $p<0.05$), compared with the three other groups.
Conclusion: Milk-fed piglets show clinical and tissue response to doxorubicin that are similar to chemotherapy-induced toxicity symptoms in patients. Gut structural damage may be most pronounced within 6 days of treatment while clinical symptoms continue after this time. Increased structural and functional parameters in the DOX2-COL pigs indicate that gut restitution after chemotherapy may be enhanced by colostrum feeding.

Disclosure of Interest: None Declared

ESPGHAN 2013 - Abstract Submission

GI INFECTIONS

ESPGHAN13-1503

ESCHERICHIA COLI MODEL OF DIARRHEA IN NEWBORN PIGS

M. L. Jensen [1,*], S. O. Petersen [1], M. S. Cilieborg [1], S. B. Bering [1], P. T. Sangild [1]

[1]Department of Nutrition, Exercise and Sports, Faculty of Science, University of Copenhagen, Frederiksberg, Denmark

Please select your preferred presentation type: Poster only

Has this abstract previously been presented?: No

Has this abstract previously been published?: No

Objectives and Study: Enterotoxigenic *Escherichia coli* causes diarrhea in infants worldwide. Reliable animal models of pathogen-induced diarrhea are of importance to investigate preventive dietary effects. *E. coli* F18 is a common porcine pathogen causing diarrhea in newly-weaned pigs. We have previously shown that artificially-reared newborn pigs deprived of sow's milk from birth, show high susceptibility to *E. coli* F18. We hypothesized that neonatal *E. coli* F18-induced diarrhea is dose-dependent and that bovine colostrum and maternal flora reduces the disease severity.

Methods: Term pigs were delivered by cesarean section. In experiment 1, pigs were fed infant formula (Milex, Arla Foods) and inoculated with either no bacteria (controls, n=8) or a low (n=9), medium (n=7) or high (n=7) dose of *E. coli* F18 ($1x10^7$, $2x10^8$ and $8x10^9$ CFU/d, respectively) for 5 days. In experiment 2, pigs were kept for 8 days and received either no bacteria (controls, n=7), *E. coli* F18 ($2.6x10^{11}$ CFU/d, n=7), *E. coli* F18 ($2.6x10^{11}$ CFU/d) plus maternal flora on day 1 ($4x10^7$ CFU, n=5), and *E. coli* F18 ($2.6x10^{11}$ CFU/d) plus 50% dietary substitution of the Milex formula with bovine colostrum (n=4). The degree of diarrhea, body weight, amount of mucosa, intestinal permeability, hexose absorption and density of adherent bacteria were determined.

Results: In experiment 1, increasing doses of F18 increased the incidence of diarrhea ($p<0.05$). Amount of mucosa and intestinal permeability did not differ. In experiment 2, all groups inoculated with *E. coli* F18 had more diarrhea than control pigs ($p<0.05$). Co-inoculation with maternal fecal flora or inclusion of bovine colostrum in the enteral formula diet had no effect on diarrhea outcome or any other measured parameters.

Conclusion: Artificially-reared, caesarean-delivered pigs are highly susceptible to diarrhea induced by *E. coli* F18. The effect is dose-dependent but less affected by the birth colonization (maternal fecal flora) and protective diets such as bovine colostrum. The newborn pig may be a useful model to investigate dietary components preventing *E Coli* diarrhea in newborn infants.

Disclosure of Interest: None Declared

ESPGHAN 2013 - Abstract Submission

NUTRITION, METABOLISM AND EXPERIMENTAL APPROACHES

ESPGHAN13-1440

PROBIOTICS MAY INCREASE THE SENSITIVITY TO PATHOGEN-INDUCED DIARRHEA IN NEWBORN PIGS

M. S. Cilieborg [1,*], A. D. Andersen [2], M. L. Jensen [1], S. O. Petersen [1], P. T. Sangild [1]

[1]Department of Nutrition, Exercise and Sports, Faculty of Science, University of Copenhagen, [2]Microbial ecology, Technical university of Denmark, Frederiksberg, Denmark

Please select your preferred presentation type: Oral or Poster

Has this abstract previously been presented?: No

Has this abstract previously been published?: No

Objectives and Study: Pathogen induced diarrhea in neonates is a problem worldwide. Probiotics may improve gut colonization and intestinal health in neonates and thereby prevent diarrhea, but the effects are highly strain-dependent. We hypothesized that early administration of two probiotic bacteria, *Pediococcus pentosaceus* (PEP) and *Lactobacillus paracasei*(LAP) would reduce infectious diarrhea in neonates. To test this, we used an infection model in newborn piglets inoculated daily with a porcine pathogen, *E. coli* F18

Methods: Fifty-nine caesarean-delivered newborn pigs were fitted with umbilical catheters and orogastric feeding tubes. Parenteral nutrition was given for 24 h followed by full enteral formula feeding (15 mL/kg/3h) until euthanasia on day 5. To standardize initial gut colonization, maternal fecal slurry (1 mL, 2×10^7 cfu) was inoculated immediately after birth. From day one, pigs received *E. coli* F18 (10^{10} cfu/d) or water combined with PEP (10^{10}cfu/d) or LAP (10^8 cfu/d) or placebo. This resulted in five bacteria inoculated groups: F18, F18-PEP, F18-LAP, PEP, LAP (all n=10) and controls (n=9). Pigs were weighed daily and feces was scored twice daily (normal feces = 1, pasty feces = 2, droplets of diarrhea = 3, moderate diarrhea = 4, intense diarrhea = 5)

Results: Diarrhea was noted in 34, 30, 11, 4, 0 and 2% of the total observations in the F18-PEP, F18-LAP, F18, PEP, LAP and control group, respectively ($P<0.01$ for group effect), and their corresponding fecal scores were 0.8±0.3, 1.6±0.4, 1.4±0.5, 0.5±0.2, 0.3±0.1 and 0.4±0.1. Pigs given *E. coli* F18 had significantly more diarrhea than pigs not given the pathogen and both probiotic bacteria potentiated the *E. coli* F18-induced diarrhea ($P<0.05$). Compared with healthy pigs (n=47), pigs with diarrhea (with ≥2 observations of fecal score 4) showed a significant increases in mean fecal score (2.9±0.2 vs. 0.4±0.0), reduced weight gain (-3.5±18.5 vs. 108.0±9.3 g) and higher intestinal permeability measured as the urinary lactulose/mannitol ratio (0.11±0.05 vs. 0.02±0.00) (all $p<0.05$). Pigs with diarrhea also had more blood lymphocytes and monocytes (49.4±2.9 and 4.5±0.6 vs. 43.1±1.5 and 2.8±0.3%, $P=0.06$ and $P<0.01$, respectively) and less neutrophils (43.1±3.3 vs. 52.6±1.7, $P<0.05$).

Conclusion: Both probiotic bacteria increased the sensitivity to diarrhea induced by the porcine pathogen, *E. coli* F18. The results suggest that probiotics may cause unexpected detrimental effects in the un-colonized intestine of sensitive newborns and should be given with caution to vulnerable groups of newborn infants.

Disclosure of Interest: None Declared

ESPGHAN 2013 - Abstract Submission

CLINICAL NUTRITION

ESPGHAN13-1539

HUMAN MILK AND BOVINE COLOSTRUM DECREASE INCIDENCE OF NECROTIZING ENTEROCOLITIS IN PIGS

M. L. Jensen [1,*], P. T. Sangild [1], M. Lykke [1], M. Schmidt [2], T. Thymann [1]

[1]Department of Nutrition, Exercise and Sports, Faculty of Science, University of Copenhagen, [2]Department of Reproduction, Faculty of Health and Medical Sciences, University of Copenhagen, Frederiksberg, Denmark

Please select your preferred presentation type: Oral or Poster

Has this abstract previously been presented?: No

Has this abstract previously been published?: No

Objectives and Study: Preterm birth and formula feeding predispose to development of necrotizing enterocolitis (NEC) in infants. As mother's milk is often absent following preterm delivery, artificial milk formula or human donor milk are used as alternatives. We hypothesized that human donor milk may provide similar NEC-preventive effects in preterm pigs, as bovine colostrum.

Methods: Preterm pigs delivered by cesarean section received 2 days of total parenteral nutrition, followed by 2 days of total enteral feeding (15 mL/kg/3h) with bovine colostrum (BC, n=13), human donor milk (HM, n=13) or infant formula (IF, n=14) provided at isoenergetic levels. Following an in vivo hexose absorption test, pigs were euthanized on day 5 and the gastrointestinal tract was collected to record intestinal NEC lesions (macroscopic scores 1-6, NEC defined as score ≥ 3), histopathology (necrotic cells, congestion, hyperemia, subepithelial edema and loss of villi/epithelia), digestive enzyme activities and tissue concentrations of IL-6 and IL-8.

Results: Relative to IF, pigs fed BC or HM showed higher body weight gain (+22 g/d), more intestinal mucosa (+16%), higher activity of six digestive enzymes (+67-175%), higher hexose absorptive capacity (+400%), all $P<0.05$. This was associated with lower prevalence of histopathologic lesions in the distal small intestine and colon (overall range -41% to -82%) and lower NEC incidence in BC and HM pigs vs. IF (both 7/13 vs.13/14, $P<0.05$). All parameters were similar between BC and HM pigs, except that BC pigs showed increased crypt depth (+32%) and higher aminopeptidase N activity (+22%) relative to HM pigs ($P<0.01$). Relative to IF pigs, IL-6 and IL-8 levels were lower in HM pigs (-86 and -29% respectively, $P<0.05$) and IL-8 tended to be lower in BC pigs (- 31%, $P=0.06$).

Conclusion: Bovine colostrum and human milk are superior to formula with regards to effects on gut structure, function and NEC resistance in preterm pigs. Bovine colostrum may be a relevant nutritional alternative to mother's milk in sensitive newborn infants if human milk is unavailable. Further studies are required to study the effects of milk from different species, gestational ages, lengths of lactation, and product treatments (e.g. pasteurization, freezing).

Disclosure of Interest: None Declared

ESPGHAN 2013 - Abstract Submission

NUTRITION, METABOLISM AND EXPERIMENTAL APPROACHES

ESPGHAN13-1563

PREMATURITY REDUCES FUNCTIONAL ADAPTATION TOINTESTINAL RESECTION IN PIGLETS

L. Aunsholt [1,*], T. Thymann [2], N. Qvist [3], D. Sigalet [4], S. Husby [1], P. T. Sangild [2]

[1]Hans Christian Andersen Childrens Hospital, Odense University Hospital, Odense , [2]Department of Nutrition, Exercise and Sports, University of Copenhagen, Copenhagen, [3]Department of Surgery, Odense University Hospital, Odense , Denmark, [4]Department of Surgery, University of Calgary, Calgary, Alberta , Canada

Please select your preferred presentation type: Oral or Poster
Has this abstract previously been presented?: No
Has this abstract previously been published?: No

Objectives and Study: Necrotizing enterocolitis and congenital gastrointestinal disorders in infants often require intestinal resection, with subsequent risk of short bowel syndrome (SBS), especially with a dysfunctional colon. Intestinal adaptation is an important prognostic factor and we hypothesized thatadaptation to resection is diminished in preterm versus term neonates. To test the hypothesis, we studied adaptation in a novel model of SBS using preterm and term piglets with a jejunostomy.

Methods: Term or preterm two-day-old piglets were subjected to 50% distal intestinal resection with placement of a jejunostomy. For 4-5 days, resected piglets were given parenteral nutrition with gradually increasing doses of enteral nutrition. Samples of intestine were collected at birth, 2 and 6-7days to measure structural parameters and digestive enzyme activity.

Results: Preterm and term piglets showed similar increase from birth to 2days in intestinal weight and digestive enzyme activities (sucrase, maltase, and peptidases). At 6-7days, the remnant intestine had a similar density (g/cm) and mucosal mass in both groups. Villous height, crypt depth, enzyme activities (sucrase, maltase, DPPIV) and hexose uptake capacity were greater in term versus preterm pigs (all $P<0.05$). Clinically, preterm piglets were more vulnerable to resection in terms of hypoglycemia, respiratory distress, dehydration and circulatory instability. Consequently, more preterm than term pigs were euthanized prior to the end of the protocol (8/14 vs. 2/10, $P=0.13$).

Conclusion: Studies on intestinal adaptation after resection in neonates is feasible using preterm and term piglets, but extensive clinical care is required, especially for resected preterm pigs. Physiological instability and developmental immaturity may explain that intestinal functional adaptation after resection is less pronounced in preterm versus term neonates.

Disclosure of Interest: None Declared

ESPGHAN 2013 - Abstract Submission

NUTRITION, METABOLISM AND EXPERIMENTAL APPROACHES

ESPGHAN13-1577

EFFECT OF BOVINE COLOSTRUM ON ADAPTATION AFTER INTESTINAL RESECTION IN NEWBORN PIGS AND HUMAN INFANTS

L. Aunsholt [1,*], N. Qvist [2], P. T. Sangild [3], A. Vegge [3], B. Stoll [4], D. G. Burrin [4], P. B. Jeppesen [5], T. Eriksen [6], S. Husby [1], T. Thymann [3]

[1]Hans Christian Andersen Childrens hospital, [2]Department of Surgery, Odense University Hospital, Odense , [3] Department of Nutrition, Exercise and Sports, Faculty of Science, University of Copenhagen, Copenhagen, Denmark, [4] Department of Paediatrics, Baylor College of Medicine, Houston, United States, [5]Department of Gastroenterology, Copenhagen University Hospital, Copenhagen, [6]Department of Veterinary Clinical and Animal Sciences, University of Copenhagen, openhagen, Denmark

Please select your preferred presentation type: Oral or Poster
Has this abstract previously been presented?: No
Has this abstract previously been published?: No

Objectives and Study: Minimal enteral nutrition may stimulate gut adaptation following intestinal resection, whether this depends on the nature of enteral diet is unknown. Bovine colostrum contains trophic and immuno-modulatory factors and may stimulate adaptation better than a standard formula. We hypothesized that minimal enteral nutrition could stimulate intestinal adaptation in neonates, and that bovine colostrum was superior to a milk-formula.
Methods: Experiment 1: Three- d-old piglets subjected to resection of 50% of the intestine were given total parenteral nutrition (CONTROL, n=9) or parenteral nutrition supplemented with minimal enteral feeding of bovine colostrum (COL, n=5) or formula (FORM, n=6) for 7 days. Effects were assessed by a 24-hour nutrient balance study as well as intestinal histological and functional endpoints. Experiment 2: Feasibility of using bovine colostrum for humans was assessed by randomizing newborn infants subjected to intestinal resection to receive colostrum (n=5) or not (n=5) as minimal enteral nutrition. Clinical symptoms and biomarkers of allergy were collected.
Results: In experiment 1 relative wet weight absorption was higher in COL versus CONTROL pigs (52.5 ± 5.80% and 22.7 ± 6.80 %, $p < 0.05$). Relative Na^+ absorption was higher in COL and FORM versus CONTROL (-447 ± 65%, -655 ± 76% versus -916 ± 82%, $p< 0.05$).
In experiment 2, colostrum was well tolerated and did not induce allergy in infants.
Conclusion: Minimal enteral nutrition improved gut adaptation with limited effects of type of diet. Bovine colostrum was well-tolerated in newborn piglets and infants after intestinal resection.

Disclosure of Interest: None Declared

ESPGHAN 2013 - Abstract Submission

CLINICAL NUTRITION

ESPGHAN13-1644

A NUTRITION-RELEVANT COGNITION-BEHAVIOR MODEL IN NEWBORN PIGLETS

M. M. Maibom [1,*], S. O. Petersen [1], T. Thymann [1], A. M. Plomgaard [2], G. Greisen [2], C. Thomsen [2], P. T. Sangild [1]
[1]University of Copenhagen, Frederiksberg C, [2]Copenhagen University Hospital, Copenhagen, Denmark

Please select your preferred presentation type: Oral or Poster
Has this abstract previously been presented?: No
Has this abstract previously been published?: No

Objectives and Study: Nutrition is important for early maturation of the gut and the brain. Lack of mother´s milk or specific nutrients, may inhibit infant brain development, but the most sensitive stages of development and the responsible diet factors remain unknown. We hypothesized that preterm and term newborn pigs can be used to document diet-related neurodevelopmental functional and structural outcomes.
Methods: Clinical variables and brain-related functions were followed in preterm and term newborn piglets after different nutritional regimens. Term pigs were sow-reared for 3 days and fed formula for 4 weeks with a standard or low protein level (46 or 23 g/L, n=36). Clinical variables, physical activity, and a visual discrimination test were used to investigate neurodevelopmental outcome. Preterm pigs were delivered at 90% gestation and fed increasing doses of bovine colostrum or infant formula until day 12 of life (n=8).
Results: Newborn term pigs are mobile and have open eyes within a few minutes of birth. Feeding a low protein diet to 3-20 d-old term pigs reduced the body weight gain (7 vs. 15 g/kg/d, $P<0.05$), but this did not affect the number of trials taken to reach competent visual discrimination in the test cage (70±3 vs. 60±10 trials, $P=0.67$). Competence was defined as 80% correct learning responses in 10 consecutive trials. No differences were observed in total brain weight (46.7±0.8 vs. 46.6±0.7 g), relative to controls. Preterm, low birth weight piglets (700-900 g) showed signs of neurodevelopmental immaturity during the first days after birth as reflected by delayed and unstable locomotion, slow eyelid opening and poor sucking reflexes. Colostrum-fed preterm pigs were more active (67 vs. 55% activity time during the first 12 days, $P<0.05$) and developed sucking reflexes earlier, relative to formula-fed pigs (78 vs. 168 h, $P<0.05$). One week-old preterm pigs showed explorative behavior in the visual discrimination test cage, and some limited capacity to understand the test at 3 weeks of age. Magnetic resonance imaging (MRI) of the brain showed increased brain myelination in 12 d-old vs. newborn preterm pigs (each n=2), but both groups had markedly less myelination than term pigs of a similar postnatal age.
Conclusion: The newborn pig may be a suitable model to study diet effects on infant neuronal development. Moderate protein undernutrition does not affect cognitive performance in term pigs. Preterm pigs show impaired and diet-dependent behavioral characteristics that may reflect their immature brain structure and function.

Disclosure of Interest: None Declared

ESPGHAN 2013 - Abstract Submission

NUTRITION, METABOLISM AND EXPERIMENTAL APPROACHES

ESPGHAN13-1662

INFANT FORMULA WITH REDUCED PROTEIN CONTENT AND OPTIMIZED AMINO ACID COMPOSITION DOES NOT COMPROMISE GROWTH OR ORGAN DEVELOPMENT IN PIGLETS

M. Lykke [1,*], T. Thymann [1], H. V. Goudoever [2], B. Koletzko [3], E. V. D. Beek [4], B. Pennings [5], M. Abrahamse [5], B. Stoll [6], D. Burrin [6], P. Sangild [1]

[1]University of Copenhagen, Frederiksberg C, Denmark, [2]VU University Medical Center, Amsterdam, Netherlands, [3]Ludvig-Maximilian University of Munich, Munich, Germany, [4]Danone research center for specialized nutrition, Singapore, Singapore, [5]Danone research center for specialized nutrition, Wageningen, Netherlands, [6]Children´s Nutrition Research Centre, Houston, United States

Please select your preferred presentation type: Oral or Poster
Has this abstract previously been presented?: No
Has this abstract previously been published?: No

Objectives and Study: Excess protein intake in early life has been related to later life development of obesity and metabolic syndrome. We tested whether a modified infant formula with 20% less protein and with an optimized amino acid (AA) composition based on recent studies in infants, would display similar growth rate and organ development, relative to a standard formula. We used artificially-reared piglets on restricted dietary intake as a model for infant growth because of their high sensitivity to dietary AA, related to fast growth in early life.

Methods: Seven day-old piglets were fed isoenergetic amounts of an AA-based formula for 14 days (700 kJ/kg/d) with a standard suboptimal protein level (100%, 8 g/kg/d n=22), 20% less protein (80%, n=19), 20% less protein and optimized AA composition (80% opt AA, n=17) or 50% less protein (50%, n=13). Growth rate, body composition, organ weights and intestinal brush border enzyme activities were measured.

Results:

	Protein intake, g/kg/d	Weight gain, g/kg/d	Protein efficiency, Weight gain/protein intake
100%	7.68	14.85	1.93
80%	6.08	13.88	2.28
80% opt AA	6.14	15.38	2.50**
50%	3.80	7.80*	2.05

Body weight gain was significantly reduced in the 50% group (*P<0.05, -50%, Table), relative to the three other groups which showed comparable growth. The efficiency of utilization of protein was higher in the 80% opt. AA versus the 100% group (**P<0.01, +30%, Table). Organ weights showed no differences among groups, except for kidney weight that was reduced in the 50% group. This group also showed decreased blood platelet count and increased platelet volume at day 7, compared with the 100% group. No other differences were seen in hematology, fat mass and fat-free mass. The 50% group showed lowered bone accretion compared with the other groups. Groups with reduced protein did not show any decreases in activities of six brush border enzymes, compared with the 100% group.

Conclusion: No developmental effects were detected when reducing the protein content to 80% of a standard formula. This suggests that 20% reduction of the protein load with an optimal AA composition does not induce any acute growth deficits or disproportional growth effects in young artificially-reared pigs fed a restricted diet.

Disclosure of Interest: None Declared

ESPGHAN 2013 - Abstract Submission

NUTRITION, METABOLISM AND EXPERIMENTAL APPROACHES

ESPGHAN13-1669

EARLY LIFE MALNUTRITION INDUCES GUT ATROPHY AND INCREASE HEPATIC FAT INFILTRATION IN A PAEDIATRIC PIGLET MODEL

M. Lykke [1,*], A. Hother [1], P. Sangild [1], K. F. Michaelsen [1], C. Mølgaard [1], T. Thymann [1]

[1]Department of Nutrition, Exercise and Sport, University of Copenhagen, Frederiksberg C, Denmark

Please select your preferred presentation type: Oral or Poster

Has this abstract previously been presented?: No

Has this abstract previously been published?: No

Objectives and Study: Temporal changes leading to moderate or severe acute malnutrition in infants is poorly understood although it remains a tremendous problem in many developing countries. Our objective was to develop a prospective study of nutritional depletion using a pig model. We specifically aimed to describe changes in growth parameters and blood profile measurements as well as end stage markers of function and structure of the gut and liver.

Methods: Four-week old pigs were weaned from their mothers and given *ad libitum* access to either pure maize flour (maize, n=12) or a nutritionally optimized diet (reference, n=12). Weekly blood samples and growth parameters including body weight (BW), crown-rump length (CRL), thoracic circumference (TC) and length of the metatarsus (LM) were collected. Blood was sampled weekly for haematology and biochemical profiling. After 7 weeks, pigs were euthanized and intestinal and hepatic morphology, brush border enzyme activity and triglyceride content of the liver were measured.

Results: Relative to reference group, body weight of maize-fed pigs was reduced from 2 weeks onwards with final bodyweights of 8.2 kg vs. 29.7 kg at 7 weeks ($P<0.001$). Similar patterns were seen for CRL, TC and LM. Blood alanine aminotransferase (ALAT) and bilirubin levels were increased in maize pigs from week 3 and 1, respectively ($P<0.001$), while albumin levels were reduced from week 1 ($P<0.05$) and dropping to 20 g/L in week 7 ($P<0.001$). After 4 weeks haemoglobin concentration, mean cell volume and hematocrit were reduced in the maize pigs ($P<0.01$) with increasing clinical signs of anemia throughout the study period. There was lower villous height and crypt depth in maize-fed pigs ($P<0.001$) and lower brush border activity of lactase and aminopeptidase A ($P<0.05$). Activity of sucrase, maltase, aminopeptidase N and dipeptidylpeptidase IV were not affected. Liver triglyceride content tended to be higher in maize pigs ($P=0.05$) and was associated with histopathological changes in hepatic tissue.

Conclusion: Feeding pure maize for 7 weeks induces severe stunting and mild to moderate wasting. Changes in levels of blood cells, ALAT, bilirubin and albumin were evident from an early stage. Malnutrition induces gut atrophy but largely maintains mucosal function in terms of digestive enzyme activity. Hepatic fat infiltration and increasing levels of ALAT, bilirubin and decreased levels of albumin suggest progression of liver disease which is commonly seen in children with severe acute malnutrition. This model provides information about changes during the course of malnutrition, which is helpful to device refeeding strategies to restore normal physiological function after malnutrition.

Disclosure of Interest: None Declared

ESPGHAN 2013 - Abstract Submission

CLINICAL NUTRITION

ESPGHAN13-1744

UNDERNUTRITION CAUSES CARDIAC DYSFUNCTION IN A PIGLET MODEL

C. Fabiansen [1], M. Lykke [1], A.-L. Hother [1], I. Hunter [2], J. Koch [2], J. P. Gøtze [3], O. B. Nielsen [4], H. Friis [1], P. T. Sangild [5], T. Thymann [6,*]

[1]Department of Nutrition, Exercise and Sports, Faculty of Science, [2]Department of Veterinary Clinical and Animal Sciences, University of Copenhagen, Frederiksberg C, [3]Department of Clinical Biochemistry, Copenhagen University Hospital, Copenhagen, [4]Department of Biomedicine, Aarhus University, Aarhus, [5]Department of Nutrition, Exercise and Sports, Faculty of Science, Copenhagen University Hospital, Frederiksberg C, [6]Department of Nutrition, Exercise and Sports, Faculty of Science, University of Copenhagen, Copenhagen, Denmark

Please select your preferred presentation type: Oral or Poster
Has this abstract previously been presented?: No
Has this abstract previously been published?: No

Objectives and Study: The association between undernutrition and cardiac function in pediatric patients is still poorly understood. A possible link is important for an estimated 60 million children up to 5 years of age that are suffering from undernutrition. The objective of this study was to investigate cardiac function with respect to undernutrition, using an experimental piglet model.

Methods: Four-week old piglets were given *ad libitum* access to either a low-nutrient diet consisting of pure maize flour (MAIZE, n=12) or a control diet (CON, n=12) for 7 weeks. Temporal changes in plasma levels of pro-atrial natriuretic peptide (proANP) and troponin T (TNT) were measured as markers for cardiovascular disease. Echocardiography was performed at 7 weeks when cardiac tissue was collected for analysis of Na/K ATPase density. For comparison, echocardiography was also performed on a reference control group consisting of pigs with a body weight similar to maize-fed pigs without undernutrition.

Results: Body weight was lower in MAIZE relative to CON pigs (-72%, $P<0.001$). There was an initial decline in proANP for both MAIZE and CON pigs during the first 3-4 weeks, then a marked increase in MAIZE pigs at 5-7 weeks, relative to CON pigs ($P<0.05$). Likewise, mean TNT tended to be higher in MAIZE ($P=0.07$) suggesting myocardial damage. Echocardiography, as indicated by the myocardial performance index, showed left ventricle dysfunction in MAIZE relative to both weight- and age-matched control pigs. Heart to body weight ratio was similar between groups but the heart had a flabby appearance in the MAIZE group. Myocardial Na/K ATPase levels were 50% higher in MAIZE vs. age-matched control pigs ($P<0.01$).

Conclusion: Undernutrition in a piglet model causes adverse cardiac remodeling and dysfunction. The results suggest that assessment of cardiac function is important in undernourished patients and that proANP may be a relevant plasma biomarker of cardiac dysfunction.

Disclosure of Interest: None Declared

ESPGHAN 2013 - Abstract Submission

NUTRITION, METABOLISM AND EXPERIMENTAL APPROACHES

ESPGHAN13-1412

SHORT-TERM EFFECTS OF HUMAN MILK OLIGOSACCHARIDES IN A PRETERM PIG MODEL OF NECROTIZING ENTEROCOLITIS

S. O. Petersen [1,*], M. M. Maibom [1], Y. Li [1], T. Thymann [1], P. T. Sangild [1], S. B. Bering [1] and Clinical and Experimental Nutrition group, Faculty of Science, University of Copenhagen, Denmark

[1]Department of Nutrition, Exercise and Sports, University of Copenhagen, Denmark, Faculty of Science, University of Copenhagen, Denmark, Copenhagen, Denmark

Please select your preferred presentation type: Oral or Poster

Has this abstract previously been presented?: No

Has this abstract previously been published?: No

Objectives and Study: Human milk oligosaccharides (HMO) may mediate a major part of the known prebiotic and anti-inflammatory effect of human milk in the newborn intestine. Such effects may be particularly important for immature newborns that are highly sensitive to microbiota- and diet-induced inflammatory insults. We hypothesized that initial feeding with an HMO-enriched formula diet just after birth would improve the short-term resistance to diarrhea and necrotizing enterocolitis (NEC) in preterm pigs.

Methods: For five days after birth, caesarean-delivered preterm pigs were fed increasing doses (3-15 mL/kg/3 h) of a maltodextrin-based enteral milk formula, with (n=17) or without (n=15) an HMO mixture (5.0 g/L formula). Clinical conditions, NEC lesions, amount of mucosa and organ weights were recorded on day 5.

Results: Mean NEC incidence was lower in the HMO group, relative to controls but the difference did not reach statistical significance (35 vs. 53%). Mucosal weight in the proximal intestine was elevated in the HMO pigs ($p<0.05$), while body weight, organ weights and diarrhea scores were similar.

Conclusion: HMO-enriched formula may induce a moderate positive effect on NEC incidence, possibly by increasing mucosal growth in the proximal intestine. Inclusion of HMO in milk formula did not improve the short term diarrhea resistance or organ development. More long term studies, using different HMO combinations and doses, are required to verify how HMOs support defense against bacterial pathogens and inflammatory conditions in the sensitive newborn intestine.

Disclosure of Interest: None Declared

ESPGHAN 2013 - Abstract Submission

GI MOTILITY AND FUNCTIONAL GI DISORDERS

ESPGHAN13-1727

A GLUCAGON-LIKE PEPTIDE 2 ANALOGUE INCREASES BODY WEIGHT AND GUT GROWTH IN NEWBORN PIGS SUBJECTED TO INTESTINAL RESECTION

T. Thymann [1,*], B. Stoll [2], D. G. Burrin [2], A. Vegge [1], N. Qvist [3], P. B. Jeppesen [4], T. Eriksen [5], H. Heinze [6], L. Mecklenburg [6], P. T. Sangild [1]

[1]Department of Nutrition, Exercise and Sports, Faculty of Science, University of Copenhagen, Copenhagen, Denmark, [2] Department of Paediatrics, Baylor College of Medicine, Houston, United States, [3]Department of Surgery, Odense University Hospital, Odense , [4]Department of Gastroenterology, Copenhagen University Hospital, Copenhagen, [5] Department of Veterinary Clinical and Animal Sciences, University of Copenhagen, Frederiksberg C, Denmark, [6] Nycomed GmbH, Konstanz, Germany

Please select your preferred presentation type: Oral or Poster
Has this abstract previously been presented?: No
Has this abstract previously been published?: No

Objectives and Study: Pediatric short bowel syndrome (SBS) following gut resection results from a variety of etiologies. Reports from pediatric SBS patients indicate that the endogenous level of the intestinotrophic factor glucagon-like peptide 2 (GLP-2) is decreased. The long-acting synthetic human GLP-2 analogue, teduglutide (ALX-0600, Nycomed GmbH) is effective in adult SBS patients whereas less is known from pediatric SBS patients. We tested the efficacy of teduglutide in a neonatal piglet jejunostomy model of SBS that exhibits a deficient endogenous GLP-2 secretion.
Methods: Two-day old, term pigs were subjected to resection of 50% of the small intestine starting from the ileo-cecal junction, and the remnant proximal intestine was exteriorized on the abdominal wall as a jejunostomy. All pigs were subsequently given total parenteral nutrition for 7 days and a single daily injection of the following doses of teduglutide: 0.01 (n=6); 0.02 (n=6); 0.1 (n=5) or 0.2 mg/kg/day (n= 6) and compared with placebo (n=9). Digestive capacity was studied during a 24 h enteral nutrition balance study where stoma output was collected quantitatively.
Results: A regression analysis showed dose-dependent increase in weight per length of the remnant intestine ($P<0.01$). Body weight increment was similar for all four teduglutide groups but higher than for placebo pigs ($P<0.05$). Activity of disacharidases and aminopeptidases in the intestinal mucosa was similar for all groups and digestive capacity was not affected by the end of the experiment. Villus heights and crypt depths were numerically higher in teduglutide groups but not significantly different from placebo. Immunohistochemistry showed no apparent differences in the staining intensities for Ki67 (cell proliferation), villin, fatty acid binding protein, chromogranin A and GLP-2 receptor in the remnant intestine. Pharmacokinetic measurements after teduglutide injection showed a plasma half-life of ≈ 30 min during the elimination phase.
Conclusion: A single daily injection of teduglutide dose-dependently increases the weight per length of the neonatal remnant intestine after distal gut resection, but has limited effect on intestinal function. Significant effects of teduglutide on nutrient digestion and gut function may require a longer adaptation period and/or a more frequent administration of the peptide. In perspective GLP-2 or its analogues may be relevant to improve intestinal adaptation in pediatric SBS patients.

Disclosure of Interest: T. Thymann Consultant for: Nycomed GmbH, B. Stoll: None Declared, D. Burrin: None Declared, A. Vegge: None Declared, N. Qvist: None Declared, P. Jeppesen Consultant for: Nycomed GmbH, T. Eriksen: None Declared, H. Heinze Employee of: Nycomed GmbH, L. Mecklenburg: None Declared, P. Sangild Consultant for: Nycomed GmbH

ESPGHAN 2013 - Abstract Submission

NUTRITION, METABOLISM AND EXPERIMENTAL APPROACHES

ESPGHAN13-1068

ANTIBIOTICS MARKEDLY AFFECT URINE AND PLASMA METABOLOMES OF PRETERM PIGS SUSCEPTIBLE TO NECROTIZING ENTEROCOLITIS

P. Jiang [1, 2,*], T. Berri [2], M. L. Jensen [2], J. Stanstrup [2], J. M.-F. Wan [1], L. O. Dragsted [2], P. T. Sangild [2]

[1]School of Biological Sciences, The University of Hong Kong, Hong Kong, China, [2]Department of Nutrition, Exercise & Sports , University of Cophenhagen, Frederiksberg, Denmark

Please select your preferred presentation type: Oral or Poster

Has this abstract previously been presented?: No

Has this abstract previously been published?: No

Objectives and Study: Antibiotics (AB) treatment is commonly used to prevent and treat necrotizing enterocolitis (NEC), a severe microbiota-dependent gut disorder in preterm infants. Neonatal AB treatment affects the intestinal and plasma proteome and protects against NEC, at least short term. We hypothesize that reduced bacterial colonization following AB treatment would also affect the plasma and urine metabolomes and help to explain how AB may induce NEC protection in neonates.

Methods: Preterm pigs, used as a model of infants, were given broad-spectrum antibiotics (n=11) or control treatment (saline, n=13) from just after birth by caesarean section. After five days, urine and blood plasma were collected and their metabolite profiles were analyzed with ultra-performance liquid chromatography-mass spectrometry (UPLC-MS) using a non-targeted approach. Potential metabolite candidates for biomarkers with significantly different abundance in urine or plasma between AB and control group were identified based on mass spectral information and verified with commercial chemical standards.

Results: AB treatment prevented NEC development, relative to control (0/11 versus 11/13, $P < 0.001$). The principal component analysis (PCA) of metabolomes showed a significant effect of the AB treatment on both urine and plasma metabolomes. Twenty and eight putative markers were identified based on mass spectra in urine and plasma, respectively. The most notable feature of differentiated metabolome is the significantly lower abundance of bacterial metabolic products and/or intermediates of amino acids in the AB pigs, which reflects that a major part of the microflora is eradicated while the intestinal permeability is still intact. These metabolites include indolylacryloylglycine and 3-methyldioxyindole from metabolism of tryptophan, 3-phenyllactic acid and phenylacetylglycine from phenylalanine and tyrosine, 2-aminoadipic acid from lysine. Besides, 3-methyladipic acid and pimelic acid from the metabolism of long-chain fatty acids showed lower abundance in the AB piglets relative to the control ones.

Conclusion: The close relations among AB treatment, NEC disease, and identified metabolites make it possible to test the metabolite signature in urine and/or plasma as biomarkers of NEC in preterm neonates. Metabolites such as 3-phenyllatic acid and 2-aminoadipic acid, bacterial metabolic intermediates, have a potential to indicate the progression of NEC which could be important for timely clinical interventions. More research is required to understand how the affected metabolites relate to gut microbial colonization and NEC pathology.

Disclosure of Interest: None Declared