Vlasova Olena Vasylivna, Hrytsiuk Mariana Ivanivna, Kolyubakina Larisa Viktorovna, Homma Natalia Vasylivna. Necrotic Enterocolitis: Clinical and Anamnestic Parallels in Premature Infants. Journal of Education, Health and Sport. 2020;10(3):265-271. eISSN 2391-8306. DOI http://dx.doi.org/10.12775/JEHS.2020.10.03.028
https://apcz.umk.pl/czasopisma/index.php/JEHS/article/view/JEHS.2020.10.03.028
https://zenodo.org/record/3857732

The journal has had 5 points in Ministry of Science and Higher Education parametric evaluation. § 8. 2) and § 12. 1. 2) 22.02.2019.

Received: 09.03.2020. Revised: 18.03.2020. Accepted: 31.03.2020.

Necrotic Enterocolitis: Clinical and Anamnestic Parallels in Premature Infants

[1]Olena Vasylivna Vlasova, [1]Mariana Ivanivna Hrytsiuk, [1]Larisa Viktorovna Kolyubakina, [2]Natalia Vasylivna Homma

[1]HSEE of Ukraine "Bukovinian State Medical University"
[2]Regional Children's Clinical Hospital of Chernivtsi

Olena Vasylivna Vlasova - Candidate of Medical Sciences, Doctoral Student of the Department of Pediatrics and Children's Infectious Diseases of HSEE of Ukraine "Bukovinian State Medical University", Chernivtsi, Ukraine, E-mail: vlasovaolena01@gmail.com
https://orcid.org/000-0003-4253-0731
Mariana Ivanivna Hrytsiuk - Doctor of Medical Sciences, Head of the Department of Social Medicine and Public Health of HSEE of Ukraine "Bukovinian State Medical University", Chernivtsi, Ukraine;
E-mail: m.grytsiuk@gmail.com;
http://orcid.org/0000-0003-1000-6417
Larisa Viktorovna Kolyubakina - Candidate of Medical Sciences, Associate Professor of the Department of Pediatrics and Children's Infectious Diseases of HSEE of Ukraine "Bukovinian State Medical University", Chernivtsi, Ukraine.
Natalia Vasylivna Homma – medical doctor, Regional Children's Clinical Hospital of Chernivtsi, Ukraine;

Abstract

Necrotic enterocolitis (NEC) in neonatal practice remains one of the major causes of morbidity and mortality in premature infants due to the combined effect of various pathogenic factors: infectious, metabolic, circulatory on the relatively immature bowel. Most often the onset of the disease occurs at the gestational age of the baby 29-32 weeks at the age of 2-3 weeks of life.

Objective of study: evaluation of anamnestic, clinical and paraclinical data and course of NEC in premature infants who were hospitalized in the neonatal unit of Regional Children's Clinical Hospital (RCCH) of Chernivtsi.

Materials and methods. A retrospective analysis of the diseases of 28 premature infants who were hospitalized in the neonatal intensive care unit (NICU) of RCCH was performed. While in the hospital, all children underwent general clinical, biochemical, instrumental methods of investigation and determination of immunological parameters of the infectious-inflammatory process in the blood serum, namely the level of C-reactive protein and pressepsin was made.

Results. Among the examined, the proportion of deeply premature infants (up to 32 weeks of gestation) was 50%, including extremely low weight 17.8%. About 80% of children were born with signs of asphyxia of varying severity. It was shown that the development of NEC in premature children is associated with a burdened infectious history in mothers amid anemia (r = + 0.79), a short gestation period (r = + 0.44), and a low Apgar score in the fifth minute (r = + 0.45), the severity of the condition at admission to the hospital (r = + 0.74), the need for long-term mechanical ventilation (r = + 0.67), hemodynamic support with the vasoactive drugs (r = + 0.39), apnea development (r = + 0.83), feeding intolerance (r = + 0.45) and thrombocytopenia (r = +0.68). It was established that the determination of serum presepsin content makes it possible to verify the genesis of the development of NEC.

Conclusion. The formation of NEC in premature infants is associated with the development of multiple organ failure in the anamnesis due to asphyxia, and its chances are increased due to the presence of a generalized infectious inflammatory process.

Key words: necrotic enterocolitis; premature infants; presepsin; generalized-infectious inflammatory process.

Introduction

Despite the introduction of modern perinatal technologies into neonatal practice, necrotic enterocolitis remains one of the leading causes of infant morbidity and mortality in neonatal intensive care units [NICU] [1, 2]. Thus, numerous epidemiological studies have shown that the incidence of NEC is between 5 and 13% of infants with gestational age less than 32 weeks gestation and body weight at birth less than 1500 grams. The highest incidence rate among this category of patients is in children with extremely low weight. The mortality rate varies in the group of children with a traditional NEC diagnosis of 28-54% of cases, and after surgery to 60% [3, 4].

Selective circulatory ischemia of the intestine is considered to be the most important triggering mechanism for the development of NEC due to the transferred perinatal hypoxia and / or asphyxia on the background of immaturity of the gastrointestinal tract and immaturity of mechanisms of immune protection, as well as bacterial colonization of the intestine. Today, generalization of information on NEC diagnostics, use of standardized feeding protocols for premature infants, antibacterial therapy, and erythrocyte transfusions have contributed to the stabilization of morbidity for this pathology (an average of 10% among extremely low birth weight children) and has led to recognition. different groups of newborns have excellent risk factors for developing the disease [4].

Thus, it is proved that for a newborn's intestine at a certain post-conceptual age is characterized by a hyperreactive condition associated with an increase in the level of intrauterine activity TLR-4, which are required for differentiation of the intestine of the fetus [5]. In premature infants, TLR-4 levels remain elevated, leading to enterocyte apoptosis followed by bacterial translocation of gram-negative bacteria through the intestinal mucosa. In addition to the model of development of innate immune responses, a specific role belongs to the peculiarities of the development of the intestinal microvessels and the state of the microbiota, in particular, the impact of antibacterial therapy on its formation. It is proved that the onset of the disease most often falls at the post-conceptual age of 29-32 weeks of pregnancy [6].

Based on this, the aim of the study was to assess the relationship of anamnestic, clinical and paraclinical data with the course of NEC in premature infants undergoing inpatient treatment in the neonatal unit of Regional Children's Clinical Hospital (RCCH) of Chernivtsi.

Materials and method. A retrospective analysis of the diseases of 28 premature infants who were hospitalized in the NICU of RCCH was performed. Criteria for inclusion in the study: premature infants with clinical and paraclinic features of NEC, exclusion criteria: malformations of the gastrointestinal tract, the presence of errors and hereditary diseases in the family history, infectious and inflammatory diseases of the gastrointestinal tract. While in the hospital, all children underwent general clinical, biochemical, instrumental methods of investigation and determination of immunological parameters of the infectious-inflammatory process in the blood serum, namely the level of C-reactive protein and pressepsin was made.

Results. The gender distribution among newborns was uniform, accounting for 50%. When analyzing the peculiarities of the course of the perinatal period, it was noted that 64.5% of babies were born in maternity hospitals, the rest - 35.5% in maternity wards of central

district hospitals. The proportion of preterm infants (up to 32 weeks gestation) was 50%, of which 17.8% were infants with extremely low birth weight. About 80% of infants were born in asphyxia of varying severity. Thus, severe asphyxia was diagnosed in 17.8% and moderate in 67% of children. The volume of examinations, urgent and after resuscitation care was in accordance with the clinical protocols “Initial, resuscitation and post-resuscitation neonatal care” protocol of the Ministry of Health of Ukraine No. 225 of March 28, 2014 and Clinical Protocol "Assistance to Newborns with Respiratory Disorders" # 484 of 8/21/2008. In the intensive care unit in maternity hospitals, in 60.7% of cases, the condition of infants was assessed as severe, and in 39.3% of patients it was moderate. By birth parity, infants (50%) from the first pregnancy prevailed, 71.4% of mothers were housewives, 18 infants (64.3%) were born by caesarean section.

In the analysis of the anamnesis data it was noted that pregnancy and childbirth were complicated in all mothers of premature babies. In every second woman, during pregnancy, the threat of miscarriage was dominated on the background of anemia, and in every fourth, preeclampsia of varying severity was noted.

According to the prevalence of the most important perinatal infectious factors, chorionamnionitis was noted in 17.8% of cases, chronic pyelonephritis in 6 women (21.4%), and a long anhydrous period of more than 5 days in five women (17.7%).

Further treatment of children consisted of providing respiratory support, including mechanical ventilation in 67.8% of children, among which in 42.8% of cases respiratory support lasted more than 6 days. All children received hemodynamic support with partial parenteral nutrition and antibiotic therapy. It should be noted that only 35.7% of newborns received breastfeeding versus 64.3% of children who were fed highly adapted mixtures.

While staying in the neonatal intensive care unit (NICU) in city maternity hospital, the diagnosis of bacterial sepsis of newborns was established in 43% of children, and hypoxic-ischemic damage to the central nervous system in 57% of infants. On average, children were in maternity hospitals for 6 days, but due to the severity of their condition, 11 children needed to be transferred to the specialized department of the RCCH on the first day. Severe condition with symptoms of multiple organ failure at admission to NICU of RCCH was observed in 100% of infants.

On admission, all children underwent general clinical, biochemical and instrumental research methods. Further treatment included providing support for vital functions: 42.8% of infants needed mechanical ventilation within 5 days, and 28.5% more than 10 days; hemodynamic for the use of vasoactive drugs and antibiotic therapy. In the course of dynamic

observation and further examination, the diagnosis was corrected: neonatal sepsis was verified in 75% of infants, and hypoxic-ischemic central nervous system (CNS) damage in 25% of cases. Thus, the average serum presepsin level in newborns, as a modern marker of the development of a generalized infectious and inflammatory process, was 711.9 ± 111.7 pg/l versus 110.0 ± 39.8 pg/l ($p < 0.01$) newborns diagnosed with NEC on the background of hypoxic-ischemic damage to CNS.

During the dynamic observation and treatment within the first and second week, signs of the development of necrotic enterocolitis I-II degree appeared. Among the clinical signs, the systemic manifestations of the disease dominated in the form of fever (21%), apnea (17.8%), tachycardia (10 7%), edematous syndrome (25%), cyanosis (3.5%), on the background of jaundice (39.2%) and a decrease in food tolerance (100%). Abdominal symptoms in the form of abdominal distention, regurgitation, the appearance of congestive gastric contents, impaired passage of the intestines and moderate edema of the anterior abdominal wall were observed in all infants. According to a survey radiography of the chest and abdominal organs, NEC I-II degree was diagnosed.

All children required partial parenteral nutrition and three required full parenteral nutrition. The volume of nutrition per breastfeeding ranged from 5-10 ml in 68% of patients and from 10 to 20 ml - 32% of children, with the share of infants who were breast-feeding accounting for 46.4% of cases and the remaining -53. 6% of newborns were fed with highly adapted mixtures.

In conducting paraclinical studies anemia was diagnosed in 47.5% of infants, thrombocytopenia in 50% of children, leukocytosis with rod-shift left - in 32.1% of cases. The rate of C-reactive protein in serum above 10 mg/ml was observed in every fourth child. The diagnostic value of determination of serum prespepsin content in the diagnosis of the genesis of NEC is analyzed. Thus, the level of pressepsin greater than 140 pg/l can be used as a test for the detection of infectious genesis of NEC in newborns, the indicators of which were: sensitivity -85.7%, specificity 71.4%. The odds ratio is -14.9 [95% CI 7.3 -30.4]. The analysis of correlation relationships of NEC development showed the presence of reliable relationship of NEC development with aggravated infectious anamnesis in the mother against anemia ($r = + 0.79$), gestational term ($r = + 0.44$), low Apgar score on the fifth minute ($r = + 0,45$), the severity of the condition at admission to the hospital ($r = + 0,74$), the need for long-term mechanical ventilation ($r = + 0,67$), hemodynamic support with vasoactive drugs ($r = 0.39$), apnea development ($r = + 0.83$), intolerant feeding ($r = + 0.45$), and thrombocytopenia ($r = + 0.68$).

Conclusions

1. Deeply preterm infants with signs of multiple organ failure in history due to the development of a generalized infectious-inflammatory process were predominant among children with development of NEC.

2. The content of presepsin 140 pg/ml or more with a sensitivity of 85.7% indicates the presence of an infectious-inflammatory process in the genesis of NEC, the chances of which, according to this immunological index, increase by 15 times.

3. The most significant clinical and anamnestic criteria for the development of NEC include the presence of a burdened infectious anamnesis of the mother, gestation time of less than 32 weeks of pregnancy, low Apgar score at the fifth minute, the severity of the condition at admission to hospital, the need for long-term maintenance of vital functions, intolerant feeding and the development of thrombocytopenia.

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