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Necrotizing enterocolitis: a challenge in medical approach

Enterocolite necrosante: desafio na conduta médica

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ABSTRACT

Introduction: Necrotizing enterocolitis is a multifactorial condition that mainly affects premature newborns. In these newborns, the gastrointestinal system is not yet fully developed, which compromises the ability to defend against microorganisms and makes the intestine more susceptible to lesions. Premature newborns have a less developed immune system, making it difficult to fight infections and increasing vulnerability to intense inflammatory processes. These factors, together, create an environment conducive to inflammation and necrosis of the intestinal wall, leading to the disease.

Objective: To better understand the risk factors, their management, prevention and prognosis, reducing the risk of long-term sequelae.

Method: Integrative review with synthesis of evidence. The databases chosen were Pubmed, Scielo, Scopus and Lilacs using the descriptors: "newborn, prematurity, necrotizing enterocolitis AND or OR and their respective terms in English.

Result: The searches identified 13 studies that met the search strategy and were read in full, with their key points included in this review.

Conclusion: The disease affects premature babies, with the occurrence being higher the greater the prematurity. Low birth weight is also a predisposing factor, and the lower the weight, the greater the number of cases. Apgar below 7 in the 5th min of life and hypoxia during resuscitation may induce its presence. The initial complementary diagnosis should be made by simple radiography and abdominal ultrasound. Additionally, transfontanelle ultrasound should be used when hypoxic brain injury is suspected and echocardiogram when cardiac malformations causing intestinal hypoperfusion may be present.

KEYWORDS: Newborn. Prematurity. Necrotizing enterocolitis.

RESUMO

Introdução: Enterocolite necrosante é condição multifatorial que afeta principalmente recém-nascidos prematuros. Neles, o sistema gastrointestinal ainda não está completamente desenvolvido, o que compromete a capacidade de defesa contra microrganismos e torna o intestino mais suscetível às lesões. Recém-nascidos prematuros têm sistema imunológico menos desenvolvido, dificultando o combate às infecções e aumentando a vulnerabilidade a processos inflamatórios intensos. Esses fatores, em conjunto, criam ambiente propício para a inflamação e necrose da parede intestinal, levando ao quadro da doença.

Objetivo: Compreender melhor os fatores de risco, seu manejo, prevenção e prognóstico, diminuindo os riscos de sequelas em longo prazo.

Método: Revisão integrativa com síntese de evidências. As bases escolhidas foram Pubmed, SciELO, Scopus e Lilacs utilizando os descritores: "recém-nascido, prematuridade, enterocolite necrosante AND ou OR e seus respectivos termos em inglês.

Resultado: As buscas identificaram 13 trabalhos que atenderam à estratégia de busca e foram integralmente lidos, com seus pontos-chave incluídos nesta revisão.

Conclusão: A doença acomete bebês prematuros, sendo maior a ocorrência quanto maior a prematuridade. O baixo peso ao nascer também é fator predisponente, e quanto menor o peso, maior o número de casos. Apgar abaixo de 7 no 5º. min de vida e hipóxia durante reanimação podem ser indutores de sua presença. O diagnóstico complementar inicial deve ser feito por radiografia simples e ecografia abdominais. Adicionalmente, ecografia transfontanela deve ser utilizada quando se suspeita de lesão hipóxica cerebral e ecocardiograma na verificação de malformações cardíacas que acarretem hipoperfusão intestinal.

PALAVRAS-CHAVE: Recém-nascido. Prematuridade. Enterocolite necrosante.

Central message

The study and knowledge of necrotizing enterocolitis is relevant in the hospital environment due to the high mortality among patients affected by it, which brings a very high emotional cost to families. There is an increase in the length of stay in the neonatal ICU, and sequelae in the short and long term. Due to the limited existence of articles in the literature on the subject, this study sought to update the most important aspects in the approach to this serious disease.

Perspective

This review sought to add an update on the subject in order to better understand it, which is severe and requires rapid diagnosis for the installation of appropriate therapy. Analyzing the correlation of necrotizing enterocolitis with prematurity, low birth weight, hypoxia, and difference in the number of cases between sexes is important in the prognosis, as the measures to be taken must take into account the most efficient means and methods for diagnosis.

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INTRODUCTION

Necrotizing enterocolitis (NEC) is a multifactorial condition, that is, it results from the combination of several factors that mainly affect premature newborns. In them, the gastrointestinal system is not yet fully developed, which compromises the ability to defend against microorganisms and makes the intestine more susceptible to injuries. In situations of imbalance in the intestinal microbiota, harmful bacteria can proliferate and generate inflammation, causing damage to the intestinal wall and promoting a lack of oxygen or reduced blood flow to the intestine, compromising the integrity of intestinal cells, and predisposing the tissue to necrosis. Early introduction of tube feeding (especially with artificial formula) may increase the risk of NEC as breast milk contains protective factors that reduce inflammation and promote healthy gut development. Premature newborns have a less developed immune system, making it difficult to fight infections and increasing vulnerability to intense inflammatory processes. These factors, together, create an environment conducive to inflammation and necrosis of the intestinal wall, leading to NEC. Knowledge of it is essential for health professionals and parents, as it enables early recognition of symptoms and rapid initiation of treatment. Studies show that rapid diagnosis and treatment are associated with lower rates of complications and mortality.

Thus, a better understanding of risk factors and their management can help in prevention and prognosis, reducing the risks of long-term sequelae. This is the objective of this review, which was to promote updating on concepts, diagnostic means and conducts.

METHOD

This is an integrative literature review with a synthesis of evidence. The databases chosen for the selection of the studies were Pubmed, SciELO, Scopus and Lilacs using the descriptors: "newborn, prematurity, necrotizing enterocolitis AND or OR,. Any work that discussed the proposed theme was initially included in the sample. After reading the titles and abstracts, those that did not adequately address the theme were excluded. The searches identified 13 papers that met the search strategy and were read in full, with their key points included in this review.

DISCUSSION

Pathophysiology

Necrotizing enterocolitis is a disease that affects the gastrointestinal tract of newborns, especially premature infants, who may have suffered hypoxia at birth or after. It is not uncommon for the clinical practice to be nonspecific, as well as the findings in complementary tests, which does not collaborate with diagnostic accuracy.[1]

Among its causative factors is the lesion of the intestinal mucosa, caused mainly by peri- or intrapartum hypoxia, evidenced by Apgar below 7 in the first minute. Apgar is a test that evaluates the health of the newborn in the first minutes of life, and observes 5 aspects of the baby's vitality. An Apgar score below 7 in the first minute of life indicates that the baby has suffered oxygen deprivation, which can have repercussions throughout life. Hypoxia also occurs due to congenital cardiac or intestinal malformation with low blood flow, which favors increased intestinal permeability, leading to mucosal lesions, subsequent necrosis and perforation.[1,2] Hypoxia may be due to complications of prematurity, such as hyaline membrane. Most premature infants receive exogenous surfactant to make up for production failure due to lung immaturity, and thus allow better gas exchange. Tissue hypoxia due to anemia is common in premature newborns, caused by hematopoiesis deficiency due to immaturity of the body, cerebral or pulmonary hemorrhage, and fragility of the body in formation. Consecutive blood collections, carried out to monitor the evolution, such as blood gases, blood count, blood culture, among others, are reasons for blood loss, and sometimes blood component transfusions are necessary.[3]

The presence of pathogenic bacteria is another factor that contributes to the occurrence of NEC. Microbial dysbiosis occurs due to inadequate colonization of the gastrointestinal tract of the newborn admitted to the neonatal ICU soon after birth, due to the use of antibiotic therapy, due to maternal complications in labor and premature rupture of membranes, vaginal colonization of the mother by group B streptococcal bacteria, or surgical delivery. The late start of feeding favors bacterial translocation, contributing to the performance of these microorganisms in the occurrence of the disease.[1]

Another factor is the metabolic substrate. Colostrum or fresh breast milk or pasteurized human milk provided to the baby will serve as nutrition for the microorganisms already present, or it can act as an aggressive factor to the intestinal mucosa that has already suffered injury by hypoxia. The use of infant formula instead of colostrum, breast milk or pasteurized human milk increases susceptibility to bacterial invasion, due to the risk of triggering an allergic response to cow's milk protein and causing aggression to the integrity of the intestinal mucosal barrier, in addition to the absence of protective substances in human milk that are not present in infant formula.[4]

Prematurity, a reality of many babies who have NEC, is accompanied by the immaturity of the gastrointestinal tract, known as dysmotility of the premature infant's intestine, allowing greater permeability of the organ's epithelium, aggravated by the decrease in the mucin barrier that works to protect the intestine, and low levels of immunoglobulins leading to reduced immunity. This probably explains why most cases occur in premature newborns: and in the literature, 90% of newborns operated on for this diagnosis have a gestational age of less than 37 weeks.[2]

Signs and symptoms

The newborn may initially present systemic clinical symptoms such as pallor, tachycardia, tachypnea, fever, hypoactivity, apnea, hypotension, bradycardia, impaired perfusion, and thermal lability. Frequent gastrointestinal signs are abdominal distension, food intolerance, increased gastric residue, bilious vomiting, presence of blood in the stool, relief of loops, and pain on abdominal palpation, which will have repercussions on changes in laboratory and imaging tests. Alterations of the abdominal wall, such as erythema, edema, mowering, and pallor, suggest the diagnosis, but are only observed in 10% of patients.[5]

Source: Prematurity.com[6]

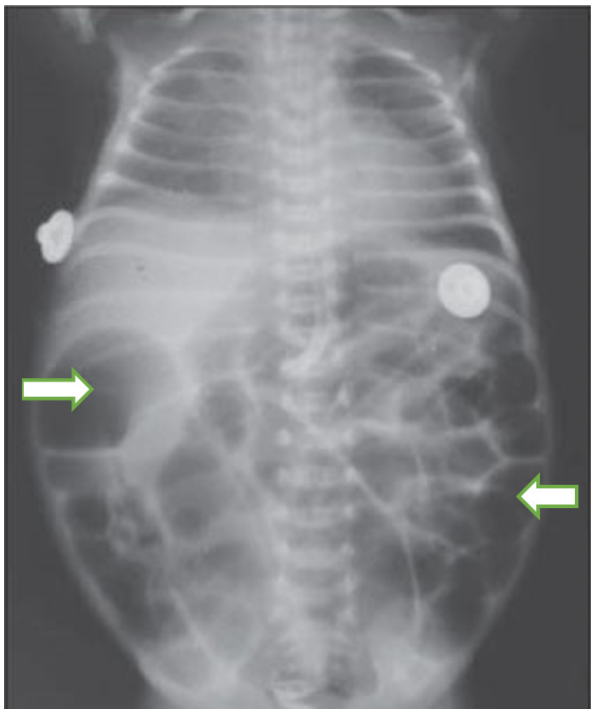
FIGURE 1 — Abdominal distension in a newborn with necrotizing enterocolitis

Diagnosis

Diagnosis is made considering the initial clinical manifestations such as food intolerance, increased gastric residue, abdominal distension, bilious vomiting, presence of blood in the feces (Figure 1).[5,7]

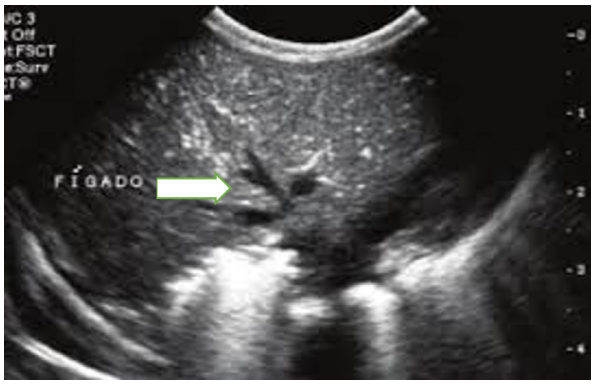
Laboratory findings serve as diagnostic aids but are not specific to NEC. These are leukopenia, thrombocytopenia, hyponatremia, hypokalemia, increased levels of C-reactive protein, instability of blood glucose, alteration of coagulation tests, and mixed acidosis. Radiological findings are dilated bowel loops, little gas in the intestine, fixed loops, which are intestinal loops distended with gas that do not change on serial radiographs (Figure 2). Pathognomonic findings on abdominal radiography are intestinal pneumatosis, air in the portal venous system, and pneumoperitoneum, which is a sign of intestinal perforation.[4,8]

Abdominal ultrasound may suggest the presence of abdominal fluid, thickening of the abdominal wall, decreased perfusion of the intestinal wall, which can be visualized early,[10] it is also possible to observe air in the portal system (Figure 3) and intestinal pneumatosis. In a study evaluating postoperative outcomes, the location of intestinal injury and subsequent perforation is more common in the ileum in preterm infants, and in extremely preterm infants in the jejunum.[2]



Source: Alvares et al.[9]

FIGURE 2 — Radiographic image of distended loops (arrows) suggestive of necrotizing enterocolitis



Source: Miranda et al.[12]

FIGURE 3 — Abdominal ultrasound showing air in the portal system

The clinical signs associated with the findings in imaging exams, abdominal X-ray or abdominal ultrasound, help in the classification of the so-called Bell Classification, and direct the treatment. It is divided into stages based on suspicion; signs and symptoms are added to the picture, contributing to locate it in the staging of the Bell et al classification. In 1978, these authors proposed the criteria classifying the disease into stages in order to guide therapeutic decisions. Subsequently, other authors[1,11] modified this criterion, including systemic, intestinal and radiographic signs (Table).

Auxiliary diagnostic tests

Most hospitals use radiographic anteroposterior study of the abdomen, lateral and supine position with serial horizontal rays for diagnosis and follow-up of the evolution of abominal conditions. The image obtained

TABLE — BELL staging modified by Walsh and Kleigman

Internship	Systemic signs	Intestinal signs	Picture Signs	Treatment
WOULD Suspicion ECN	thermal instability apnea, bradycardia, lethargy.	gastric residue, abdominal distension, vomiting, occult blood +	normal or with mild distension	Swim orally, antibiotics for 3 days, dependent on cultures
IB Suspicion ECN	thermal instability apnea, bradycardia, lethargy.	gastric residue, abdominal distension, vomiting, blood in the stool, enterorrhagia or melena.	normal or with mild distension	Swim orally, antibiotics for 3 days, dependent on cultures
IIA BCE set mildly ill	thermal instability, apnea, bradycardia, lethargy.	Same as above plus decreased or absent abdominal noises, with or without abdominal pain	Intestinal dilatation, ileus, intestinal pneumatosis	Nothing by mouth, antibiotics for 7-10 days, if the test is normal in 24-48 hours
IIB ECN Defined Moderately ill	As above, more mild metabolic acidosis and thrombocytopenia	Same as above, plus definite abdominal pain with or without abdominal cellulitis or mass in the right lower quadrant, absent bowel noises	Same as IIA, plus air in the portal vein, with or without ascites	Nothing by mouth, antibiotics for 14 days, correction of acidosis
IIIA ECN advanced. Seriously ill	Same as IIB plus hypotension, bradycardia, severe apnea, combined respiratory and metabolic acidosis	As above, more signs of generalized peritonitis, severe pain, abdominal distension	Same as IIB, plus definite ascites	Same as above, plus 200 ml/kg/day of fluids, inotropic agents, mechanical ventilation, paracentesis; if the patient does not improve within 24 to 48 hours, surgical intervention
IIIB ECN advanced. Seriously ill, intestinal perforation	Same as IIB plus hypotension, bradycardia, severe apnea, respiratory and metabolic acidosis combined, disseminated intravascular coagulation, neutropenia	As above, more signs of generalized peritonitis, severe pain, abdominal distension	Same as IIIA, plus pneumoperitoneum	Same as above, plus surgical intervention

Source: Hachem, Lyra, Scarpa, et al.[1]

is static, not allowing visualization or identification of the blood flow situation, where there is potentially an area subject to necrosis and perforation. The presence of air in the submucosa of the intestine, resulting from the fermentation produced by bacteria in addition to the intestinal lumen, is pneumatosis and can be visualized on X-rays. Distension of intestinal loops is the first sign to draw attention on imaging, and reflects the abdominal distension already seen clinically.[9] The radiographic study does not require a high-cost device, such as ultrasound, or a specialized professional to perform the exam, because not every neonatologist is prepared to perform ultrasound. On the contrary, the radiographic study is performed by a technician who waits to be reported later, but can be interpreted by the attending physician himself.[3]

It should always be borne in mind to provide the least radiation to the patient. Ultrasonography, in turn, uses high-frequency sound waves to give rise to an anatomical image. It is widely used to evaluate the central nervous system, presence of periventricular leukomalacea, intraventricular hemorrhage, i.e., hypoxic ischemic lesion, compatible with a history of fetal distress at birth.[3] Images may reveal a metabolically less active borderline zone, reflected by a deep gray image. Areas of tissue necrosis may appear in the form of cavitation, cysts, or decreased white matter. Intracranial hemorrhage may also be visualized, or areas of hydrocephalus may appear in the course. Neonatal heart diseases, which include structural abnormalities with consequent impairment of cardiac function and organ oxygenation, can be detected through echocardiography. Congenital heart tumors that cause obstruction of blood flow, congenital malformations, and pulmonary hypertension due to hypoxia or bronchial aspiration at birth may also be diagnosed.[3]

Treatment

Medical treatment should be initiated as soon as NEC is suspected and consists of initially transferring the newborn from rooming-in or intermediate inpatient unit to the neonatal ICU, placement in an incubator to avoid cross-infection, and close monitoring of vital data. Contact isolation and bowel rest measures should be installed by suspending feeding, prescribing fasting, placing a large gastric tube leaving it open to control gastric stasis, and prescribing parenteral nutrition to avoid severe weight loss. It is important to institute supportive measures, maintain fluid and electrolyte balance, cardiocirculatory support due to the risk of septic shock, respiratory support, and analgesia due to the discomfort and pain that may be present. All procedures must follow pre-existing protocols in the service according to the recommendations for infection control and based on the management practices of the little patient.[5,7]

Complementary tests should be requested to assist in the diagnosis and verification of elements that contribute to the decision of the treatment to be instituted. It is recommended to collect laboratory tests and cultures for the prescription of antibiotic therapy if necessary, monitoring the evolution and decision to change medication.[1,3,5]

Blood component replacement should be carefully evaluated, since authors suggest a relationship between blood transfusion and the pathogenesis of NEC, probably because it needs to be due to anemia that causes tissue hypoxia.[7]

Radiographic study for the acute abdomen (anteroposterior, lateral and supine views with horizontal rays) should be requested every 6/8 h, or abdominal ultrasound, and discussion of the neonatology team with the pediatric surgery about the imaging findings.[13]

The construction of medical records according to the evolutionary sequence is important for monitoring and decision-making, and should be carried out based on the results of complementary tests, laboratory tests, imaging, and the appearance or disappearance of new signs and symptoms. Recording the stage of the disease according to the modified Bell classification directs the clinical management, beginning of fasting or resumption of diet, initiation of antibiotic therapy, and the choice of drugs to be used or their suspension. Indicate the use of vasoactive drugs and surgical options, keeping in mind the prevention of sequelae and complications, such as short bowel. Precise surgical intervention is indicated

when pneumoperitoneum or paracentesis occurs with the presence of feces or bile; Relative indication is the presence of wall cellulitis, persistent fixed loop, fixed abdominal mass, diffuse pneumatosis (4 quadrants), and air in the portal system.

CONCLUSION

NEC affects premature babies, and the occurrence is greater the greater the prematurity. Low birth weight is also a predisposing factor, and the lower the weight, the greater the number of cases. Apgar below 7 on the 5th. minute of life and hypoxia during resuscitation can be inducers of his presence. Initial complementary diagnosis should be made by plain abdominal x-ray and ultrasound. In addition, transfontanelle ultrasound should be used when hypoxic brain injury is suspected, and echocardiogram to verify cardiac malformations that lead to intestinal hypoperfusion.

Authors' contributions

Wilma Lilia de Castro e Souza Silva: Conceptualization, Methodology
Luiz Martins Collaço: Research, Project Administration

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