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Abstracts

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ABS 1

DETRIMENTAL MUCOSAL EFFECT OF IBUPROFEN IN THE IMMATURE HUMAN INTESTINE

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INTRODUCTION

Patent ductus arteriosus (PDA) is a common problem in preterm infants. The use of nonsteroidal anti-inflammatory drugs such as indomethacin (INDO) and ibuprofen (IBU) has been shown to be effective for the closure of PDA. However, this treatment has been associated with an increased risk of developing enteropathies in neonates. We have recently reported that INDO exerts deleterious effects on the immature human intestine [1]. Whether the use of IBU is safer than INDO for the immature intestine remains to be elucidated. In this study we investigated the direct impact of IBU on the human immature intestinal transcriptome using serum-free organ culture.

METHODS

After determining the optimal dose of 100 μM of IBU (90% inhibition of intestinal prostaglandin E2 production and in the range of circulating levels in treated preterm babies), global gene expression profiles were determined using Illumina BeadChip microarrays in the small intestine after 48 h of IBU treatment (4 control ileums and 4 matched IBU-treated ileums). Differentially expressed genes were determined using the Mann-Whitney test ($p < 0.05$), and further analyzed with Ingenuity Pathway Analysis software (IPA 8.8) to identify biological functions and canonical pathways modulated by IBU. Validation of differentially expressed genes was confirmed by qPCR.

RESULTS

By establishing gene expression profiles induced by IBU on the immature intestine, we identified several statistically significant biological processes that were modulated by IBU. Among them, we found metabolic pathways that were known to be affected by IBU such as "Glycolysis/gluconeogenesis", "Fatty acid activation", and "Xenobiotics metabolism". However, we also noted important metabolic pathways less well known to be associated with IBU, namely "Antimicrobial response" and "Mucus production", that were significantly modulated. For instance, we noted that the gene expression of antimicrobial molecules such as LCN2, REG1A and PI3, were highly downregulated by IBU. In addition, we observed that the intestinal epithelial barrier was affected by IBU in the immature intestine, which decreased expression of several genes involved in mucus production such as AGR2, CLCA1, FCGBP, MUC2 and TFF3.

CONCLUSIONS

In summary, our study identified that IBU modulates several metabolic and physiological pathways in the immature human intestine. Indeed, our findings suggest that IBU could favor bacterial colonization in preterm infants by decreasing intestinal epithelial defense. Our results also suggest that the use of IBU is not safer than INDO for the closure of PDA and emphasize the risk of using a NSAIDs-based therapy on the immature gut.

ACKNOWLEDGMENTS

Supported by Canadian Institutes of Health Research (CIHR)

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ABS 2

CORRELATION BETWEEN CALPROTECTIN LEVELS IN MECONIUM AND VITAMIN D STATUS IN CORD BLOOD: ASSOCIATION WITH

INTESTINAL DISTRESS DURING NEONATAL PERIOD

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INTRODUCTION

Vitamin D has been considered as potential immune modulator, and also associated with severity and activity of inflammatory bowel disease in adolescents and adults. Fecal calprotectin derived mainly from activated neutrophils presents in the intestinal mucosa and lumen. It has been investigated as a biomarker of mucosal inflammation in diverse conditions such as necrotizing enterocolitis (NEC), and an inflammatory bowel disease. Korea is one of the most prevalent areas of maternal and neonatal vitamin D deficiency. We aimed to investigate the correlation between vitamin D status in cord blood and fecal calprotectin in meconium and find the association with intestinal distress during neonatal period.

METHODS

One hundred and forty-four newborns were enrolled who were delivered at Kyungpook National University Children's Hospital between July 2016 and February 2017. The cord blood concentrations of 25-hydroxyvitamin D (25-OHD), C-reactive protein (CRP), and delta neutrophil index (DNI) were measured. Meconium samples were collected for fecal calprotectin analysis. Maternal medical data including history of steroid and antibiotics medication were collected. We defined NEC, and feeding intolerance as the intestinal distress.

RESULTS

Median 25-OHD concentrations in cord blood were 20.2 ng/mL (range: 2.65-86.81 ng/mL; interquartile range (IQR): 14.4-26.9 ng/mL) and median fecal calprotectin levels in meconium were 122.9 μg/g (range: 11.5-2,000.0 μg/g; IQR: 51.8-409.4 μg/g). Four infants (2.8%) were diagnosed as NEC. Fecal calprotectin levels in meconium were significantly associated with gestational age (ϱ = -0.191, p = 0.022), birth weight (ϱ = -0.289, p < 0.001), serum 25-OHD concentrations (ϱ = -0.176, p = 0.008), and DNI (ϱ = 0.268, p = 0.003) in cord blood, but not with serum CRP levels in cord blood. Serum 25-OHD concentrations were correlated with fecal calprotectin levels (r = -0.287, p = 0.046) after controlling for confounding factors. Fecal calprotectin levels were significantly higher in infants with feeding intolerance (median 177.0 μg/g; IQR: 64.8-714.8 μg/g) compared to infants without feeding intolerance (median 112.3 μg/g; IQR: 44.0-285.9 μg/g, p = 0.030). The serum 25-OHD concentrations were not different between infants with and without feeding intolerance.

CONCLUSIONS

Serum 25-OHD concentrations in cord blood were inversely correlated with fecal calprotectin levels in meconium. Infants with feeding intolerance had higher fecal calprotectin levels compared to infants without feeding intolerance.

ABS 3

COMPARISON OF FECAL CALPROTECTIN LEVELS ACCORDING TO FEEDING KINDS IN VERY PRETERM INFANTS

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INTRODUCTION

Functional and biochemical maturation of the gastrointestinal tract are established over the last trimester of gestation, which affects the digestive absorptive function of very preterm infants. Fecal calprotectin (FCP) indicates neutrophil migration to the gastrointestinal mucosa and can suggest the severity of mucosal inflammation. We investigated the fecal calprotectin level according to feeding kinds in very preterm infants with or without feeding intolerance (FI).

METHODS

We prospectively investigated 68 very preterm infants born at 28-31 weeks' gestation in Keimyung Universitiy Dongsan Medical Center between July 2016 and April 2017. All enrolled infants was fed within 3 hours of life using preterm formula, who achieved full enteral feeding (> 100 cc/kg/day) within 7 days of life. Fecal calprotectin levels were routinely investigated at 7 days and 28 days of life in fully enteral-fed very preterm infants without parenteral nutrition. FI was defined as gastric residual volume ≥ 50% of previous feeding

volume, abdominal distention or emesis, and the disruption of the patient's feeding plan. The infants with FI were temporarily fed with amino-acid based formula (AAF, Neocate®) after investigation with FCP. Infants with necrotizing enterocolitis, bacterial sepsis, and perinatal asphyxia during hospitalization were not included. FCP were measured by using a commercial quantitative enzyme-linked immunosorbent assay on the Alegria® system (ORGENTEC Diagnostika, Mainz, Germany).

RESULTS

Median gestational age was 30.1 weeks, and median birth weight was 1,488 g. The median age to achieve full enteral feeding was 3.8 days. In sixteen infants with FI, which was developed at median 3.3 days of life (range: 2-6 days of life), FCP levels in formula-fed or breast-fed infants (905 ± 133 μg/g) was significantly higher than that in infants fed amino acid based-formula (217 ± 232 μg/g) ($p < 0.01$). FCP level in formula-fed or breast-fed infants with FI (905 ± 133 μg/g) was significantly higher than that without FI (405 ± 267 μg/g) ($p = 0.05$).

CONCLUSIONS

FCP might be sensitive according to feeding kinds in very preterm infants with feeding intolerance.

ABS 4

NEONATAL MORBIDITY OF EXTREME PRETERM INFANTS BEFORE AND AFTER THE INTRODUCTION OF A DONOR HUMAN MILK BANK AT THE PERINATAL CENTER GROSSHADERN

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INTRODUCTION

The effects of human breast milk on the development of the extremely immature premature infant are very complex. A positive influence on the development and maturation of the immune system and gastrointestinal tract is assumed. Various studies have shown a reduction in nosocomial infections and necrotizing enterocolitis (NEC) in premature infants after exclusive breast milk feeding in the first days of life, with pasteurized human milk instead of preterm formula. However, pasteurization changes the composition and quality of breast milk. An exclusive breast milk feeding regime with unpasteurized donated milk may strengthen the positive effects, but profound data is rare. Since the introduction of the human milk bank (HMB) at the Perinatal Center (PNC) Großhadern in February 2012, an exclusive feeding strategy with unpasteurized donated breast and own mother's milk is being sought for children born < 32 weeks gestational age (GA).

METHODS

Retrospective analysis of all preterm infants born < 32 weeks GA age and 1,500 g at the PNC Großhadern in two observation periods (i): 02/2010-02/2012 and ii): 02/2012-03/2015; before and after the introduction of the HMB. Exclusion criteria were death < 7 days of life, severe malformations and metabolic birth defects. The infants of both study periods were compared with respect to the following parameters: GA, birthweight, chorioamnionitis, initial diet during the first days of life (human milk or formula), day of life when full enteral feeds were established, weight development and neonatal morbidity (sepsis, NEC, bronchopulmonary dysplasia, ROP, death). Primary target criteria were the incidence of NEC and nosocomial sepsis in the two observation periods.

RESULTS

142 preterm infants born before 02/2012 and 236 infants born between 02/2012-03/2015 met the inclusion criteria and data could be obtained. In the second study period 121/237 infants received donated breast milk instead of preterm formula (74% unpasteurized). Due to a shortage of stored donated breast milk 115 preterm infants received formula. With respect to the comparison of formula fed vs. donated breast milk fed infants before and after the introduction of the HMB no significant difference was found for the incidence of NEC (1/142 vs 1/121) and nosocomial sepsis (21/142 vs 21/121). Formula fed infants reached full enteral feeds after 11.2 ± 4.4 days vs 10.4 ± 4.2 days in the group of infants with donated breast milk ($p = 0.09$). In both groups 120% of birthweight was gained after 19.3 days.

CONCLUSIONS

In the first 3 years after the introduction of the HMB in our PNC, 50% of all premature infants < 32 weeks GA received donor milk during the first days of life instead of preterm formula. Three quarters were fed unpasteurized milk. Due to a low incidence of NEC before the introduction of the HMB (< 1%) no further reduction could be

observed in our cohort. Exclusive enteral feeding with donor milk instead of preterm formula tended to be faster and was associated with comparable growth.

ABS 5

IS NEAR INFRARED SPECTROSCOPY A RELIABLE TECHNIQUE TO MEASURE GUT PERFUSION IN PRETERM INFANTS?

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INTRODUCTION

Blood transfusion improves gut tissue perfusion in preterm infants; this has been demonstrated by increased gut tissue oxygenation and reduced fractional tissue oxygen extraction [1]. Whether this is a true improvement in response to blood transfusion or this is an effect of changing gut tissue oxygenation over time has remained open to conjecture. The objective of this study was to investigate the reliability of gut tissue oxygenation measured using Near Infrared Spectroscopy (NIRS) in preterm infants.

METHODS

Gut oxygenation measured using NIRS (Splanchnic Tissue Haemoglobin Index [sTHI], Tissue Oxygenation Index [sTOI] and Fractional Tissue Oxygen Extraction [sFTOE]) in preterm infants who received blood transfusion (15-20 minutes before to 15-20 minutes post-transfusion) was compared to control infants (continuously over 3 hours). Infants who received transfusion were recruited to three groups: 1 to 7 (group 1; n = 20), 8 to 28 (group 2; n = 21) and ≥ 29 days of life (group 3; n = 18). Control group: stable infants and who were not receiving blood transfusion (1-7 days = 4, 8-28 days = 5, ≥ 29 days = 3, total n = 12). The study was approved by REC and written parental consent was obtained.

RESULTS

The infant characteristics (gestational age, birth weight and haemoglobin level at birth) of the control group were similar to those of transfused infants. The mean sTHI, sTOI and sFTOE epochs over time remained unchanged over the three hours period of measurement in all the control infants. In the transfused groups, the sTHI increased by 39%, 45% and 47% in Group 1, Group 2 and Group 3 respectively (**Tab. 1**). The baseline sTOI increased by 42%, 29% and 30% following transfusion in Group 1, Group 2 and Group 3 infants respectively. The mean pre-transfusion sFTOE decreased significantly post-transfusion in all the three groups ($p < 0.01$).

CONCLUSIONS

These findings indicate that the improvement of splanchnic tissue oxygenation and extraction balance in transfused infants is a true reflection of splanchnic tissue oxygenation changes. Hence, NIRS is a reliable technique to measure splanchnic tissue oxygenation and can be used to monitor gut tissue perfusion in preterm infants.

REFERENCE

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Table 1 (ABS 5). Splanchnic Near Infrared Spectroscopy (NIRS) measurement parameters in transfused and control preterm infants.

Splanchnic oximetry parameters, mean (SD)	Group 1 (1-7 days) n = 17[a]			Group 2 (8-28 days) n = 20[b]			Group 3 (≥ 29 days) n = 15[c]			Control infants n = 12		
	Pre-BT	Post-BT	p-value	Pre-BT	Post-BT	p-value	Pre-BT	Post-BT	p-value	Initial measurement	Measurement after 3 hours	p-value
sTHI (percentage increase from baseline), %	40.6 (15.4)	56.0 (14.8)	0.001	37.0 (12.5)	53.6 (16.8)	0.001	26.6 (12.2)	37.9 (14.8)	0.001	38.9 (14.6)	40.5 (16.2)	0.74
sTOI, %	36.7 (19.3)	52.1 (20.8)	0.01	44.6 (10.4)	57.6 (14.3)	0.01	41.3 (10.4)	53.8 (16.5)	0.01	42.1 (10.4)	43.5 (11.3)	0.67
sFTOE, %	64.7 (13.4)	44.4 (20.3)	0.004	51.4 (11.5)	37.0 (14.9)	0.005	55.6 (11.8)	42.7 (15.1)	0.0004	58.6 (12.5)	57.8 (13.4)	0.78

sTHI: splanchnic tissue haemoglobin index; sTOI: splanchnic tissue oxygenation index; sFTOE: splanchnic fractional tissue oxygen extraction. [a]3 infants, [b]1 infant and [c]3 infants excluded from the analysis due to motion artefacts.

ABS 6

EARLY BIOCHEMICAL MARKERS ASSOCIATED WITH DEVELOPMENT OF NECROTIZING ENTEROCOLITIS

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INTRODUCTION

Necrotizing enterocolitis (NEC) is a major cause of morbidity and mortality in preterm infants. The pathophysiology of NEC is not fully understood but several factors contribute, such as prematurity, enteral feeding, infections, innate inflammatory response and genetic susceptibility. Early detection of infants at risk for or with early stages of NEC could improve the outcome. The aim of this study was to identify biochemical markers associated with development of NEC in extremely preterm infants.

METHODS

This prospective observational study included 46 infants born before 28 weeks' gestational age, and without any major anomalies. Blood samples were collected from arterial catheters on the second day of life and forty-five inflammatory markers and growth factors were analysed using proximity extension assay (PEA) technique. NEC was defined as stage IIa-IIIb according to the modified Bell's stages. The Mann-Whitney test was used to compare non-parametric continuous data and the Fisher's exact test was used to compare categorical data between infants that did or did not develop NEC. The Benjamini-Hochberg method was used to reduce the risk of false discoveries to an expected rate of at most 20%. All data from PEA analyses are presented as arbitrary units in linear values.

RESULTS

Eleven infants (24%) developed NEC at a median of 9 days (range: 2-18 days). All NEC were Bell's stage IIIa or IIIb. Infants with NEC tended to have lower gestational ages (median 24^{+0} weeks [range: 22^{+6}-27^{+3} weeks] vs. median 25^{+3} weeks [range: 22^{+0}-27^{+3} weeks]; p = 0.180) and lower birth weights (median 621 grams [range: 582-935 grams] vs. median 760 grams [range: 423-1,058 grams]; p = 0.060). Perinatal parameters did not differ from infants without NEC. All analysed biochemical markers are presented in **Tab. 1**. NEC was associated with high levels of proteins from the epidermal growth factor-family (AREG, TGF-α) and their linked receptors

Table 1 (ABS 6). Biochemical markers.

	NEC n = 11	No NEC n = 35	p
AREG	**74.8 (28.9-253.6)**	**44.4 (10.8-231.3)**	**0.021**[b]
CA125	**23.2 (9.3-32.5)**	**10.3 (3.2-51.5)**	**0.007**[b]
CCL20	1,563 (323-5,658)	958 (239-3,133)	0.174
CCL25	**383.8 (226.0-501.5)**	**267.0 (159.0-461.9)**	**0.018**[b]
CCL28	1.24 (1.06-1.30)	1.13 (1.06-1.75)	0.406
CD40	968.1 (598.8-1,783.3)	971.5 (503.0-2,153.5)	0.766
CD40L	10.0 (6.1-140.9)	8.7 (4.9-267.8)	0.719
EGF	30.9 (13.2-486.5)	31.7 (12.5-1,785.2)	0.913
EGFR (HER1)	43.4 (32.2-55.9)	40.0 (30.2-55.0)	0.122
ELAM-1	287.1 (136.5-804.9)	277.2 (107.3-1,960.7)	0.913
EPO	1.58 (0.94-4.11)	1.14 (0.82-15.3)	0.216
GH	1,859 (1,062-2,358)	1,923 (925-2,239)	0.766
HB-EGF	249.2 (205.6-268.1)	252.8 (224.0-275.8)	0.463
HER2	**924.7 (657.9-1,053.3)**	**860.7 (649.9-1,112.9)**	**0.047**[b]
HER3	**583.1 (473.7-665.1)**	**513.58 (402.9-620.5)**	**0.016**[b]
HER4	64.2 (45.6-92.8)	55.3 (36.5-84.9)	0.101
HGF	**227.6 (134.4-342.1)**	**157.6 (107.1-340.1)**	**0.030**[b]
IFN-γ	-[a]	-[a]	-
IL-1-α	4.21 (1.23-160.86)	3.15 (1.23-98.21)	0.584
IL-10	21.2 (10.8-237.5)	18.4 (9.3-51.0)	0.217
IL-10RB	237.9 (161.0-303.4)	252.6 (127.9-363.0)	0.502
IL-12	376.2 (161.9-578.6)	281.1 (122.8-972.0)	0.522
IL-17RB	**22.3 (14.8-37.7)**	**18.9 (9.7-45.8)**	**0.032**[b]
IL-18	77.7 (51.7-187.5)	82.4 (52.0-212.3)	0.913
IL-1RA	231.3 (161.2-291.3)	230.7 (94.9-303.2)	0.628
IL-2	-[a]	-[a]	-
IL-4	-[a]	-[a]	-
IL-5	-[a]	-[a]	-
IL-6	247.9 (99.9-3,480.1)	316.7 (105.0-2,711.9)	0.814
IL-8	963.3 (382.8-6,400.9)	713.5 (197.3-5,285.1)	0.325
MCP-1	3,267 (915-5,054)	2,505 (1,475-4,973)	0.267
MIP-1α	12.9 (4.3-181.9)	10.1 (4.7-67.0)	0.195
MMP12	221.6 (62.2-636.1)	254.0 (65.5-825.0)	0.913
MMP3	1.90 (1.43-2.46)	1.78 (1.18-4.56)	0.863
MMP7	**577.0 (412.6-809.4)**	**734.5 (367.4-1,189.4)**	**0.037**[b]
MYD88	2.02 (1.45-4.84)	1.93 (1.45-5.14)	0.673
PDGF	11.4 (8.5-319.4)	17.0 (7.1-735.6)	0.584
TGF-α	**24.4 (13.8-37.8)**	**19.4 (11.3-33.7)**	**0.051**[b]
TGF-β	**106.4 (72.6-203.1)**	**85.9 (46.1-150.9)**	**0.008**[b]
TNF-α	-[a]	-[a]	-
TNF-β	14.8 (6.0-20.3)	15.2 (7.9-26.9)	0.584
TNFR1	8,894 (7,852-9,639)	8,825 (7,291-9,712)	0.522
TNFR2	**88.0 (59.1-99.2)**	**71.0 (43.5-99.7)**	**0.020**[b]
VEGF-A	3,151 (2,122-4,013)	3,019 (1,928-4,918)	0.743
VEGFR2	244.1 (192.1-277.3)	234.6 (172.7-289.1)	0.673

Values in arbitrary units.
[a]Less than 80% of the test results in the range of quantification; [b]significant according to the Benjamini-Hochberg method.

(HER2, HER3), factors related to intestinal and peritoneal inflammation (HGF, CA125), and cytokines and cytokine receptors (TGF-β, CCL25, IL-17RB, TNFR2). NEC was also associated with low levels of matrix metalloproteinase 7 (MMP7).

CONCLUSIONS

There were significant differences in the serum levels of 11 proteins between infants that later did and did not develop NEC in this cohort. These biochemical markers could potentially give clues to the pathophysiology of NEC and maybe be used as indicators for preterm infants at risk of NEC, but further research is needed.

ABS 7

OPTICAL PROPERTIES OF EARLY STOOL FROM PRETERM INFANTS: IMPORTANT TO CONSIDER FOR ABDOMINAL OXIMETRY BASED ON NEAR-INFRARED SPECTROSCOPY

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INTRODUCTION

Necrotizing enterocolitis (NEC) is the most common gastrointestinal emergency of the preterm infant. Early detection of NEC by lowered abdominal tissue oxygen saturation (StO_2) using near-infrared spectroscopy (NIRS) may be relevant for treating or even preventing NEC. However, current commercial NIRS-oximeters provide inaccurate StO_2 values, because they neglect the relevant influence of stool as abdominal absorber. The aim of this study was to characterize the optical properties of faeces to enable to correct abdominal StO_2 readings for the presence of stool.

METHODS

A study on 25 preterm infants with mean gestational age of 30.9 ± 2.3 weeks and weight of 1,478 ± 511 g was conducted, investigating the first five stool probes excreted by each infant. The stool probes were measured with a VIS/NIR spectrometer and

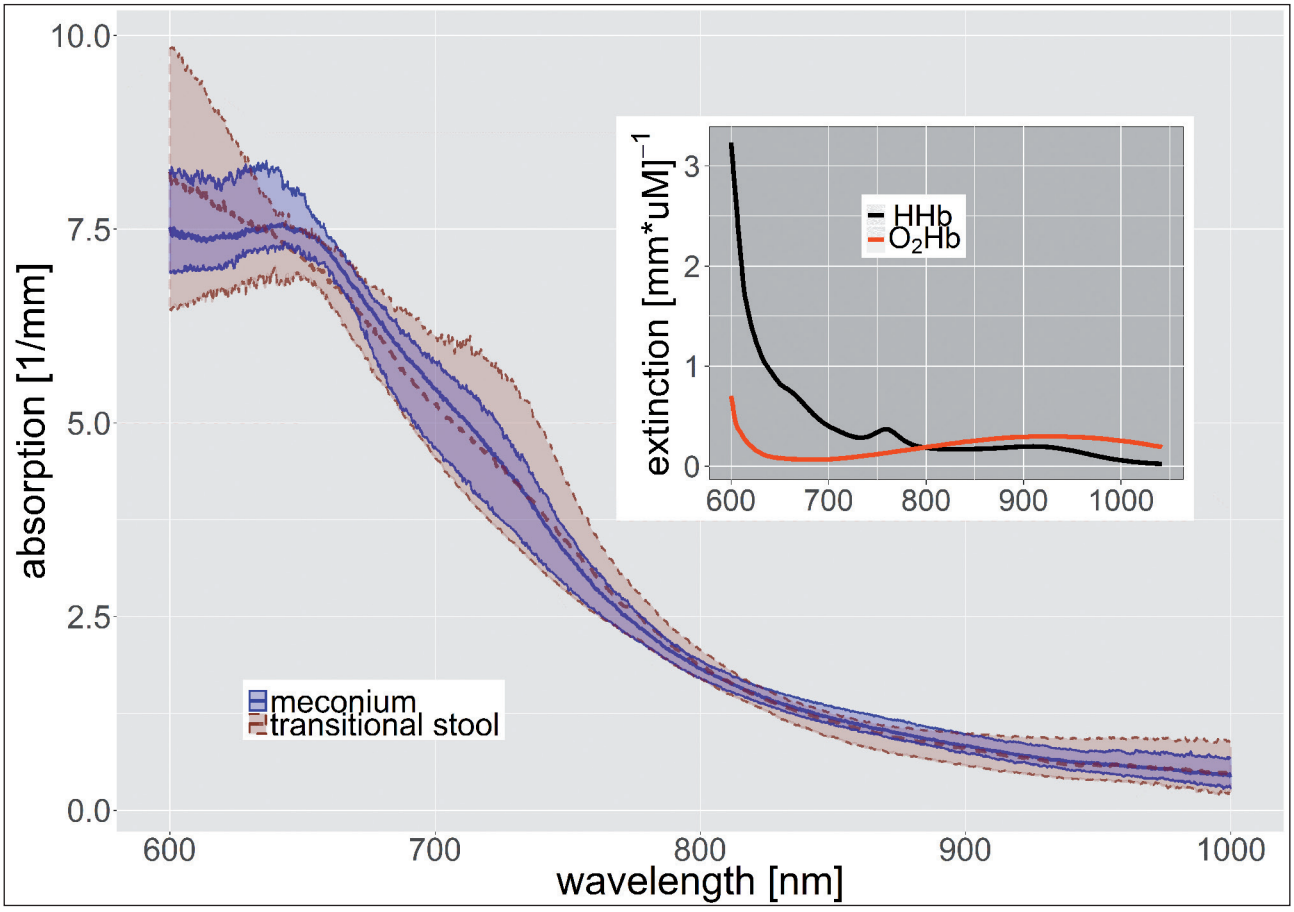

Figure 1 (ABS 7). Two differing absorption curves associated with meconium and transitional stool.

analysed for their optical properties with the inverse adding doubling software. Subsequent principal component analysis and probabilistic clustering were performed to investigate the stool probes for differing stool types and possible changes of the optical properties in time.

RESULTS

We found two differing absorption curves associated with meconium and transitional stool (**Fig. 1**). Probabilistic clustering correctly assigned 91% of all stool probes to their corresponding stool type. The probes showed a strong absorption in the near-infrared region with a decline towards longer wavelengths. For wavelengths > 700 nm, the slope of stool absorption was opposite to the absorption of oxyhaemoglobin. Consequently, the presence of stool in the abdomen erroneously lowers the measured concentration of oxyhaemoglobin if not considered appropriately. This results in erroneously low StO_2 readings whenever stool is present, causing low reproducibility and high inaccuracy of abdominal StO_2 measurements.

CONCLUSIONS

We determined the absorption spectra of meconium and transitional stool. It is obvious that their spectra lead to erroneous StO_2 values in current NIRS-oximeters. Based on the results of this study, we identified specific wavelengths for the development of a novel NIRS-oximeter that non-invasively and continuously measures abdominal StO_2 corrected for the interference of stool.

ABS 8

STOOLING PATTERN AND GASTRIC RESIDUALS ARE NOT USEFUL TOOLS FOR EARLY DIAGNOSIS OF NECROTISING ENTEROCOLITIS IN PRETERM INFANTS

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INTRODUCTION

Necrotising enterocolitis (NEC) is a devastating disease primarily affecting preterm infants. Early diagnosis is very important. Measuring of gastric residuals is a common practice in many Neonatal Intensive Care Units around Europe. There are few studies made looking at the early stooling pattern and gastric residuals in relation to NEC development. The aim of this project was to identify possible disturbances in early gut motility related to an increased risk of developing NEC in preterm infants.

METHODS

This was a retrospective case-control study looking at NEC patients born and treated in the Neonatal Intensive Care Unit at Queen Silvia children's hospital in Gothenburg between 2004 and 2016. Swedish neonatal quality register was used to identify NEC-cases (n = 115). Each case was matched to a control born closest in time to the NEC-case with the same gestational age and gender. Cases with spontaneous intestinal perforation and controls with upper gastrointestinal malformations were not included. Gut motility was studied by meconium passage, stooling frequency and gastric residuals.

RESULTS

Patients born at other hospitals (n = 35), NEC-cases who had volvulus (n = 2) and NEC-cases with missing medical records (n = 1) were excluded. This resulted in a group of 77 NEC-cases and 77 controls, in total 154 subjects. There was a significant decrease in the amount of food given ($p = 0.03$), the amount of food given per kg ($p = 0.02$) starting one day before diagnosis. GR > 3.5 ml was significantly increased for the NEC-cases one day before diagnosis ($p = 0.009$). The number of stools per day was only decreased for the NEC-cases at the day of diagnosis ($p < 0.001$). No significant difference was found looking at the time of first passage of meconium.

CONCLUSIONS

This study did not identify any significant differences in early gut motility between NEC cases and controls. However, one day before diagnosis there were a significantly increased number of large gastric residuals in NEC-cases. Measures of gastric residuals are not considered a useful tool in the early diagnostics of NEC.

ABS 9

REFERENCE VALUES OF ZONULIN IN TERM NEONATES

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INTRODUCTION
Zonulin (ZO) is postulated as a new biomarker of intestinal permeability. Preliminary data obtained in neonates hospitalised in the intensive care unit have shown that ZO concentrations in newborns with rotavirus infections and necrotizing enterocolitis are increased in relation to newborns hospitalised at neonatal pathology unit without inflammatory signs and symptoms. Interpretation of the observed values necessitates establishing reference values in healthy newborns.
METHODS
Serum ZO concentration was measured in 80 term newborns (48 males and 32 females) born after an uncomplicated pregnancy. 38 of them were delivered by Cesarean section. All patients were given high Apgar scores and during observation period the newborns remained in stable condition, did not require phototherapy, intravenous infusion or any other medical interventions. Before discharged, blood sampling was performed at the end of the second day of life due to routine testing including screening for metabolic disorders. Hematocrit (Ht), bilirubin, glucose, sodium and potassium were also measured, and ZO was assessed by ELISA.
RESULTS
The mean serum ZO concentration was 0.51 ± 0.08 ng/ml. The values of the 5th and the 95th percentiles were 0.37 and 0.60 ng/ml, respectively. There was no influence of gender, mode of delivery, birth weight, 1' and 5' Apgar score and serum bilirubin levels on serum ZO concentrations. There were, however, weak associations between hematocrit, as well as serum glucose, and assessed values of serum ZO ($R = -0.254$, $p = 0.02$; $R = -0.306$, $p = 0.006$).
CONCLUSIONS
The established reference values enable interpretation of zonulin concentrations in pathologic conditions in newborns.

ABS 10

DETERMINANTS OF THE NEED FOR TREATMENT IN PREMATURE INFANTS WITH SUSPECTED NECROTISING ENTEROCOLITIS

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INTRODUCTION
The decision to treat infants for necrotizing enterocolitis (NEC) results in a prolonged course of antibiotics in addition to discontinuation of feeds for the duration of the illness. Although a low threshold for commencing antibiotics and placing the infant "nil by mouth" (NPO) is understandable due to the low specificity of clinical symptoms, the provision of a prolonged course of antibiotics and NPO should only be justified in the presence of confirmed NEC (radiologically). We aimed to assess the adherence to this concept in a tertiary neonatal intensive care unit in infants < 1,500 grams.
METHODS
This was a retrospective review of all infants under 1,500 g admitted to the neonatal intensive care unit who underwent an abdominal radiograph for a clinical suspicion of NEC over a one year period (2016). Definite NEC was defined as the presence of typical radiological signs, and/or the need for surgical intervention or decision by the neonatal team to define the episode as clinical or non-radiological NEC. Treatment was defined as the provision of antibiotics and NPO for a minimum of 5 days. The cohort was subsequently divided into those without definite NEC receiving no treatment (No Treatment), infants with confirmed NEC who received a full course of treatment (Confirmed NEC), and infants without radiological or surgical NEC who received NEC treatment (Treatment-No NEC). We assessed the determinants of continuing NEC treatment despite ruling out of NEC.
RESULTS
Forty-two infants with a median [IQR] gestation and birthweight of 26.2 [24.7-28.5] weeks and 820 [660-1,065] grams respectively were enrolled. Twenty-one infants who had an initial clinical suspicion of NEC did not receive treatment following normal radiology; 10 infants had confirmed NEC and continued treatment and 11 infants did not have evidence of radiological NEC yet continued a full course of NEC treatment. The **Tab. 1** outlines their clinical characteristics, NEC clinical signs and symptoms, and other important outcomes. Infants in the Treated-No NEC group were of a similar birthweight to the Confirmed NEC group and had a high proportion of small for gestation infants. They also had a high rate of concerning clinical signs including temperature instability and bloody stool, abdominal tenderness and distension. There was no difference in the rate of bilious aspirates, and laboratory findings between the three groups.

Table 1 (ABS 10). Clinical characteristics, necrotizing enterocolitis (NEC) clinical and laboratory parameters, and other clinical outcomes of the infants enrolled.

	No Treatment n = 21	Confirmed NEC n = 10	Treated-No NEC n = 11	p
Demographics				
Gestation (weeks)	26.9 [25.1-28.6]	25.1 [24.2-27.5]	26.1 [24.6-29.0]	0.37
Birthweight (g)	1,030 [842-1,137]	720 [643-766]	750 [600-990]	< 0.001
Small for gestation	0	3 (30)	5 (46)	0.005
Male	13 (62)	6 (60)	7 (64)	0.99
Caesarean Section	15 (71)	6 (60)	7 (64)	0.80
Absent EDF	1 (5)	1 (10)	2 (18)	0.47
Complete ANS	15 (71)	7 (70)	5 (46)	0.61
Probiotics	10 (48)	2 (20)	8 (73)	0.05
NEC clinical and laboratory parameters				
Bilious aspirates	9 (43)	5 (50)	3 (27)	0.54
Bloody stool	0	1 (10)	2 (2)	0.15
Distension	10 (48)	7 (70)	7 (64)	0.44
Tenderness	0	2 (20)	2 (18)	0.11
Temp instability	2 (10)	0	5 (46)	0.009
pH	7.30 ± 0.07	7.30 ± 0.12	7.30 ± 0.09	0.97
HCO_3-	22 ± 2	19 ± 2.5	21 ± 1.9	0.02
Haemoglobin (g/L)	128 ± 23	132 ± 21	127 ± 20	0.34
Pneumatosis	0	2 (20)	0	
Other clinical outcomes				
Ventilation days	4 [1-14]	14 [6-20]	17 [2-40]	0.64
Days to full feeds	13 [10-17]	20 [13-35]	14 [10-33]	0.19
Death	5 (24)	4 (40)	0	0.08

Data are presented as medians [inter-quartile range], mean ± standard deviation, or proportion (%).
NEC: necrotizing enterocolitis; No Treatment: infants without definite NEC receiving no treatment; Confirmed NEC: infants with confirmed NEC who received a full course of treatment; Treatment-No NEC: infants without radiological or surgical NEC who received NEC treatment; EDF: end diastolic flow; ANS: antenatal steroids.

CONCLUSIONS

In this review, we identified that clinicians continue NEC treatment in a sizable proportion of infants who do not have radiological signs of NEC. They appear to be guided by clinical concerns and continue to do so despite the lack of objective evidence of the condition. Prolonged use of antibiotics and NPO have significant implications on gut flora colonisation and weight gain and this practice needs to be revised.

ABS 11

EFFECT OF ANTIBIOTIC PROPHYLAXIS DURING REMOVAL OF A CENTRAL VENOUS CATHETER ON DEVELOPMENT OF THE NEONATAL INTESTINAL MICROBIOTA

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INTRODUCTION

Administration of two dosages of an anti-staphylococcal agent during the procedure of removal of a central venous catheter (CVC) in preterm infants < 1,500 grams is effective in preventing catheter removal associated sepsis within the critical period of 48 hours after removal [1]. At the same time, increasing knowledge is elicited about the negative effects of antibiotics on development of the intestinal microbiota in premature infants and its lifelong consequences. Objective: Study the effect of vancomycin prophylaxis to prevent sepsis after removal of a CVC on the intestinal microbiota in preterm infants.

METHODS

A prospective pilot study was performed from 2012 through 2013 in our level III NICU. Fourteen preterm infants < 1,500 g with a CVC, but without episodes of (suspected) late-onset sepsis requiring antibiotics, were included. Prophylaxis consisted of 2 dosages of vancomycin (10 mg/kg) 1 hour before and 12 hours after removal of a CVC. Faecal samples were collected before (< 5 days) and after prophylaxis (< 7 days). Microbiota composition was determined by sequencing of the 16S-rRNA gene (Illumina MiSeq).

RESULTS

In faecal samples of 14 preterm infants, GA 28 (26-30) weeks, BW 1,245 (1,050-1,445) g, microbiota diversity decreased significantly after prophylaxis ($p = 0.035$). Also a trend towards decreased richness ($p = 0.062$) was seen. See **Fig. 1**. No significant differences were found for specific taxa (e.g. *Bifidobacterium spp.*, *Enterococcus spp.*, *Staphylococcus spp.*). There was however, a decrease of low abundant taxa (*Comamonadacea spp.* and *Pseudomonas spp.*).

CONCLUSIONS

This pilot study shows that vancomycin prophylaxis to prevent sepsis after removal of a CVC has an effect on the microbiota diversity of the premature infant. Future studies to evaluate the clinical significance and the long-term effects are needed, outweighing benefit and harm of two preventive doses of antibiotics during removal of a CVC.

REFERENCE

[1] Hemels MA, van den Hoogen A, Verboon-Maciolek MA, Fleer A, Krediet TG.Prevention of neonatal late-onset sepsis associated with the removal of percutaneously inserted central venous catheters in preterm infants. Pediatr Crit Care Med. 2011;12(4):445-8.

DECLARATION OF INTEREST

Funded by Nutricia Research, I. Renes and J. Knol are employees of Nutricia research.

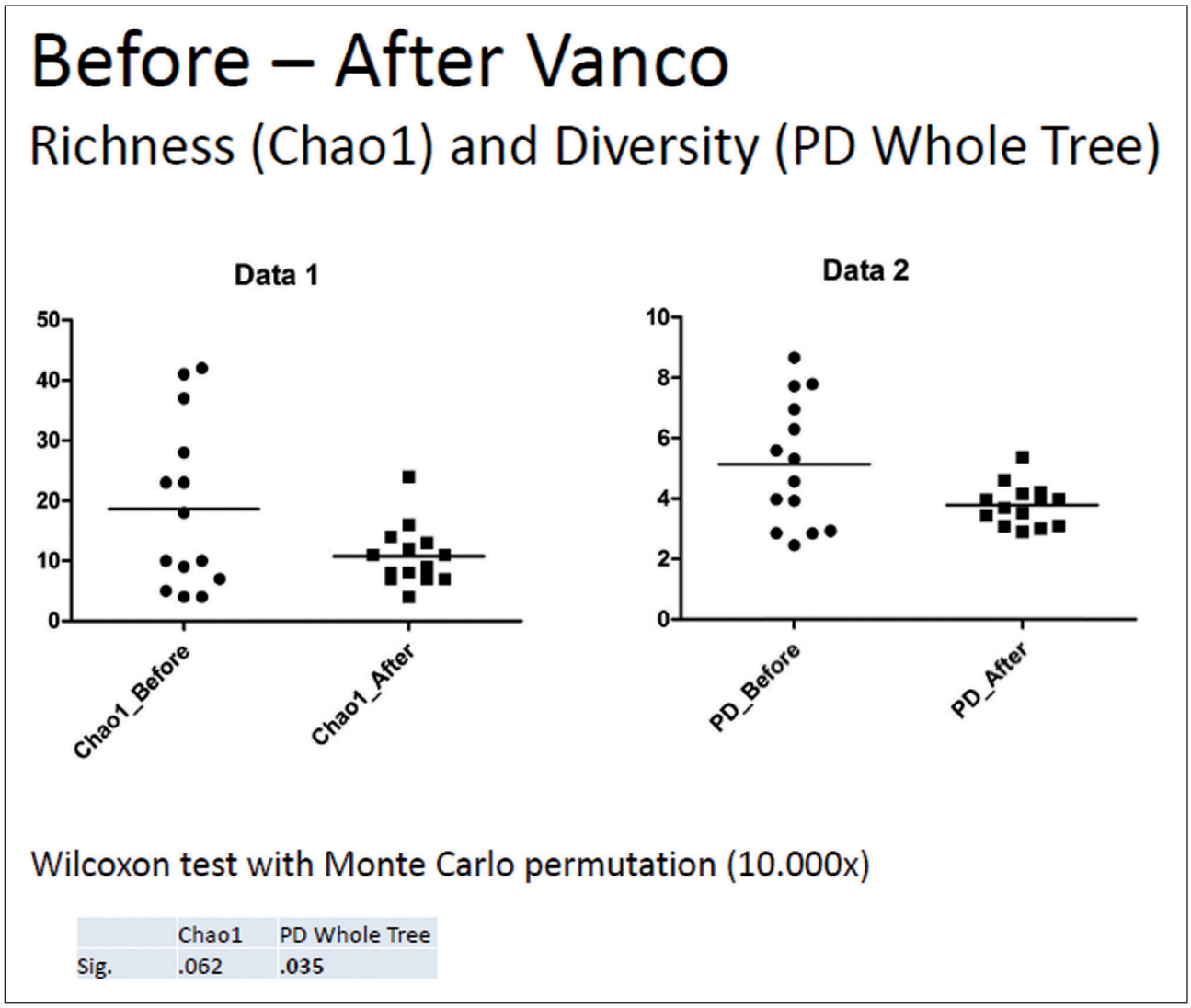

Figure 1 (ABS 11). Richness (Chao1) and diversity (PD whole tree) before and after vancomycin.

ABS 12

NEWBORNS WITH ULTRASOUND FINDING OF GAS IN HEPATIC PORTAL VENOUS SYSTEM: ANALYSIS OF RISK FACTORS, CLINICAL AND LABORATORY FINDINGS AND DEVELOPMENT OF ALLERGY

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INTRODUCTION

According to Bell's classification detection of gas in hepatic portal venous system (HPVG) is considered a sign of necrotizing enterocolitis (NEC) in newborns. Nowadays by routine use of ultrasonography, hepatic portal venous gas (HPVG) is more often found in asymptomatic patients or in benign conditions as well as in patients with NEC. We aimed to determine the differences in risk factors, clinical and laboratory findings and development of childhood allergies between the group of newborns with HPVG and the diagnosis of NEC and the group of newborns with US finding of HPVG who were not considered to have NEC.

METHODS

Infants, hospitalized at UMCL between January 2011 and March 2016, with US finding of HPVG were studied retrospectively. Group 1 consisted of newborns with HPVG and NEC and group 2 of those with HPVG without the diagnosis of NEC. Demographic characteristics, perinatal and postnatal factors, clinical and laboratory findings and parents answers regarding childhood allergies were compared between the groups.

RESULTS

59 infants with US finding of HPVG were identified, 30 in group 1 and 29 in group 2. Gestational age in the group 1 was 35.7 weeks (min = 28 max = 40) vs 37.2 weeks (min = 26, max = 41) in the group 2. There were no statistically significant differences in demographic characteristics, perinatal factors, feeding modalities, antibiotic treatment and umbilical catheter placement prior of identification of HPVG between the groups, but the groups differed in frequency of congenital heart defects (Group 1 vs Group 2, 40% vs 22%, p = 0.06). Meteorism, weak peristaltic, vomiting and blood in stool were more frequently found in the group 1 ($p < 0.05$). There was statistically significant difference between the two groups in the occurrence of leukopenia ($p < 0.05$). Cow's milk allergy later in infancy was diagnosed in the third of patients, but the difference between the groups was not statistically significant (**Tab. 1**).

Table 1 (ABS 12). Comparison of laboratory findings and risk factors between newborns with hepatic portal venous system (HPVG) and necrotizing enterocolitis (NEC) (group 1) and newborns with HPVG without the diagnosis of NEC (group 2).

		Group 1	Group 2	p
Leukopenia	**Yes**	4	0	**0.02**
	No	25	28	
Leukocytosis	**Yes**	9	4	0.13
	No	20	24	
Thrombocytopenia	**Yes**	2	4	0.38
	No	26	24	
Eosinophil count (%)		5.67 ± 5.32	4.33 ± 3.69	0.34
Elevated CRP	**Yes**	9	6	0.56
	No	21	20	
Resuscitation after birth	**Yes**	4	7	0.25
	No	25	20	
Apgar 1 min		8.1 ± 1.8	7.5 ± 2.4	0.31
Apgar 5 min		8.9 ± 1.0	7.9 ± 2.6	0.06
Feeding before detection of HPVG	**Only PN**	2	2	0.99
	Only HM	8	7	
	HM + formula	20	18	
Early sepsis	**Yes**	7	6	0.86
	No	23	22	
Umbilical venous catheter	**Yes**	10	8	0.63
	No	19	20	
Congenital heart disease	**Yes**	12	5	0.06
	No	18	23	

HPVG: gas in hepatic portal venous system; PN: parenteral nutrition; HM: human milk.

CONCLUSIONS

The group of newborns with US finding of HPVG and the diagnosis of NEC did not differ in perinatal and postnatal risk factors from the group in which HPVG was accidental finding. Our results show that careful clinical observation and finding of leucopenia could be helpful in therapeutic decisions. Although the groups did not differ in the development of allergies the fact that allergy on cow's milk was present in the third of patients with US finding of HPVG needs further evaluation.

ABS 13

NEONATAL FECAL BIOMARKERS OF NECROTIZING ENTEROCOLITIS

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INTRODUCTION

NEC remains the major cause of gastrointestinal morbidity and mortality in preterm infants. The pathophysiology of NEC remains incompletely understood. It is presumed to involve translocation of bacteria through immature defence barriers of the intestinal epithelium, leading to tissue invasion and damage. Since the early symptoms of NEC are often rather non-specific, the diagnosis of NEC can be difficult. Therefore, the search for diagnostic inflammatory markers for NEC remains warranted. These biomarkers must be non-invasive with fast, easy, and inexpensive detection. The samples stools are an ideal way to search biomarkers. Myeloperoxidase (MPO) and alkaline phosphatase (AP) are typical inflammatory intestinal markers but their use as no-invasive biomarkers has not been much studied. Since MPO and AP are enzymes, their activity is cost-effective and easily quantifiable. Fecal calprotectin has been extensively used as a biomarker in gastrointestinal diseases. Objective: to evaluate the fecal MPO and AP activity in children as possible non-invasive biomarker of intestinal inflammation.

METHODS

We studied the MPO and AP activity in meconium of term (AT, n = 21) and preterm (PT, n = 26) newborns and in samples stools of children suffering of NEC (NEC, n = 9) hospitalized in the neonatal intensive care unit (NICU) of our hospital. MPO and PA activity were obtained by spectrophotometry and the calprotectin concentration by ELISA.

RESULTS

MPO activity and calprotectin levels were high in the NEC group compared with the two other. In addition, they were moderate high in PT group regarding the AT group. Non-significantly variations in PA activity were observed.

CONCLUSIONS

Since of the severity of this disease is acknowledged, the search for biomarkers for early diagnosis and prognosis of the evolution of NEC is a priority in the actual research. This preliminary study stresses that fecal activity MPO may be a good and early NEC marker.

ABS 14

THE OPEN ABDOMEN: A CHALLENGE FOR NEONATOLOGISTS AND NEONATAL SURGEONS. THE KAROLINSKA EXPERIENCE

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INTRODUCTION

The open abdomen (OA) is a particular postsurgical condition that is used in complicated patients aimed to limit the intestinal damage (so called "damage control" surgery). The choice to perform a "damage control" surgery is aimed to reduce the time of the laparotomy (which in turn may reducing bleeding complication), to promptly treat high intra abdominal pressure (IAP) and to prevent from occurring in the postoperative phase in in critically ill newborn infants that are physiologically unstable. The open abdomen technique may also be used in cases where it is important to visually monitor the colour of the intestine at limit of viability. The open abdomen is usually closed after 2-3 days, even if sometimes the closure of the abdominal wall cannot be performed due to high risks to develop abdominal compartment syndrome. The OA is a challenging condition for neonatologists due to the several physiological ramifications on mechanical ventilation strategies, fluid balance and circulatory support, and finally pain treatment. In this study we want to present the experience on open abdomen at our tertiary NICU. Aim: To analyse the mortality and the treatment strategies regarding ventilator, BP, fluid balance and pain in OA newborn infant.

METHODS

We retrospectively assess all cases of OA during the period January 2009-November 2016.

RESULTS

44 patients were treated with OA, 23 (52.3%) of them died. Necrotising enterocolitis was the most common indication for laparotomy. A vast majority of cases developed complications in fluid balance,

transitory liver insufficiency, difficulties in pain assessment and treatment, and particular respiratory problem requiring high frequency oscillatory ventilation.

CONCLUSIONS

The open abdomen is correlated with high mortality. Special strategies for fluid balance and ventilation support has to be taken into account when treating newborn infants after damage control surgery. Closed collaboration between neonatal surgeons and neonatologist is essential for the choice of timing for closing the abdomen. The analysis of the data is still on-going and we will provide more extensive results soon.

ABS 15

ANOGENITAL STIMULATION IN RATS DOES NOT INCREASE GASTRIC EMPTYING

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INTRODUCTION

Whether delayed meconium passage is a risk factor for the presence of gastric residual and feeding intolerance in premature neonates remains controversial. Rectal stimulation via glycerin suppositories or enemas is routinely employed in some centers to prevent feeding tolerance in these neonates. The newborn rat is a good animal model to study the impact of rectal stimulation on gastric emptying since these pups require maternal anogenital region stimulation to eliminate urine and fecal material. In addition, the newborn rats' gastrointestinal function is developmentally comparable to 32-week gestation in humans. The objective of this study was to evaluate the anogenital stimulation effect on the newborn rat gastric emptying rate. We hypothesized that anogenital stimulation increases the rate of gastric emptying in newborn rats.

METHODS

52 rats aged 1 to 7 days of age were studied. The pups were separated from their mother and divided in two groups. The experimental group received anogenital stimulation with a wet cotton swab during 1 minute, each 2 hours until next exam, while the not stimulated pups served as controls. The gastric emptying rate was measured by ultrasound immediately after 6 hours following maternal separation.

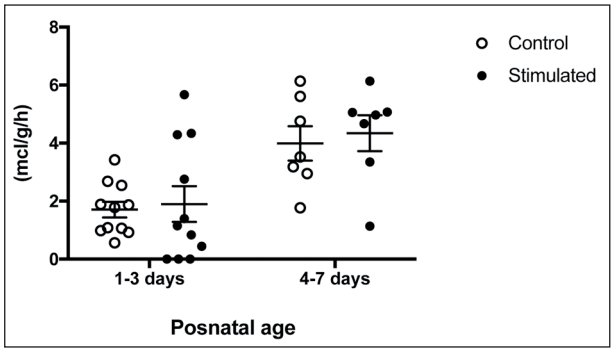

Figure 1 (ABS 15). Gastric emptying 6 h after feeding (mcl/g/h), p = 0.6.
All data expressed in Mean (SE).
Data analyzed by two-way ANOVA.

RESULTS

No statistically significant difference in gastric emptying rate was observed between groups at either 1-3 or 4-7 days of age (p = 0.6) (**Fig. 1**).

CONCLUSIONS

The present study shows that anogenital stimulation of newborn pups, although physiologically required to eliminate urine and feces, does not increase their gastric emptying rate. Such finding from a suitable animal model is in keeping with data reported from several clinical trials that failed to show that inducing meconium elimination after birth prevents feeding intolerance in preterm infants.

ABS 16

THE PRETERM INFANT GASTRIC EMPTYING RATE IS DEPENDENT ON THE FEED VOLUME AND NOT ON POSTNATAL AGE

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INTRODUCTION

Feeding intolerance, is a common finding in preterm neonates and often manifests as increased gastric residual post feed. The factors accounting for the reduced gastric emptying rate and the regulation of its muscle motility in preterm infants are poorly known. Gastric residual are usually present at the initiation of enteral feeding and often not documented as the milk intake is progressively increased. This is believed to be related to postnatal

maturation. Limited studies conducted in human and animals during adulthood suggest that gastric content emptying rate is volume-dependent. This has not been previously evaluated in preterm neonates. Hypothesizing that the stomach milk volume is a key determinant factor, we evaluated the gastric emptying rate in enterally fed, clinically stable preterm neonates during the first four weeks of life.

METHODS

Utilizing a validated ultrasound methodology, we assessed the gastric milk content volume of 28-32 weeks gestation neonates without overt feeding intolerance (n = 42). Measurements were obtained immediately after, 30 and/or 60 min following a routinely prescribed feed. Gastric emptying rate was calculated as the final-initial volume difference over the measured time period. 65% of the infants were studied more than once during the first month of life. The enteral feeding protocol for this population involved advancing the milk volume at a rate of 20 ml/kg/day, if well tolerated.

RESULTS

The gastric emptying rate was independent of postnatal age and significantly higher at 30 min, when compared with 60 min post feed. Hypothesizing that these findings related to the larger content at 30, as opposed to 60 min, we proceeded to evaluate the relationship between stomach content volume and the rate of gastric emptying. A direct and significant correlation was found between the initial content volume and the gastric emptying rate for that corresponding time period ($R^2 = 0.72$; $p < 0.01$) (**Fig. 1**). When expressed as % of initial volume, the highest emptying rates corresponded to the largest gastric content volumes, independently of age.

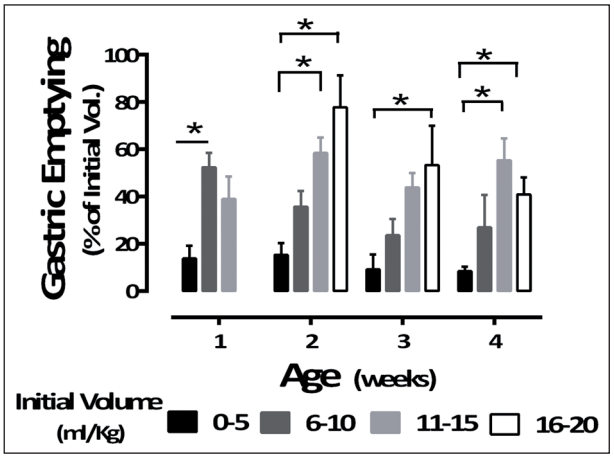

Figure 1 (ABS 16). Gastric emptying rate for infants 1-4 weeks of age according to their initial stomach content volume.
* $p < 0.01$

CONCLUSIONS

We conclude that preterm infants' gastric emptying is determined by the feed volume independently of postnatal age. Further investigation on the potential beneficial benefit of initiation of enteral feeding with volumes larger than currently employed for preterm neonates is warranted.

ABS 17

NECROTIZING ENTEROCOLITIS IN A NEONATAL INTENSIVE CARE UNIT

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INTRODUCTION

Necrotizing enterocolitis (NEC) is one of the most frequent gastrointestinal emergencies in the neonatal period. It is predominantly a disease of the preterm infant with an incidence, severity and mortality inversely related to birth weight and gestational age. The aim was to analyze the cases of NEC admitted in a level III Neonatal Intensive Care Unit (NICU).

METHODS

Retrospective study with review of the clinical files of patients admitted in the NICU from January 2008 to December 2016, with NEC diagnosis.

RESULTS

The diagnosis of NEC was established in 46 newborns, with an incidence of 1.5 per 1,000 live births, corresponding to 3.6% of very low birth weight infants and 6% of extremely low birth weight infants. The mean gestational age and birth weight was 29.5 weeks and 1,218 g, respectively. The mean age at diagnosis was 15.8 days. The most frequent risk factors were previous prolonged antibiotic therapy (73.9%), hemodynamically significant patent ductus arteriosus (28.3%), anemia requiring blood transfusion (26.1%) and umbilical arterial catheterization (10.9%). NEC grade I, II and III occurred in 37%, 32.6% and 30.4% of the cases, respectively. At diagnosis, all newborns were on enteral feeding and 64% of NEC III cases were exclusively breastfed. Surgical management was performed in 26.1%. There were 3 deaths (2 before surgery).

CONCLUSIONS
The incidence of NEC was similar to that described in the literature and occurred exclusively in preterm newborns. We point out the high rate of previous prolonged antibiotic therapy. In the prevention of NEC, few proven strategies are effective, so efforts to minimize the frequency and severity of NEC should be directed at reducing risk factors.

ABS 18

SPONTANEOUS INTESTINAL PERFORATION: A DIAGNOSTIC CHALLENGE IN THE NEWBORN

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INTRODUCTION
Spontaneous intestinal perforation (SIP) is a perforation in the gastrointestinal tract of a newborn with no demonstrable cause that is typically found in the terminal ileum. It's the second most common cause of neonatal intestinal perforation and has been very well documented in the very low birth weight neonates. The etiology of SIP remains unknown and risk factors are not yet well established. The aim was to analyze the cases of SIP in a level III Neonatal Intensive Care Unit (NICU) over a period of seven years.
METHODS
Retrospective study with review of the clinical files of patients admitted in the NICU from January 2010 to December 2016, with SIP diagnosis.
RESULTS
SIP was documented in five newborns, with an incidence of 0.2 per 1,000 live births. The mean gestational age and birth weight was 26.8 weeks and 795 g, respectively. The mean age at presentation was 10.6 days and there were 3 males. Four newborns were on enteral feeding. Abdominal distention and bluish coloration were the presenting symptoms in all patients, with systemic manifestations in three cases. All neonates had pneumoperitoneum on X-ray and in two a microbiological agent was isolated in the blood culture. Placental chorioamnionitis was not identified and postnatal steroids were not administrated in any case. One patient died before intervention and surgical management was performed in the remaining four. Perforation was located in the terminal ileum in three cases and in the transverse colon in one case. There were 2 deaths.
CONCLUSIONS
SIP is a distinct clinical entity from necrotizing enterocolitis and this differentiation is important because of management and outcome considerations. The authors highlight the high mortality rate in this case series. It is essential to maintain a high index of clinical suspicion in order to institute early appropriate management.

ABS 19

OUTCOMES OF EXTREMELY LOW BIRTH WEIGHT BABIES RECEIVING SURGICAL TREATMENT FOR NECROTISING ENTEROCOLITIS

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INTRODUCTION
Necrotising enterocolitis (NEC) remains a challenging condition to manage on the neonatal intensive care unit (NICU). Surgery is often needed to manage NEC in preterm infants, particularly those born at the earliest gestation. A recent UK population based study showed an incidence of "severe NEC" (NEC confirmed at laparotomy, histology or autopsy) among infants born < 32 weeks gestation to be 3.2%, with a mortality rate of 35% among those receiving surgical treatment. Hence the decision to provide surgical treatment for NEC is often one that needs careful consideration of parents' wishes and it is the duty of health care professionals to provide as accurate outcome information to parents as possible. The aim of our study aims is to record outcomes of extremely low birth weight (< 1,000 g at birth; ELBW) infants treated surgically for NEC at a single large NICU in England.
METHODS
All ELBW babies treated for NEC at our NICU between 1/1/2010 and 31/12/2015 were identified retrospectively using electronic patient records (Badgernet®). 174 neonates identified were then categorised as having received conservative (123) or surgical (51) management for NEC. 5 babies were excluded – 1 meconium ileus, 1 duodenal atresia, 1 Meckel's diverticulum, 2 received NEC treatment elsewhere. A retrospective notes review of the remaining 46 babies was performed to

record the major neonatal outcomes as discussed below.

RESULTS

17 (37%) babies died following surgical management of NEC. The number of days between surgery and death ranged from 0 to 72; 12% (median; 4 babies) died within 7 days of surgery and 28%(13 babies) within 30 days of surgery. Mortality was higher in those with birth weight of < 700 g. 3 (7%) babies were discharged to home, 26 (56%) were transferred to another hospital (12 to a surgical unit, 14 to another neonatal unit for ongoing management). Median age at discharge was 61 days of life (range 6-116). 27 babies (59%) were given a diagnosis of bronchopulmonary dysplasia (BPD) at 36 weeks corrected gestational age. Prior to surgery, 4 babies had evidence of Grade III/IV intraventricular haemorrhage (IVH). Post-surgery, 13 babies (28%) had Grade III/IV IVH.

CONCLUSIONS

Our results suggest that the overall mortality rate of ELBW babies undergoing surgery for NEC is not dissimilar to babies born at 50% of babies born at < 700 g died before discharge from our NICU. The incidence of other significant morbidities i.e. BPD and grade III/IV IVH, is particularly high in this cohort. These results provide useful information that will further enable parents to take informed decisions about these babies. Larger studies need to provide specific data about ELBW babies undergoing surgical management of NEC, including long term neurodevelopmental outcomes.

ABS 20

ASSESSMENT OF ENZYMOTHERAPY EFFICACY IN CASE OF LACTASE INSUFFICIENCY IN PRETERM INFANTS

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INTRODUCTION

The objective of the study was to assess the efficacy of substitution enzymotherapy in case of lactase insufficiency in preterm infants on the basis of clinical-anamnesis data and application of non-invasive methods of diagnostics.

METHODS

26 preterm infants were examined in the neonatal center of the Regional Pediatric Clinical Hospital. The first (I) group included 13 preterm infants who in addition to their comprehensive treatment received substitution therapy with the medicine "Mamalac" during 2 weeks. The second (II) group included 13 preterm infants without administration of this medicine. The groups were comparable by the main clinical signs. The main complaints in case of indication of "Mamalac" were: decreased tolerance to food, periodical abdominal bloating and anxiety of a child.

RESULTS

At the moment of administration of the medicine the volume of food for one meal in I group was 10 ml in 15.4% infants, from 10 to 30 ml – in 15.4% cases and 69.2% infants received more than 30 ml of food for one meal. Corresponding indices in II clinical group were: 7.6% ($p < 0.05$); 30.8% ($p < 0.05$) and 61.6% ($p > 0.05$). In the process of administration substitution therapy to a comprehensive treatment in I clinical group a tendency to quicker weight gain was marked. Thus, a part of preterm infants with the body weight more than 2,500 g was 53.8% against 38.4% cases ($p < 0.05$) of a comparison group, and the volume of meals more than 30 ml increased from 69.2% to 84.6% against 38.5% to 15.4% cases (p I/II group < 0.05).

CONCLUSIONS

The percentage of infants with the carbohydrate level more than 0.6% according to Benedict test decreased from 84.5% to 30.7% in the main group, while from 61.4% to 38.3% in the group of comparison (p I/II group < 0.05), which is indicative of the efficacy of early application of substitution enzymotherapy in case of feeding of preterm infants with a low tolerance to food at hospital.

ABS 21

THE NORWEGIAN PRETERM INFANT GUT (PINGU) STUDY: A METAGENOMIC APPROACH TO GUT MICROBIOTA COMPOSITION AND RESISTOME IN INFANTS SUPPLEMENTED WITH PROBIOTICS

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INTRODUCTION
Probiotics protect against necrotizing enterocolitis (NEC) in preterm infants. Early probiotic supplementation with Infloran® (*B. longum* and *L. acidophilus*) for preterm infants at high risk for NEC was therefore routinely implemented in Norway in 2014. In this study we aimed to evaluate the composition and trajectory of the infant gut microbiota (taxonomy and resistome) in preterm infants supplemented with probiotics (probiotic-group) versus preterm infants not supplemented with probiotics (no-probiotic group).
METHODS
Explorative multicenter study in six Norwegian neonatal units. We included 66 preterm infants: 31 infants < 28 weeks gestation (mean BW 826 g) weeks in the probiotic group and 35 infants 28-31 weeks gestation (mean BW 1,290 g) in the no-probiotic group. Ten healthy breast-fed term infants were included as control group. Faecal samples were collected at 7 days, 28 days, 4 months and 1 year of age. We used a commercially available kit (OMNIgene®) enabling us to store samples at ambient temperature. Metagenome sequencing was performed using the Illumina Miseq. We collected clinical data from the Norwegian Neonatal Network. We analyzed and stratified data by probiotic-group and by use of antibiotics during hospitalization and up to 4 months of age.
RESULTS
Among the 66 preterm infants, 57 received antibiotics in the first week of life. After the first week of life, infants in the probiotic-group received more antibiotics than the no-probiotic group. Probiotic *Bifidobacteria* and *Lactobacilli*, to a lesser extent, were established early and persisted in the probiotic-group. The no-probiotic group displayed a more diverse repertoire of different bifidobacterial species. For both groups the alpha diversity increased with increasing postnatal age, but was not significantly influenced by mode of delivery or antibiotic exposure. Despite being less mature and exposed to more antibiotics, the probiotic group had a very similar taxonomic profile (gut microbiota composition) compared to the no-probiotic group at 28 days and 4 months. The gut resistome of infants exposed to prolonged antibiotic therapy had significantly more multidrug efflux pump genes.
CONCLUSIONS
Probiotic supplementation enabled extremely preterm infants to obtain a very similar gut microbiota composition compared to a more mature and healthy preterm group, with less antibiotic exposure. The duration of antibiotic exposure was associated with an increased enrichment of antibiotic resistance genes in the gut.
Clinicaltrials.gov: NCT02197468.

ABS 22

NECROTIZING ENTEROCOLITIS: WHAT ASPECTS IN 2017?

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INTRODUCTION
Necrotizing enterocolitis (NEC) is the most common acquired disease of the gastrointestinal tract (GIT) in premature infants and newborns. Ulcerative necrotizing enterocolitis: it is defined as an ulcerative inflammation of the intestinal wall. Its incidence is inversely proportional to gestational age. Despite the progress of neonatal reanimation, NEC stills burdened with heavy mortality. Our study aims to describe the clinical, biological and radiological aspects, as well as management and outcome of NEC in a Tunisian Neonatal Resuscitation and Intensive Care Unit.
METHODS
A retrospective descriptive study of patients with NEC hospitalized in our Neonatal Resuscitation and Intensive Care Unit over two-years period (March 2015-2017).
RESULTS
We collected 17 patients, 8 male and 9 female. The median weight at birth was 1,500 g. 8 patients were small for gestational age. 6 patients had perinatal asphyxia. 16 had an umbilical catheter. 10 patients were infected. 11 patients required mechanical ventilation at birth. Abdominal distension was noted in 13 cases, gastric residue in 13, apnea in 10, abdominal sensitivity in 8 and bradycardia in 4 cases. Symptoms were considered severe in 5 cases.

Rectal bleeding was noted in 3 cases. Abdominal X-ray was normal in 10 cases. It showed dilated handles in 6 cases, pneumatosis in 2 and perforation in one case. According to the Bell classification, 10 cases were classified as stage I, 6 as stage II and 1 as stage III. 15 patients underwent broad-spectrum antibiotic therapy, 12 in absolute diet. Mechanical ventilation was used in 11 cases. Only one patient underwent surgery. 4 patients died.

CONCLUSIONS

NEC represents only 8 to 12% of neonatal infections, but it remains a serious life-threatening condition for newborns. The authors recall the risk factors and the different clinical aspects.

ABS 23

ROUTINE PROBIOTICS FOR PRETERM NEONATES: EXPERIENCE IN A TERTIARY AUSTRALIAN NEONATAL INTENSIVE CARE UNIT

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INTRODUCTION

Probiotic supplementation significantly reduces the risk definite (≥ stage II) necrotizing enterocolitis (NEC) and all cause mortality in preterm neonate [1-3]. Based on the current evidence, experts favour routine probiotic supplementation (RPS) in preterm neonates, if safe and effective products are available. We aimed to implement a stepwise plan for introducing RPS for preterm neonates and compare key outcomes with a retrospective cohort that did not receive probiotic.

METHODS

Steps: 1) Develop evidence-based guidelines for RPS; 2) Select a suitable probiotic product; 3) Approval from institutional drug and therapeutics committee; 4) Endorsement from ethics committee; 5) Authorized prescriber approval from Therapeutic Goods Administration, Australia; 6) Approval for importing the product from overseas; 7) Independent quality assessment (Taxonomy, antibiotic susceptibility); 8) Prospective audit comparing key outcomes (NEC, mortality, sepsis) before (retrospective cohort) vs. after introducing RPS.

RESULTS

RPS (Infloran®: *Lactobacillus Acidophilus* and *Bifidobacterium Bifidum*) was introduced in December 2011, for preterm neonates (gestational age ≤ 32 weeks, birth weight ≤ 1,500 g). Over 24 months (December 2011-2013). 148 neonates (Median gestational age: 28.8 [IQR: 26-30] weeks) received RPS. Majority (95.0%) received breast milk. The incidence of definite NEC was significantly reduced after introducing RPS (0.6% vs. 5.5%) compared to the retrospective cohort (n = 144) with comparable demographic characteristics (Median gestation: 28.5 [IQR: 25.2-30.6] weeks). The prospective audit was continued for another 24 months January 2014 - January 2016 (n = 187) and the incidence of NEC remained very low (0.5%). Supplementation was well tolerated with no adverse events. No parents refused consent. Results are presented in **Tab. 1**.

CONCLUSIONS

Our results support the benefits of probiotics in preterm neonates. Our experience, as the first Australian neonatal unit to introduce RPS may help others wishing to adopt this intervention.

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Table 1 (ABS 23). Key outcomes – routine probiotics December 2011-January 2016 compared to historic controls (December 2009-2011).

	Historic control n = 144 December 2009-December 2011	Probiotics n = 148 December 2011-December 2013	Probiotics n = 187 January 2014-January 2016
NEC (≥ stage II)	8 (5.5%)	1 (0.6%)	1 (0.5%)
NEC (≥ stage II) BW < 1,000 g	6/65 (9.2%)	0/61	1/72 (1.3%)
Death (≥ 7 days)	5	4	5

NEC: Necrotising Enterocolitis; BW: birth weight.

ABS 24

MATERNAL RISK FACTORS FOR NEC IN PREMATURES INFANTS WITH GA UNDER 28 WEEKS

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INTRODUCTION

Identify risk maternal factors predictive for NEC in prematures infants with GA less than 28 weeks.

METHODS

The study was retrospective and we included 988 newborn in five years (2012-2016) with GA less than 28 weeks, from nine level III Centers from Romania. The predictors factors that we watched were: chorioamnionitis, prolonged rupture of the membranes more than 18 hours, pregnancy-induced hypertension, eclampsia, maternal diabetes, antepartum hemorrhage, antenatal corticosteroids, type of birth, place of birth as possible involved in a develop of NEC.

RESULTS

The incidence of NEC was 10.4% and the maternal predictive factors involved were statistically analyzed by multiple regression. They are identifiers in order of significance: the lack of antenatal steroids ($p = 0.001$), birth outside the center ($p = 0.002$), eclampsia ($p = 0.03$), prolonged rupture of membranes > 18 hours ($p = 0.02$). The factors not involved in NEC were: chorioamnionitis ($p = 0.15$), antepartum hemorrhage ($p = 0.37$), maternal diabetes ($p = 0\ 40$), type of births ($p = 0.19$), maternal hypertension ($p = 0.16$).

CONCLUSIONS

The key to prevention NEC is to reduce premature birth. In our study, born outside the center without maternal corticosteroid administration need a rigorous control of infections.