SCIENTIFIC JOURNAL OF RESEARCH IN MEDICINE (SJRM)

Article available online : https://savanticjournals.uz Volume 1 Issue 2 August 2022

CURRENT VIEW ON NECROTIZING ENTEROCOLITISE IN NEWBORNS

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Abstract: Necrotizing enterocolitis (NEC) of newborns is an inflammatory bowel disease and is one of the most dangerous diseases in neonatal gastroenterology. The average incidence of necrotizing enterocolitis is 2.4:1000 newborns (from 1 to 10: 1000), or about 2.1% (from 1 to 7%) of the total number of children admitted to neonatal intensive care units. The frequency of occurrence of the disease increases with a decrease in the gestational age of the child at birth. Full-term newborns account for 10-20% of cases of NEC. The paper summarizes the results of our own research and literature data on this problem.

Key words: necrotizing enterocolitis; newborn; children.

Introduction

Necrotizing enterocolitis (NEC) of newborns is an inflammatory bowel disease that is one of the most dangerous diseases in neonatal gastroenterology. The average mortality rates for NEC range from 10 to 45% and depend, in addition to the degree of maturity, also on the stage and prevalence of the process. Children who develop intestinal perforations and peritonitis have the highest mortality rate, especially when the inflammatory process spreads to the jejunum and proximal: to the duodenum 12 and stomach (up to 63%). The average incidence of necrotizing enterocolitis is 2.4:1000 newborns (from 1 to 10: 1000), or about 2.1% (from 1 to 7%) of the total number of children admitted to neonatal intensive care units. The frequency of occurrence of the disease increases with a decrease in the gestational age of the child at birth. Full-term newborns account for 10-20% of cases of NEC. NEC is considered as a polyethological inflammatory bowel disease. Risk factors for developing NEC include: 1) prematurity, 2) hypoxia/asphyxia, 3) bacterial colonization of the intestine by pathogenic microflora, 4) enteral nutrition. The paper summarizes the results of our own research and literature data on this problem.

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under Volume: 1 Issue: 1 in June-2022 https://savanticjournals.uz/view-journal?journal=399263992

SCIENTIFIC JOURNAL OF RESEARCH IN MEDICINE (SJRM)

Article available online : https://savanticjournals.uz Volume 1 Issue 1 July 2022

In the increased frequency of intrauterine hypoxia and asphyxia in child birth; features of the formation of the intestinal biocenos is in intensive care; features of the interaction of intestinal cells with immunocompetent cells in newborns and excessive activity of the inflammatory response, immaturity of the intestinal nervous system and mechanisms of regulation of intestinal motility; violation of the mechanisms of adaptation to enteral nutrition in premature infants due to immaturity and lack of early natural feeding; imperfection of local immunity. One of the leading links in the pathogenesis of NEC, according to most authors, is a violation of microcirculation in the intestine. Hypoxia, especially in utero, can significantly alter the blood supply to the gastrointestinal tract. In children who have had intrauterine hypoxia, changes in blood flow in the mesenteric vascular system persist postnatally, while in this group of children symptoms of gastrointestinal dysadaptation to enteral nutrition are much more common (in 86% compared to 24% in the control group). Hypoxia as a powerful stress factor activates the immune system, which is reflected in an increase in the synthesis of pro-inflammatory cytokines and other regulatory substances. However, intestinal wall ischemia is not the only pathogenetic factor in NEC. Clinical and pathomorphological changes in NEC indicate a synergistic effect of ischemia and bacterial aggression factors during the development of the disease. Ischemia followed by reperfusion contributes to maintaining the increased permeability of the intestinal wall characteristic of premature infants. Increased permeability facilitates the translocation of bacteria into the intestinal wall and then into the systemic circulation. It is important that massive contamination of the intestinal cavity with bacteria can lead to translocation even in the absence of changes in permeability and violations of intercellular contacts, for example, in a number of full-term children with NEC. In children with NEC, in a high percentage of cases, microorganisms that can have a damaging effect on the intestinal wall are sown: E. coli, Klebsiella, Staphilococcus, Bacteroides fragilis, Clostridium perfringens, Clostridium deficile, Enterobacter. However, statistical analysis of the risk factors for the occurrence of NEC does not allow us to identify any single microorganism, the contamination of which would be an independent risk factor for the occurrence of enterocolitis. Lipopolysaccharide (LPS) of gram-negative bacteria plays a special role in initiating the inflammatory process in the intestinal wall in NEC. The content of LPS in the stool of children with NEC is significantly higher than in children without NEC; there is also a difference in the severity of lipopolysaccharide excretion in the stool at different stages of the disease. LPS, as a result of interaction with TLR2 receptors on the enterocyte, activates the production of cyclooxygenase 2, which provides reactions for the synthesis of prostaglandins, thromboxanes and leukotrienes in the enterocyte. In NEC, a higher level of interleukin 1b (IL-1b) and a higher level of mRNA were found (compared to the level in bowel malformations). 1b (IL-1b), mRNA tumor necrosis factor a (TNF-a), IL-8, IL-11, IL-18, IL-12. 84% of children with NEC have all the signs of not only a local, but also a systemic inflammatory reaction, with the development of intestinal perforations, the frequency of occurrence of a systemic inflammatory

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reaction reaches 100%. NEC develops in 70-80% of cases after the start of enteral nutrition, so it is accepted that the presence of enteral nutrition is considered a risk factor for the development of NEC. However, the disease may also occur on a full parenteral diet (PPP). The practice of recent decades, as well as a number of scientific works, prove the important role of breastfeeding practice in the development of NEC. More careful administration of enteral nutrition under strict control of assimilation has reduced the incidence of the disease in many neonatal centers. Currently, there is no doubt about the need for strict clinical and laboratory monitoring of the assimilation of enteral nutrition in premature infants. An increase in the proportion of breast milk in the diet of children with very low body weight reduces the incidence of NEC and sepsis compared to children fed preterm formulas. The incidence of NEC decreases directly proportionally, depending on the proportion of breast milk in the diet of preterm infants. The preventive role of natural feeding probably lies in the ability to reduce the pro-inflammatory response and ensure mucosal repair. NEC is histologically characterized by inflammation and extensive damage to the intestinal wall tissues. Specific histopathological changes in the initial stages are edema and detachment of the villi epithelium, pronounced leukocyte infiltration, then signs of villi destruction, submucosal edema, the appearance of microhemorrhages, microthrombosis, and blood stasis in the capillaries appear. In severe cases, complete disappearance of the villi structure, ulceration of the mucosa may occur, gas bubbles (pneumatosis) are visualized in the submucosa and under the serous membrane. Pneumatosis of the intestinal wall is often found in NEC in newborns, but it is not a specific symptom, as it occurs in other pathologies and at an older age. Some authors regard gastric pneumatos is as a marker of fulminant NEK currents. The serous membrane thickens due to edema. At the stage of progression, areas of necrosis and perforation occur against the background of diffuse inflammation of the intestinal wall. As the process progresses, transmural necrosis of the intestinal wall develops, followed by perforation. In some cases, multiple necrotic segments of the intestine are interspersed with affected but viable tissues. Both in the presence of perforation and with massive necrosis of the intestine without perforation, peritonitis develops. The most common locations of perforations are the terminal ileum, cecum, hepatic and splenic corners of the colon. Typical symptoms of secondary neuronal dysplasia were found in patients with NEC. Degenerative changes in the submucosal and intermuscular plexus of the intestinal nervous system are detected. The plexuses lose glial cells and neurons, the ganglia show areas of lysis in the center, and the ganglia resemble empty baskets." Lesions resembling focal agangliosisare found. The production of neurotransmitters that inhibit muscle tone, such as vasoactive intestinal peptide and nitric oxide, decreases. Changes in the submucosal plexus are dominant, and they are more pronounced the stronger the damage to the mucosa. Thus, in NEC, degenerative changes in the intestinal nerve plexuses are observed, possibly secondary to hypoxemia. Repair processes in the intestinal wall during convalescence occur slowly. Destructive changes in the mucosa (edema, detachment of the villous epithelium) can persist for up to a month

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or more. As a result of inflammation, areas of stenosis may form in some intestinal fragments. The classification of NEC was first proposed in 1978 by M. Bell et al. According to Bell's classification, the following stages of NEC are distinguished: stage I: 1. the presence of blood in the stool; 2. large residual volume in the stomach during probe feeding; 3. bloating and abdominal tension, palpation of tight intestinal loops; 4.on the X — ray-stretching of intestinal loops, intestinal pneumatosis. Stage II: 1. increasing abdominal enlargement and tension of the anterior abdominal wall, its redness or cyanosis against the background of deterioration; 2. increasing thrombocytopenia and acidosis; 3. on the X-ray-the presence of fluid in the abdominal cavity. Stage III: 1. development of perforation and peritonitis; 2. development of shock. Subsequently, a classification was proposed by Walsh and Kleigman (1986), which takes into account the stage changes in general clinical, gastroenterological, and radiological symptoms.

In Russian practice, it is customary to distinguish 4 stages in the clinical course of NEC. The principal difference from Bell's classification is the identification of the prodrome stage, when there are no reliable signs of NEC. A great contribution to the study of the problem of NEC was made by representatives of the national school of pediatric surgeons, in particular T. V. Krasovskaya. Highlighting this stage reduces the risk of untimely diagnosis and allows you to change the patient's management tactics in time.

Children with NEC should be considered as a high-risk group for sepsis. 84% of children with NEC show signs of a systemic inflammatory reaction. In 60% of children during the course of NEC, other purulent-inflammatory diseases are detected. At least 75% of children with NEC have multiple organ failure involving 2 or more systems; NE is characterized by acid-base balance disorders such as metabolic acidosis, hypo— and hyperglycemia, and DIC syndrome. The incidence of systemic inflammation and multiple organ failure increases with the progression of the disease. The course of the disease is often cyclical, but relapses of the disease are possible, including after the closure of intestinal stomas. Diagnosis is based on the assessment of the above-mentioned risk factors, clinical picture, and X-ray examination. Ultrasound examination of the abdominal cavity is also used, in doubtful cases — laparocentesis.

Treatment. If NEC is suspected, the following conservative measures are immediately carried out:: 1. Stop enteral nutrition and stop taking medications per os. 2. Decompression of the stomach is performed (naso-or orogastric probe is opened and the probe opening is lowered below the level of the child's stomach, the volume and nature of discharge is recorded). 3. Conduct post-syndrome therapy: respiratory support, relief of hemodynamic disorders, correction of CBS, electrolyte disorders, exicosis, hemostasis disorders, pain syndrome. 4. Complete parenteral nutrition is performed (according to postconceptual age and taking into account the presence of sepsis, multiple organ failure). 5. Current antibiotics are replaced taking into account the possible role of anaerobic flora in combination with hospital strains of Gr– and Gr+ bacteria, followed by a change taking into account sensitivity. Conducting cleansing enemas for enterocolitis can provoke

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intestinal perforation. Indications for surgical treatment: 1. Tumoral formation of the abdominal cavity. 2. Inflammatory changes in the abdominal wall. Compaction, swelling, or fibrous inflammation of the subcutaneous tissue of the abdominal wall are menacing signs that usually appear in the presence of the underlying abscess, peritonitis, or intestinal gangrene.3. Specific X-ray picture (pneumoperitoneum, ascites signs, "static loop" symptom). 4. Laboratory data. Acute thrombocytopenia, coagulation disorders, severe hyponatremia and persistent acidosis confirm the presence of necrosis of the intestinal wall. 5. Abdominal paracentesis. Necrosis of the intestinal wall is indicated by the following data: turbid brown liquid, detection by staining on the skin.Gram of extracellular bacteria, a large number of white blood cells, a predominance of neutrophils — more than 80%. The resumption of EP in patients with NEC is carried out gradually. EP administration is possible in case of complete relief of pain, absence of signs of peritoneal irritation, regurgitation syndrome, hemorrhagic syndrome, restoration of peristalsis (usually not earlier than 3 days), relief of systemic inflammation and DIC. After the elimination of these clinical symptoms, enteral nutrition may begin. In a number of institutions, nutrition is preceded by the introduction of an isoosmolar liquid: saline or glucose-salt solution in a volume corresponding to trophic nutrition (about 0.5 ml / kg / hour), for 0.5–1 days. With satisfactory fluid absorption: the absence of stagnant contents in the stomach, regurgitation, increased bloating, maintaining satisfactory peristalsis, the presence of independent stool without admixture of blood, it is possible to prescribe products for enteral nutrition. The appearance of the listed symptoms of NEC at any stage of nutrition is an indication for its cancellation and resumption of full parenteral nutrition. As the first product for enteral nutrition, if the mother has milk, it is possible to prescribe native breast milk from her own mother in combination with lactase preparations. In the absence of native breast milk after a period of parenteral nutrition, it is preferable to feed with mixtures based on high-grade protein hydrolysate in a dilution of 3:1 water (25% mixture), then 1:1 (50% mixture), then in a standard concentration. After complete relief of the inflammatory process and transfer to full enteral nutrition with mixtures based on protein hydrolysate, preterm infants are gradually introduced mixtures for premature infants, full-term infants-standard adapted mixtures or lactose-free mixtures, depending on the presence of secondary lactase deficiency. According to indications, pancreatic enzymes are prescribed, and dysbiotic disorders are corrected. Feeding of children who have undergone surgery due to perforation or necrosis of the intestine is carried out according to the appropriate protocols for managing children with post-resection syndrome. Outcomes. In children who have had NEC but did not require bowel resection, intestinal motility disorders and secondary lactase deficiency may persist for 1-3 months after the disease, but by 3 months in most cases, the digestive and absorption functions are normalized. In children who have undergone bowel resection due to bowel necrosis, perforation, or peritonitis, the prognosis will be determined by the volume of resection (the most unfavorable options are with extensive jejunal resection), the level of stoma application (if the first surgical intervention was performed with the

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removal of the stoma), the condition of the intestinal region located distal to the perforation. Children with NEC are the largest group of children with short bowel syndrome (intestinal insufficiency due to loss of the absorption surface).

References

1. Khodzhaeva D. I. Changes in the Vertebral Column and Thoracic Spinecells after Postponement of Mastoectomy //International Journal of Innovative Analyses and Emerging Technology. – 2021. – Т. 1. – №. 4. – С. 109-113.
2. Ilkhomovna K. D. Modern Look of Facial Skin Cancer //Барқарорлик ва Етакчи Тадқиқотлар онлайн илмий журнали. – 2021. – Т. 1. – №. 1. – С. 85-89.
3. Ilkhomovna K. D. Morphological Features of Tumor in Different Treatment Options for Patients with Locally Advanced Breast Cancer //International Journal of Innovative Analyses and Emerging Technology. – 2021. – Т. 1. – №. 2. – С. 4-5.
4. Khodjayeva D. I. MORPHOLOGY OF IDIOPATHIC SCOLIOSIS BASED ON SEGMENT BY SEGMENT ASSESSMENT OF SPINAL COLUMN DEFORMITY //Scientific progress. – 2022. – Т. 3. – №. 1. – С. 208-215.
5. Ходжаева Д. И. СОВРЕМЕННЫЕ ВОЗМОЖНОСТИ УЛЬТРАЗВУКОВОЙ ДИАГНОСТИКИ ПРИ РАКЕ КОЖИ ЛИЦА //Жизнеобеспечение при критических состояниях. – 2019. – С. 111-112.
6. Aslonov S. G. et al. Modern Approaches to Oropharyngeal Cancer Therapy //International Journal of Discoveries and Innovations in Applied Sciences. – 2021. – Т. 1. – №. 3. – С. 38-39.
7. Khodjaeva D. I. MAGNETIC-RESONANCE IMAGING IN THE DIAGNOSIS OF BREAST CANCER AND ITS METASTASIS TO THE SPINAL COLUMN //Scientific progress. – 2021. – Т. 2. – №. 6. – С. 540-547.
8. Ilkhomovna K. D. MANIFESTATIONS OF POST-MASTECTOMY SYNDROME, PATHOLOGY OF THE BRACHIAL NEUROVASCULAR BUNDLE IN CLINICAL MANIFESTATIONS //Innovative Society: Problems, Analysis and Development Prospects. – 2022. – С. 225-229.
9. Ходжаева Д. И. АНАЛИЗ СРАВНЕНИЯ МОРФОТОПОМЕТРИЧЕСКИХ ПАРАМЕТРОВ СТРУКТУР ПОЯСНИЧНОГО ОТДЕЛА ПОЗВОНОЧНОГО СТОЛБА В НОРМЕ И ПРИ ДЕГЕНЕРАТИВНО-ДИСТРОФИЧЕСКИХ ИЗМЕНЕНИЯХ //Uzbek Scholar Journal. – 2022. – Т. 5. – С. 192-196.
10. Sultonova N. A. Treatment of hypercoagulable conditions in women with misscarriage in early gestation //Asian Journal of Multidimensional Research (AJMR). – 2020. – Т. 9. – №. 12. – С. 13-16.

Articles Published by "Global Research Network LLC"
under Volume: 1 Issue: 1 in June-2022 https://savanticjournals.uz/view-journal?journal=399263992

11. Султонова Н. А. ИНДИВИДУАЛЬНЫЙ ПОДХОД К ПРОГНОЗИРОВАНИИЮ САМОПРОИЗВОЛЬНЫХ ВЫКИДЫШЕЙ У ЖЕНЩИН ДО 24 НЕДЕЛЬ ГЕСТАЦИИ //Современные вызовы для медицинского образования и их решения. – 2021. – Т. 406.
12. Султонова Н. А. ПРОГНОСТИЧЕСКИЕ КРИТЕРИИ САМОПРОИЗВОЛЬНЫХ ВЫКИДЫШЕЙ В СТРУКТУРЕ ПРЕВЫЧНОГО НЕВЫНАШИВАНИЯ НА РАННИХ СРОКАХ БЕРЕМЕННОСТИ НА ФОНЕ ПАНДЕМИИ COVID-19 //ЎЗБЕКИСТОН РЕСПУБЛИКАСИ СОҒЛИҚНИ САҚЛАШ ВАЗИРЛИГИ ТОШКЕНТ ТИББИЁТ АКАДЕМИЯСИ. – С. 60.
13. Султонова Н. А., Негматуллаева М. Н. Значимость Применения Витамина И Минеральной Комплексной Терапии В Профилактике Невынашивания Беременности //CENTRAL ASIAN JOURNAL OF MEDICAL AND NATURAL SCIENCES. – 2021. – С. 388-392
14. Харибова Е. А., Тешаев Ш. Ж. Морфофункциональные особенности тканевой организации энтероэндокринных клеток в возрастном аспекте //Проблемы биологии и медицины. – 2020. – №. 2. – С. 168-173.
15. Харибова Е. А. Особенности морфологии нейрональных ансамблей в тройничном узле человека //Морфология. – 2011. – Т. 140. – №. 5. – С. 123-124.
16. Махмудов З. А., Нечай В. В., Харибова Е. А. Железисто-лимфоидные взаимоотношения в стенке илеоцекального перехода на разных этапах постнатального онтогенеза //Морфология. – 2008. – Т. 133. – №. 2. – С. 85.
17. Адизова Д. Р., Адизова С. Р., Иброхимова Д. Б. Место депрессивных расстройств у пациенток с хронической сердечной недостаточностью //Биология и интегративная медицина. – 2021. – №. 4 (51). – С. 79-90.
18. Адизова Д. Р., Джураева Н. О., Халилова Ф. А. ROLE OF DEPRESSION AS A RISK FACTOR IN THE COURSE OF CHRONIC HEART FAILURE //Новый день в медицине. – 2019. – №. 4. – С. 15-18.
19. Adizova D. R. et al. Rational approach to standard therapy //Central Asian Journal of Pediatrics. – 2019. – Т. 2. – №. 2. – С. 49-53.
20. Адизова Д. Р., Иброхимова Д. Б., Адизова С. Р. Приверженность лечению при хронической сердечной недостаточности //Биология и интегративная медицина. – 2020. – №. 6 (46). – С. 112-122.
21. Rakhmatovna T. D. Enterobiosis in Children Current Diagnostic Problems //European Multidisciplinary Journal of Modern Science. – 2022. – Т. 7. – С. 89-95.
22. Rakhmatovna T. D. HELICOBACTER PYLORI IN CHILDREN WITH GASTRIC DYSPEPSIA SYNDROME //BARQARORLIK VA YETAKCHI TADQIQOTLAR ONLAYN ILMIY JURNALI. – 2022. – Т. 2. – №. 3. – С. 155-159.

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23. Rakhmatovna T. D. CLINICAL AND EPIDEMIOLOGICAL ASPECTS OF THE COURSE OF ENTEROBIOSIS IN SCHOOL-AGE CHILDREN //BARQARORLIK VA YETAKCHI TADQIQOTLAR ONLAYN ILMIY JURNALI. – 2022. – С. 95-98.
24. Kurbanovna S. I. Functioning of the Immune System in Children, After Surgical Correction of Congenital Heart Defects //European Journal of Life Safety and Stability (2660-9630). – 2021. – Т. 12. – С. 439-446.
25. Шарифбаевич, Р. Н. (2021). Роль Социального Партнерство В Установлении Нормативов В Сфере Охраны Окружающей Природной Среды (Правовой Аспект). CENTRAL ASIAN JOURNAL OF THEORETICAL & APPLIED SCIENCES, 2(8), 45-55. Retrieved from https://cajotas.centralasianstudies.org/index.php/CAJOTAS/article/view/222
26. Sadulloeva I. K. Ashurova NG CLINICAL AND IMMUNOLOGICAL FEATURES OF CONGENITAL HEART DEFECTS IN ADOLESCENT GIRLS //Europe's Journal of Psychology. – 2021. – Т. 17. – №. 3. – С. 172-177.
27. Тешаев Ш. Ж., Хасанова Д. А. Сравнительная характеристика морфологических параметров лимфоидных структур тонкой кишки крыс до и после воздействия антисептика-стимулятора Дорогова фракции 2 на фоне хронической лучевой болезни //Оперативная хирургия и клиническая анатомия (Пироговский научный журнал). – 2019. – Т. 3. – №. 2. – С. 19-24.
28. Тешаев Ш. Ж., Хасанова Д. А. Макроскопическое строение пейеровых бляшек тонкой кишки крысы и изменения кишки при воздействии хронического облучения //Оперативная хирургия и клиническая анатомия (Пироговский научный журнал). – 2020. – Т. 4. – №. 1. – С. 41-45.
29. Тешаев Ш. Ж. и др. Морфологические изменения лимфоидных структур тонкой кишки крыс при хронической лучевой болезни //Морфология. – 2019. – Т. 155. – №. 2. – С. 278-278.
30. ТЕШАЕВ Ш. Ж., МУСТАФОЕВ З. М. СРАВНИТЕЛЬНАЯ ХАРАКТЕРИСТИКА МОРФОМЕТРИЧЕСКИХ ПАРАМЕТРОВ ПОЧЕК ПРИ ПОЛИПРАГМАЗИИ ПРОТИВОВОСПАЛИТЕЛЬНЫМИ ПРЕПАРАТАМИ //ЖУРНАЛ БИОМЕДИЦИНЫ И ПРАКТИКИ. – 2022. – Т. 7. – №. 1.
31. Тешаев Ш., Худойбердиев Д., Тешаева Д. Воздействие экзогенных и эндогенных факторов на стенку желудка //Журнал проблемы биологии и медицины. – 2018. – №. 4 (104). – С. 213-215.

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