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The inflammatory status of the intestine in premature infants depending on gestational age

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ABSTRACT

Background and objectives (Aim). To identify the features of the inflammatory status of the intestine in premature infants depending on gestational age.

Materials and methods. The study included 36 premature babies. All children were divided into two groups, according to gestational age (GA): group 1-12 newborns with GA of 22 (0/7) - 28 (6/7) weeks; and group 2-24 newborns with GA of 29(0/7) - 32(6/7) weeks. The exclusion criteria were: the presence of congenital malformations, septic conditions, surgical pathologies.

Results. The level of fecal calprotectin, as well as CRP in the 1st group of children was significantly higher than in the 2nd group, which demonstrates an inverse relationship between the severity of inflammation and the gestational age of premature newborns: the lower the gestational age, the higher the rates of inflammation in the intestines. The permeability of the intestinal barrier was high in both groups, which was reflected in increased values of fecal alpha-antitrypsin on the 3rd and 14th days of the examination, and did not have statistically significant differences between the groups. Children of group 1 required longer treatment than children of group 2, both in the ICU. Clinical manifestations of digestive disorders in premature infants were manifested by decreasing in body weight gain, the appearance of discharge from the tube with pathological impurities, while no significant difference was found between the groups.

Conclusions. Premature neonates less than 28 weeks of age show greater signs of acute inflammation in the intestinal tract.

Keywords: preterm, inflammatory status, intestine, gestational age

INTRODUCTION

According to the World Health Organization (WHO), 13.4 million babies were born preterm in 2020, more than one tenth of all babies born [1]. The state of prematurity, in itself, predisposes to the occurrence of various disorders of the gastrointestinal tract, which, in turn, leads to increased morbidity rates among this group of children [2]. However, the state of the intestine and its functions in premature infants receiving respiratory therapy has not been sufficiently studied.

The gastrointestinal tract is an integral part of the body, that is response not only the digestion and absorption of nutrients depends, but also immunological function, modulation of the inflammatory response and the launch of autoimmune diseases.

The complexity of the morphological structure of the intestine is not fully understood, and new discoveries are revealing the broader significance and importance of this organ [3].

An immature gastrointestinal tract and emerging digestive system disorders from birth put children at risk for delayed psychophysical development and contribute to the development of negative long-term neurological consequences.

Many of these complications have long-term consequences for health, growth and development, both in infancy and later life.

Adaptation of premature newborns depends on many factors, the leading of which are: gestational age, degree of maturity; severity of disorders of the central nervous system; optimal use of the arsenal

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of modern achievements in intensive care medicine; timely provision of rehabilitation assistance and subsequent recovery treatment [4].

MATERIALS AND METHODS

The study included 36 premature babies born and nursing in the intensive care and resuscitation units of the Republican Perinatal Center (born in late 2022-early 2023). All studied children were divided into two groups according to gestational age: group 1-12 newborns with a gestational age of 22 (0/7) - 28 (6/7) weeks; and group 2-24 newborns with a gestational age of 29(0/7) - 32(6/7) weeks. The exclusion criteria were: the presence of congenital malformations in newborns, septic conditions, also children with surgical pathologies.

All children underwent general clinical methods: general blood test, stool and biochemical research methods (total protein, bilirubin, glucose, CRP, etc.). To assess the general condition of newborns at birth and further during treatment in intensive care and resuscitation units, generally accepted methods, rating scales and tables were used.

Assessment of the state of the functions of the digestive system was carried out according to standard methods, taking into account the specifics of the neonatal period. In this regard, non-invasive markers of intestinal inflammation were included in the laboratory parameters: α-1-antitrypsin (A1AT) using the immunoturbidimetry method, fecal calprotectin (FC) using the PhiCal® enzyme-linked immunosorbent assay. Statistical data processing was carried out using statistical programs StatSoft "STATISTICA-6" Correlation analysis based on the linear Pearson correlation coefficient r)

RESULTS

The research results showed that the average gestational age in the first group was 24.3±0.5 weeks (22.6-28), in the second group - 29.1±0.2 weeks (29.0-32).

Body weight at birth was significantly low in children of group 1 and averaged 986±70.2 g, and in group 2 it was 1563±67.5 g. (p<0.05).

TABLE 1. Characteristics of the examined newborns

Features	Group 1 n= 12, (M±m)	Group 1 n= 24, (M±m)
Gestational age (weeks)	24,3±0,5 (22,6-28)	29,1±0,2* (29,0-32)
Birth weight (grams)	986±70,2 (870-1238)	1563±67,5* (895,0-2308,0)
Body length at birth (cm)	33,4±0,8 (27-36)	36,5±0,4* (27-36)

* p <0.05 when comparing the indicators of the first and second groups

Gestational age also determined its influence on the average body length at birth, so in group 1 these indicators were significantly low compared to the data in group 2 (33.4±0.8 versus 36.5±0.4 cm; P< 0.05).

A correlation was observed between gestational age and body weight (r=0.689; p<0.05) and body length (r=0.705; p<0.05) of the child.

The Apgar score (Table 2) at the 1st and 5th minutes of life was significantly lower in newborns of group 1 compared to the indicators of children in group 2 (p <0.001).

TABLE 2. Some clinical and laboratory parameters of the examined children

Features	Group 1 n= 12	Group 1 n= 24
Apgar score at 1st minute	5,2±0,6	6,7±0,4*
Apgar score at 5th minute	6,1±0,2	7,7±0,3*
Duration of antibiotic therapy (days)	21,5±0,2	16,9±0,4
Weight gain after day 7	5,3±1,4	6,3 ±1,4*
On what day did stable weight gain begin	10,8±0,7	10,9±1,0
Weight gain after day 14 (average over 5 days)	11,3±1,6	12,4±1,9*
Duration of CPAP (days)	13,4±1,80	11,4±1,81

* - reliability of data between groups (P <0.05)

As can be seen from Table 2, the duration of antibiotic therapy in children of both groups does not differ significantly.

Weight gain on the 7th day was observed most often in children of group 2 (P<0.05). Similar indicators of body weight gain were obtained on the 14th day of life.

In children of group 1, the duration of CPAP was on average 2 days longer.

The nosological characteristics of the examined newborns are presented in Table 3.

TABLE 3. Nosological characteristics of the examined children

Main diagnosis	Group 1 n= 12	Group 1 n= 24
Respiratory distress syndrome (RDS)	9 (75%)	19 (79,1%)
Infections of the perinatal period	4 (33,3%)	4(16,6%)
NEC	2 (16,6%)	5 (20,8%)
Concomitant pathology		
HIE	6 (50,0%)	7 (29,1%)
Asphyxia	1 (8,3%)	2(8,3%)

As can be seen from Table 3, the main nosology is SDR, which amounted to 75% in group 1 and 79.1% in group 2, infections were diagnosed in a third of patients in group 1 and in 16.6% of cases in group 2, NEC was more common in newborns of group 1 (16.6%), but the difference compared with the indi-

cators of group 2 was not statistically significant (p>0.05).

In both study groups, all preterm infants were fed from the first 3 hours of life, starting with expressing a few drops of colostrum in the delivery room, and then bolus feeding was carried out every 3 hours according to the protocol. Feeding was done through a tube, since in 91.6% of the examined premature babies the sucking reflex was absent, and in three it was weakly expressed. In the examined newborns, we identified gastrointestinal disorders presented in Table 4. As can be seen from the table, in both groups, disorders such as gastric, duodenal regurgitation and functional constipation occurred with different frequencies, and gastric regurgitation and functional constipation occurred significantly more often in group 1.

TABLE 4. Gastrointestinal disorders in examined children

Type of violations	Group 1 n= 12	Group 1 n= 24
Gastric regurgitation	3 (25,0%)	3(12,5%)*
Duodenal regurgitation	4(33,3%)	6 (26,0%)
Dyschezia	3 (25,0%)	2(8,3%)*

* p<0.05 when comparing the indicators of the first and second groups

In stool analyzes (Table 5), we did not find a significant difference between indicators such as fatty acids, the amount of mucus, epithelium and neutral fat between groups, while the number of leukocytes in feces was significantly higher in children of group 2, but was not pathological.

When assessing the length of stay of premature newborns in the hospital, it was found that the children of group 1 spent statistically significantly longer in the neonatal intensive care unit - 38.5±4.4 days (p<0.05), and the total duration of their stay in the neonatal pathology department was 61.4±6.9 days (p<0.05).

TABLE 5. Analysis of feces of examined children on days 3-4 of life

	Group 1 (n=12)	Group 2 (n=24)	p
Fatty acid (0-3)	0,63±0,18	0,76±0,10	>0,05
Mucus in stool (0-3)	0,81±0,21	1,24±0,14	>0,05
Leukocytes	1,41±0,43	3,28±0,75	<0,05
Epithelium	0,50±0,24	0,87±0,18	>0,05
Neutral fat	1,13±0,26	1,16±0,10	>0,05

Children of group 1 required longer treatment than children of group 2 both in the intensive care unit and in the neonatal pathology department.

Clinical manifestations of digestive disorders in premature infants were manifested by such signs as a decrease in body weight gain below normal (56%), discharge from the tube with pathological impurities (32%), and no significant difference was found between the indicators of children with different gestational ages.

Functional disorders of the digestive organs in premature infants are more often represented by gastric and duodenal regurgitation (in 16 children out of all examined), detected in approximately half of the cases (16.6% and 27.7% of all examined, respectively, and these indicators did not depend on gestational age). age of children.

Taking into account the importance of intestinal barrier permeability in the development of conditions associated with digestive disorders of varying severity, we set out to study the level of fecal alpha-1-antitrypsin in premature infants under 14 days of age.

TABLE 6. Fecal alpha-1-antitrypsin values in preterm infants depending on gestational age (mg/dl)

Days of life	Group 1 (n=12)	Group 2 (n=24)	p
3rd day	367,1± 92,8	533,0 ±64,1	p<0,05
14th day	481,2±72,6	543,9±53,6	p<0,05

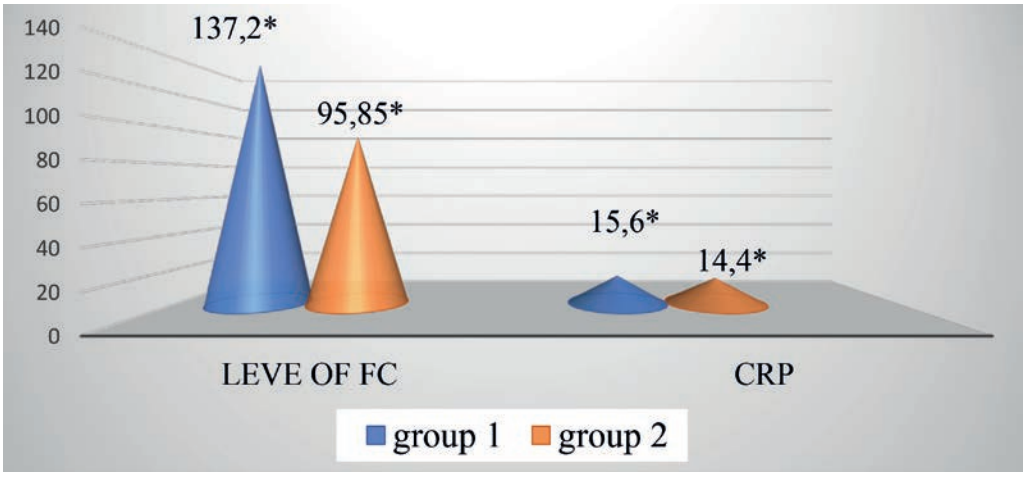

FIGURE 1. Level of inflammatory markers in premature infants depending on gestational age on day 3

The values of fecal alpha-1-antitrypsin were lower in children of group 1 compared to those in children of group 2, but at all stages of the examination they did not have statistically significant differences.

Our studies showed that the level of fecal calprotectin, as well as CRP in children of group 1 were significantly higher than the indicators in children of group 2, which demonstrates an inverse relationship: the lower the gestational age, the higher the indicators of inflammation in the intestine.

DISCUSSION

A unique characteristic of the gastrointestinal system is its lining by a single epithelial layer in continuous contact with intestinal bacterial flora. This layer is a key host defence mechanism critical for confining pathogenic bacteria to the intestinal lumen, but must also allow passage of nutrients. Preterm infants have increased intestinal permeability, perhaps to allow expected passage of important macromolecules from amniotic fluid or breast milk [5].

However, this same increased permeability could lead to increased bacterial translocation. The inflammatory response of immature intestinal epithelial cells can be triggered by either commensal or pathogenic bacteria. Disruption of the intestinal epithelial barrier increases this interaction and is thought to be an early event in the pathogenic cascade of NEC [6].

Immaturity of the intestines and immune system is a physiological feature of newborns, which is especially aggravated in the case of premature babies.

This fact, combined with factors such as diet, microbiota colonization, or mode of delivery, has been associated with both intestinal and systemic diseases, including necrotizing enterocolitis or allergy.

Despite these well-recognized health risks associated with prematurity, few studies have assessed the presence of intestinal inflammation in preterm infants, while systemic inflammation has received more attention [7,8]. Our results suggest that the study of intestinal inflammatory status in preterm infants requires further research.

CONCLUSION

The level of fecal calprotectin and CRP is significantly higher in preterm infants with a gestation period of 22-28 weeks, which demonstrates an inverse relationship: the lower the gestational age, the higher the intestinal inflammation.

At the same time, the permeability of the intestinal barrier in newborns of group 1, the values of fecal alpha-1-antitrypsin are higher at all stages of the examination.

Clinical manifestations of digestive disorders in premature infants, regardless of gestational age, are manifested by such signs as a decrease in body weight gain below normal, discharge from the tube with pathological impurities.

Children with a gestational age of 22-28 weeks require longer treatment, both in the intensive care unit and in the neonatal pathology department.

Premature neonates less than 28 weeks of age show greater signs of acute inflammation in the intestinal tract, which requires further exploration of ways to prevent and treat this condition to prevent severe complications and systemic damage.

Conflict of interests: I undersign, certificate that I do not have any financial or personal relationships that might bias the content of this work.

REFERENCES

1. World Health Organization. Preterm birdh. 2023 May 10. [Russian]. Available: https://www.who.int/ru/news-room/fact-sheets/detail/preterm-birth
2. Rodríguez-Benítez MV, Gámez-Belmonte R, Gil-Campos M, Hernández-Chirlaque C, Bouzas PR, Sánchez de Medina F et al. Premature Birth Infants Present Elevated Inflammatory Markers in the Meconium. *Front Pediatr.* 2020;8:627475. PMCID: PMC7848191
3. Khasanova SS, Akhmedova DI, Kamilova AT. The Clinical Significance of Fecal Zonulin in Extremely Premature Babies. *Am J Med Medical Sci.* 2019;9(8):289-92. doi: 10.5923/j.ajmms.20190908.03
4. Alekseenko N.Yu. The main problems and prospects for caring for children with very low and extremely low birth weight // Symbol of Science. 2017;-T.2(1):C.158-163. https://cyberleninka.ru/article/n/problemy-katamnesticheskogo-nablyudeniya-nedonoshennyh-detey-obzor-literatury/viewer
5. Rouwet EV, Heineman E, Buurman WA, ter Riet G, Ramsay G, Blanco CE. Intestinal permeability and carrier-mediated monosaccharide absorption in preterm neonates during the early postnatal period. *Pediatr Res.* 2002;51(1):64-70. doi: 10.1203/00006450-200201000-00012
6. Claud EC, Lu L, Anton PM, Savidge T, Walker WA, Cherayil BJ. Developmentally regulated IkappaB expression in intestinal epithelium and susceptibility to flagellin-induced inflammation. *Proc Natl Acad Sci USA.* 2004;101(19):7404-8. doi: 10.1073/pnas.0401710101
7. Rasquin-Weber A, Hyman PE, Cucchiara S, DR Fleisherd, JS Hyamse, PJ Milla et al. Childhood functional gastrointestinal disorders. *Gut.* 1999;45(Suppl 2):II60-8. PMID: 10457047; doi: 10.1136/gut.45.2008.ii60
8. Cuestas E, Aguilera B, Cerutti M, Rizzotti A. Sustained neonatal inflammation is associated with poor growth in infants born very preterm during the first year of life. *J Pediatr.* 2019;205:91-7. doi: 10.1016/j.jpeds.2018.09.032