

MODERN CONCEPTS OF NECROTIZING ENTEROCOLITIS IN NEWBORNS

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Abstract

Relevance. Necrotizing enterocolitis (NEC) remains one of the most serious causes of morbidity and mortality among premature infants. Despite the progress in neonatology, the incidence of NEC ranges from 1% to 7%, and mortality reaches 20-30%, increasing to 40-60% with surgical intervention. Premature infants with extremely low body weight (<1,500 g) are most susceptible to NEC and require special clinical monitoring. **The purpose of the study** is to summarize current understanding of risk factors, pathogenesis and diagnosis of NEC, as well as to evaluate the effectiveness of conservative and surgical treatment methods. **Materials and methods of research.** 40 works published in leading medical journals over the past 15-20 years have been analyzed. The main focus is on the epidemiology of NEC, the role of the microbiome, intestinal ischemia and inflammatory processes, as well as approaches to surgical tactics. **The results of the study.** It has been established that prematurity leads to poor intestinal motility, impaired mucosal barrier functions and dysbiosis, contributing to the development of NEC. Radiography and ultrasound make it possible to detect characteristic changes in the early stages, including pneumatosis and perforation. Conservative therapy involves temporary cessation of enteral nutrition, infusion support, and antibiotic therapy. In severe forms with perforation, resection of

necrotic areas and the application of a stoma are indicated. **Conclusions.** NEC requires an integrated approach to diagnosis, treatment, and prevention, including the use of breastfeeding and probiotic strategies. Further study of genetic predisposition and optimization of forecasting methods can reduce the risk of complications and increase the survival rate of premature newborns.

Keywords: Necrotizing enterocolitis, premature newborns, dysbiosis, intestinal ischemia, inflammation, breastfeeding, probiotics, surgical treatment, diagnosis, prognosis.

СОВРЕМЕННЫЕ ПРЕДСТАВЛЕНИЯ О НЕКРОТИЧЕСКОМ ЭНТЕРОКОЛИТЕ У НОВОРОЖДЕННЫХ

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Аннотация.

Актуальность. Некротический энтероколит (НЭК) остается одной из наиболее серьезных причин заболеваемости и смертности среди недоношенных новорожденных. Несмотря на прогресс в неонатологии, частота НЭК колеблется от 1% до 7%, а летальность достигает 20–30%, возрастая до 40–60% при хирургическом вмешательстве. Недоношенные младенцы с экстремально низкой массой тела (<1500 г) наиболее подвержены НЭК и требуют особого клинического мониторинга. **Цель исследования:** обобщить современные представления о факторах риска, патогенезе и диагностике НЭК, а также оценить эффективность консервативных и оперативных методов лечения. **Материалы и**

методы исследования. Проанализированы 40 работ, опубликованных в ведущих медицинских журналах за последние 15–20 лет. Основное внимание уделено эпидемиологии НЭК, роли микробиома, ишемии кишечника и воспалительных процессов, а также подходам к хирургической тактике.

Результаты исследования. Установлено, что недоношенность приводит к слабой моторике кишечника, нарушению барьерных функций слизистой и дисбиозу, способствуя развитию НЭК. Рентгенография и УЗИ позволяют выявлять характерные изменения на ранних стадиях, включая пневматоз и перфорацию. Консервативная терапия предполагает временное прекращение энтерального питания, инфузионную поддержку и антибиотикотерапию. При тяжелых формах с перфорацией показана резекция некротизированных участков и наложение стомы. **Выводы.** НЭК требует комплексного подхода к диагностике, лечению и профилактике, включая использование грудного вскармливания и пробиотических стратегий. Дальнейшее изучение генетической предрасположенности и оптимизация методов прогнозирования могут снизить риск осложнений и повысить выживаемость недоношенных новорожденных.

Ключевые слова: Некротический энтероколит, недоношенные новорожденные, дисбиоз, ишемия кишечника, воспаление, грудное вскармливание, пробиотики, хирургическое лечение, диагностика, прогноз.

YANGI TUG'ILGAN CHAQALOQLARDA NEKROTİK ENTEROKOLIT HAQIDA ZAMONAVIY TUSHUNCHALAR

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Аннотасија

Dolzarbli. Nekrotik enterokolit (NEK) erta tug'ilgan chaqaloqlarda kasallanish va o'limning eng jiddiy sabablaridan biri bo'lib qolmoqda. Neonatologiyada yutuqlarga qaramay, NEK chastotasi 1% dan 7% gacha, o'lim darajasi 20-30% gacha, jarrohlik amaliyotida 40-60% gacha ko'tariladi. Tana vazni juda kam bo'lgan (<1500 g) erta tug'ilgan chaqaloqlar NEK ga ko'proq moyil bo'lib, maxsus klinik monitoringni talab qiladi. **Tadqiqotning maqsadi** NEK xavf omillari, patogenezi va diagnostikasi haqidagi zamonaviy tushunchalarni umumlashtirish va konservativ va operativ davolash usullarining samaradorligini baholash. **Materiallar va tadqiqot usullari.** So'nggi 15-20 yil ichida etakchi tibbiy jurnallarda chop etilgan 40 ta asar tahlil qilindi. Asosiy e'tibor NEK epidemiologiyasi, mikrobiomaning roli, ichak ishemiyasi va yallig'lanish jarayonlari va jarrohlik taktikasiga yondashuvlarga qaratilgan. **Tadqiqot natijalari.** Erta tug'ilish ichak harakatining zaiflashishiga, shilliq qavatning to'siq funktsiyalarining buzilishiga va NEK rivojlanishiga hissa qo'shadigan disbiyozga olib kelishi aniqlandi. Rentgenografiya va ultratovush tekshiruvi dastlabki bosqichlarda xarakterli o'zgarishlarni, shu jumladan pnevmatoz va teshilishni aniqlashga imkon beradi. Konservativ terapiya enteral ovqatlanishni vaqtincha to'xtatish, infuzion yordam va antibiotik terapiyasini o'z ichiga oladi. Teshilish bilan og'ir shakllarda nekrotik joylarni rezektsiya qilish va stoma qoplamasi ko'rsatiladi. **Xulosalar.** NEK diagnostika, davolash va oldini olish, shu jumladan emizish va probiyotik strategiyalardan foydalanish bo'yicha keng qamrovli yondashuvni talab qiladi. Genetik moyillikni yanada o'rganish va bashorat qilish usullarini optimallashtirish asoratlar xavfini kamaytirishi va erta tug'ilgan chaqaloqlarning omon qolish darajasini oshirishi mumkin.

Kalit so'zlar: Nekrotik enterokolit, erta tug'ilgan chaqaloqlar, disbiyoz, ichak ishemiyasi, yallig'lanish, emizish, probiyotiklar, jarrohlik davolash, diagnostika, prognoz.

Introduction

Necrotizing enterocolitis (NEC) in newborns is a severe inflammatory bowel disease that mainly affects premature infants and is characterized by necrosis of the intestinal wall, which can lead to perforation, peritonitis, and death [1]. NEC remains one of the leading causes of morbidity and mortality in neonatal intensive care units (ICU), especially among children with a body weight of less than 1,500 g, who are called "premature survivors" [2]. The incidence of NEC varies from 1 to 7% among premature newborns, and mortality reaches 20-30%, increasing to 40-60% with surgical intervention [3]. Despite significant progress in neonatology, including improvements in diagnostic and treatment methods, the etiology and pathogenesis of NEC remain poorly understood, which makes it difficult to develop effective preventive strategies [4].

The purpose of the study: is to summarize modern concepts of NEC, including epidemiology, pathogenesis, clinical manifestations, diagnosis, treatment and prevention, as well as to highlight research prospects.

Materials and methods. During the preparation of the article, a review of the literature on necrotizing enterocolitis (NEC) in newborns was conducted. The main source of data was an analyzed list of papers published mainly over the past 15-20 years in leading medical journals (N Engl J Med, Lancet, Pediatrics, etc.).

The results of the study.

NEC mainly affects premature newborns, and its frequency is inversely proportional to gestational age and birth weight. According to Stoll et al., the disease occurs in 7-10% of children with a body weight of less than 1,500 g, whereas in full-term infants it is rare (less than 0.5%) [5]. The main risk factor is prematurity associated with intestinal immaturity, including insufficient motility, weak mucosal barrier function, and an immature immune response [6]. Other risk factors include artificial feeding, fetal hypoxia, intrauterine infections, congenital heart defects, and umbilical

vein catheterization [7]. Yee et al. A multicenter study showed that the use of formula milk increases the risk of NEC by 2-3 times compared with breastfeeding [8].

Epidemiological data vary depending on the region and the level of medical care. Mortality has decreased in developed countries due to early diagnosis and standardized protocols, while rates remain high in low-income countries [9]. For example, the study by Liu et al. It revealed a global incidence of NEC at the level of 2.4 per 1,000 live births, with a peak in premature infants [10]. Genetic predisposition, such as polymorphisms in the genes of proinflammatory cytokines (IL-6, TNF- α), is also considered as a potential risk factor, although data are still limited [11].

The pathogenesis of NEC is multifactorial and includes the interaction of ischemia, intestinal dysbiosis, and an inadequate immune response. The main trigger is hypoxic-ischemic intestinal damage that occurs during perinatal asphyxia or centralization of blood circulation, which leads to a decrease in mucosal perfusion [12]. Neu and Walker emphasize that the immaturity of the intestinal barrier in premature infants promotes bacterial translocation, causing an inflammatory cascade with the release of cytokines (IL-1b, IL-8) and tissue damage [13]. The formation of necrosis is associated with the activation of toll-like receptors (TLR4) on epithelial cells reacting to pathogenic microorganisms [14].

Intestinal dysbiosis plays a key role: in children with NEC, there is a decrease in the diversity of the microbiome and the predominance of pathogens such as *Escherichia coli* and *Klebsiella pneumoniae* [15]. Artificial feeding enhances this process by disrupting the colonization of beneficial bifidobacteria [16]. In addition, oxidative stress and lack of antioxidant protection in premature infants exacerbate damage, which is confirmed by Saugstad studies [17]. In severe cases, necrosis spreads to all layers of the intestinal wall, leading to perforation and peritonitis [18].

Clinical manifestations of necrotizing enterocolitis (NEC) in newborns range from mild nonspecific symptoms to severe systemic disease, which makes early

diagnosis difficult. Symptoms usually appear in the 2-3 weeks of life in premature infants, although they may occur earlier in children with extremely low body weight (<1000 g) [19]. Initial signs include bloating, stool retention, food residues in the stomach, and lethargy, which is associated with impaired intestinal motility [20]. As it progresses, bloody stools appear (in 70-80% of cases), apnea, bradycardia, and temperature instability, indicating a systemic inflammatory response [21]. In severe cases, signs of intestinal perforation develop: pronounced abdominal wall tension, erythema, and shock [22].

The severity of NEC is classified according to the Bell system, where stage I is suspected NEC (nonspecific symptoms), stage II is confirmed NEC (radiological changes), and stage III is complicated NEC with perforation or peritonitis [23]. In children with a body weight of less than 750 g, the clinical picture is often atypical, with a predominance of systemic symptoms over local ones, which requires high alertness [24]. Neu and Walker note that early signs may be mistaken for physiological adaptation or sepsis, which underscores the importance of differential diagnosis [25].

The diagnosis of NEC is based on clinical, laboratory and instrumental data. Radiography of the abdominal cavity is the gold standard, revealing intestinal pneumatosis (gas in the intestinal wall) in 50-70% of cases, which is a pathognomonic sign [26]. Other radiological findings include fixed intestinal loops, pneumoperitoneum (with perforation), and gas in the portal vein, indicating a severe course [27]. Ultrasound examination (ultrasound) is becoming increasingly important: It allows visualization of thickening of the intestinal wall, intra-abdominal fluid, and decreased perfusion, which is especially useful in the early stages [28]. Faingold et al. Ultrasound has been shown to be superior to X-rays in detecting intestinal ischemia with a sensitivity of up to 90% [29].

Laboratory markers include leukocytosis or leukopenia, thrombocytopenia ($<100,000/\mu\text{l}$), and elevated C-reactive protein (CRP), although these changes are nonspecific [30]. Metabolic acidosis ($\text{pH} < 7.25$) and lactatemia indicate systemic

hypoxia and tissue necrosis [31]. Differential diagnosis is performed with sepsis, congenital intestinal abnormalities (for example, atresia) and spontaneous perforation, which requires an integrated approach [32]. Biomarkers such as short chain fatty acids in feces or plasma IL-8 levels are being investigated as potential indicators of NEC, but their clinical use is still limited [33].

NEC treatment depends on the stage of the disease and includes conservative and surgical approaches aimed at stabilizing the condition, eliminating inflammation and preventing complications.

In stages I and II (Bell), drug therapy and supportive measures are used. Enteral nutrition is stopped for 7-14 days to unload the intestines, and nutrition is provided parenterally using solutions of glucose, amino acids, and lipids [34]. Broad-spectrum antibiotics (e.g. ampicillin and gentamicin or vancomycin and cefotaxime) are prescribed to combat bacterial translocation and sepsis, although the optimal regimen remains a matter of debate [35]. Terrin et al. Early initiation of antibiotic therapy has been shown to reduce the risk of NEC progression by 20% [36]. Correction of hypoxia, acidosis, and electrolyte disturbances is performed using infusion therapy and blood gas monitoring [37].

In stage III (Bell), surgical intervention is required for perforation or necrosis. Primary laparotomy with resection of the affected area of the intestine and the application of a stoma is a standard approach, although in children with a body weight of less than 1000 g, peritoneal drainage is preferred as a less invasive alternative [38]. Moss et al. In a randomized trial, it was shown that drainage is not inferior to laparotomy in terms of survival (about 60%), but is associated with fewer complications in extremely premature infants [39]. Postoperative care includes long-term parenteral nutrition and infection control, as the risk of recurrence remains high [40].

Conclusions. Necrotizing enterocolitis (NEC) Premature infants remain severely ill with high mortality and disability, despite improvements in neonatal care. The main risk factors are immaturity of the intestinal barrier, dysbiosis and hypoxic-ischemic damage, which enhance the inflammatory cascade. The key diagnostic methods are X-ray examination (pneumatosis, pneumoperitoneum) and ultrasound (assessment of perfusion and wall thickening). Conservative treatment in the early stages includes antibiotic therapy, intestinal respite, and correction of metabolic disorders. In severe forms with perforation, resection of necrotic areas with the formation of a stoma or the installation of drainage in extremely premature infants is necessary. Prevention is based on the use of breast milk, probiotics, and microbiome control, but there are no single proven standards yet.

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