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ORIGINAL ARTICLE

Analysis of cases of necrotizing enterocolitis of the São Francisco na Providencia de Deus University Hospital in the period of january 2015 to october 2017

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Abstract

Necrotizing enterocolitis (NEC) is the most frequent surgical emergency in the neonatal period and with a high mortality rate. It is characterized by gastrointestinal and systemic signs and symptoms of variable and progressive intensity, of a multifactorial pathology resulting from the interaction between loss of intestinal mucosal integrity and host response to this damage. This article is a retrospective study in which the study population consisted of newborns admitted to a neonatal intensive care unit diagnosed with perforated necrotizing enterocolitis who were born at the São Francisco University Hospital in Providência de Deus, in the period from January 2015 to October 2017. We searched for the various forms of clinical and evolutionary presentation of the NEC and evaluated the factors associated with the disease, in order to seek a better knowledge regarding this pathology by professionals working in the therapy units of neonatal intensive care, as well as the adequate management of the patient in an attempt to reduce its incidence and associated complications. With regard to the prevention of NEC, few strategies were proven effective; all attempts to minimize the frequency and severity of the disease were directed at eradicating the risk factors involved.

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INTRODUCTION

Necrotizing enterocolitis (NEC) is the most common surgical emergency during the neonatal period and has a high rate of mortality.[1] This pathological clinical syndrome is characterized by progressive systemic and gastrointestinal signs and symptoms of variable intensity. This multifactorial pathology results from the interaction between loss of intestinal mucosal integrity and the host's response to this damage. The pathophysiological mechanism stems from an intestinal mucosal lesion that leads to ischemia and necrosis. It results from an inflammatory process that promotes intestinal vasoconstriction in response to inflammation, tissue ischemia, and loss of mucosal integrity, culminating in the necrosis of affected areas, with varying degrees of intestinal lesion that permit bacteria and toxins to pass into the systemic circulation.[2]

This disease most commonly affects premature infants, especially those with very low birth weight. Incidence is inversely proportional to gestational age, with a mortality rate of 1%–8%. It affects 5%–10% of premature newborn (NB) infants and up to 7% of full-term NBs. This is because of the combination of the immature gastrointestinal mucosa and the immature immune system, which makes preterm NBs (PTNBs) more susceptible to the disease.[3]

The spectrum of NEC is broad and varies from mild to fulminant. The clinical onset correlates inversely with gestational age, appearing in the first days of life of PTNBs and during the first few weeks of early premature babies. Diagnosis is based on clinical suspicion, supported by X-rays and laboratory tests. Clinical gastrointestinal signs include increased abdominal circumference, abdominal distension, reduced bowel sounds, fecal changes, hematochezia, erythema of the abdominal wall, and a palpable abdominal mass. Systemic clinical signs are respiratory failure, circulatory collapse, and decreased peripheral perfusion. Laboratory findings associated with NEC are leukocytosis, leukopenia, neutropenia, acute drop in hematocrit, and especially thrombocytopenia.[4]

Radiological signs include generalized intestinal distension, localized distension, intestinal pneumatosis that can spread to the portal venous system, and pneumoperitoneum.[2]

Treatment is defined according to Bell's staging criteria, ranging from Ia to IIb.[2,4]

At stage I, there is a suspicion of NEC.

- Ia: Signs of thermal instability, hypoactivity, apnea, increased gastric residue, vomiting, abdominal distension, and microscopic enterorrhagia. X-ray shows loop distension and paralytic ileus.
- Ib: Clinical and radiological signs are the same, but enterorrhagia is macroscopic.

NEC is defined at stage II.

- IIa: In addition to the signs of stage Ib, there is decreased or absent bowel sounds and pain upon abdominal palpation. X-ray shows localized intestinal pneumatosis, alongside the signs of stage Ib.
- IIb: Signs of IIa in addition to metabolic acidosis, thrombocytopenia, leukopenia, signs of peritonitis, cellulitis of the abdominal wall, and a palpable abdominal mass. X-ray shows pneumatosis in two to three abdominal quadrants, pneumoportogram, and signs of ascites.

Stage III is the advanced stage, with increased likelihood of surgical intervention.

- IIIa: No intestinal perforation, with signs of stage IIb, in addition to hypotension or signs of shock, mixed acidosis, disseminated intravascular coagulation, multiple organ failure, and worsened abdominal distension. X-ray shows increased ascites.
- IIIb: Characterized by intestinal perforation; X-ray may show the presence of pneumoperitoneum in addition to the clinical and radiological signs of stage IIIa.

The general principles of treatment involve intestinal rest, oral fasting, gastric decompression, parenteral nutrition, decreased aggression to the gastrointestinal tract, identification and treatment of the infectious process, control of multiple organ failure, and identification and early correction of surgical complications. Antibiotic therapy duration varies from 3 to 14 days, according to the stage of the disease.[1,2,3]

Although NEC is still one of the great challenges of neonatology, much knowledge has emerged to clarify its etiopathogenesis, opening up new perspectives for management and prevention.

OBJECTIVES

The objective of this study is to analyze various clinical presentations and progressions of NEC and to evaluate factors associated with the disease to improve the knowledge of this pathology among professionals working in neonatal intensive care units (NICU) and patient management to reduce the incidence and associated complications of this condition.

METHODOLOGY

The sample of this retrospective study consisted of NBs born at the São Francisco na Providência de Deus University Hospital from January 2015 to October 2017, who were admitted to NICUs with a diagnosis of perforated NEC.

Data were collected via a structured instrument using medical records of NBs born at the São Francisco na Providência de Deus University Hospital and admitted to NICUs with a diagnosis of NEC through a search in the TasyRel system. All records of infants admitted with the suspicion of NEC (according to NICU records) were analyzed. Cases with confirmed diagnoses of perforated NEC were subjected to the data collection instrument, and records made by doctors and nurses were analyzed to summarize each case. Data from five cases were then manually tabulated. The tables include data expressed as medians, means, standard deviations, and frequencies.

The literature review included publications from 2000 to 2017 selected from an electronic database and manual search of databases such as the US National Library of Medicine (PubMed), ScientificEletronic Library Online, Index of Scientific and Technical Literature in Latin America and the Caribbean, national clinical protocols, and book chapters. The descriptors used were NEC, risk factors, prematurity, complications of prematurity, and intestinal perforation.

RESULTS

The sample consisted of five NBs with a diagnosis of enterocolitis who underwent surgery. The population had a gestational age of 26–31 weeks and Apgar scores at 5 min of 9–10. The majority of NBs were classified as appropriate for gestational age. The percentage of deaths was 80%, although not all deaths were necessarily an immediate consequence of the disease (Table 1).

All NBs were fed breastmilk and infant formula (Table 2), with average diet progression of 20 mL/kg/day. It is important to emphasize that anything NBs received was considered the first enteral feeding; thus, mixed feeding, i.e., breastmilk and formula, means that the NB may have had a little of each at a single meal or just one of them at different meals.

Respiratory distress syndrome (RDS) was notable among the associated pathologies as it was present in 80% of cases, followed by sepsis in 40% of cases and asphyxia in 20% of cases. As for other associated causes, it should be noted that the entire sample received umbilical catheterization and 80% received packed red cell transfusion (Table 3).

Clinical signs included abdominal distension and gastric residue in 100% of cases, followed by vomiting bile (60%) and apnea and thermal instability in some cases (20% each) (Table 4).

In terms of diagnostic methods, testing for fecal occult blood and reducing substances in feces were not performed. Diagnoses were made and confirmed via simple abdominal X-ray for all cases and was confirmed by horizontal X-ray in only 40% of the cases. Abdominal ultrasound was requested for 60% of the cases, but all were inconclusive (Table 4).

Treatment consisted of stopping food intake and initiating parenteral nutrition and antibiotics in 100% of cases.

Table 1. Population characteristics (n = 5)

Gestational age	28.5 ± 1.87
5-min Apgar score	9 ± 1
AGA	80%
SGA	20%
Onset of symptoms	9 ± 9.02
Deaths	80%

Data are expressed as mean ± standard deviation or frequency (percentage).
SGA: small for gestational age

Table 2. Characteristics of first feedings

Initiation of enteral nutrition	3 (2 a 4)
Initial volume of complete feeding (mL/kg/day)	15 (10 a 20)
First feeding with BM + formula	100%
Progression of diet	20 ± 10
PTNBs offered BM in the first 14 days of life	100%

RNPT que tiveram contato com LM nos primeiros 14 dias de vida 100%
Dados expressos em mediana, média ± desvio-padrão ou frequência (percentual).

Table 3. Pathologies and other associated causes

Sepsis	40%
Respiratory Distress Syndrome	80%
Asphyxia	20%
Umbilical catheterization	100%
Packed red cell transfusion	80%

Data are expressed as frequency (%).

Table 4. Signs/symptoms and diagnostic methods.

Thermal instability	20%
Abdominal distension	100%
Gastric residue	100%
Vomiting bile	80%
Apnea	20%
Simple abdominal X-ray	100%
Horizontal ray X-ray	40%
Abdominal ultrasound	60%

Data are expressed as frequency (%).

DISCUSSION

The mortality rate among very-low-birth-weight NBs has decreased due to advances in perinatal care. However, this success has allowed the emergence of previously unknown serious pathologies. NEC is one of these pathologies that have emerged with the growth of intensive care. It presents high rates of morbidity and mortality, with serious complications resulting from extensive intestinal necrosis.

It is known to occur in some intensive therapy units and is not seen in others. This suggests that iatrogenic factors related to care could contribute to its occurrence.

Despite the limited sample size, the results were similar to those found in the literature. The importance of prematurity in the etiology of NEC is well known; in this study, 100% of the cases were PTNBs.

Apgar scores were not considered a risk factor because all NBs had good Apgar scores; this differs from the findings of Hackett et al., who found that episodes of chronic fetal hypoxia, which were not apparent at birth, were later associated with enterocolitis.[5]

The beginning of enteral nutrition, type of milk, and progression of breastfeeding are also risk factors involved in the disease. A protective effect of breastmilk is suggested in this disease because of the immunoglobulins and secretory IgA it contains. This study shows no correlation of the type of milk and progression of enteral feeding with the severity of enterocolitis. The initial enteral nutrition of all NBs was trophic nutrition. Minimal enteral nutrition with slow progression is best indicated to prevent the onset of NEC and also proves optimal for gastrointestinal system maturation in PTNBs, gastrointestinal intolerance reduction, and shortening of weight recovery time. Studies have suggested initial complete feeding of up to 28 mL/kg/day.[6,7] However, the sample was too small to allow drawing conclusions on this issue. In addition, there was no differentiation between the exclusive diet with breast milk and infant formula, and the diets were considered as mixed diets.

All the factors that can cause problems to the mesenteric circulation were regarded as risk factors for developing NEC, and not all of them can be corrected or avoided. Of the NBs affected by NEC, 80% had RDS, which is in line with reports by Cunha & Pachi and Uras, who indicated RDS as a risk factor for NEC.[8,9] The findings demonstrated that umbilical catheterization had been performed in all infants exhibiting NEC, which is in agreement with the reports by Santos, who indicates this variable as a triggering factor due to decreased intestinal blood flow and consequent local ischemia, which may evolve to necrosis.[10] In the study sample, all NBs underwent umbilical catheterization, and none for a prolonged time (>5 days); only one NB had the catheter at symptom onset, hindering analysis.

Although intestinal colonization by potentially pathogenic microorganisms appears to be a risk factor for NEC, there was no evidence of specific bacteria associated with the disease. The mechanisms of intestinal lesion include the action of endotoxins on macrophages with the release of tumor necrosis factor and increased platelet activation factor, resulting in vasoconstriction, intestinal ischemia, and necrosis. In the study, 40% of patients were diagnosed with sepsis in the presence of symptoms, and antibiotic therapy was introduced or changed as a form of prevention and treatment. However, we cannot identify the initial condition, i.e., whether sepsis led to NEC or vice versa.

Transfusion of packed red cells was performed in 80% of NBs. Several case reports and retrospective studies have shown that up to one-third of all NBs that developed NEC may have received one or more blood transfusions in the 24–72 h after NEC onset, which is in line with the results of this study. The study population

received the packed red cells 12–72 h prior to the onset of symptoms. Several retrospective studies have been published since 2006, and although they had different demographics, disease severities, and incidences, several common elements were seen, such as later onset of enterocolitis in case of blood transfusion (appearing 2–5 weeks after birth) and enterocolitis occurring in younger infants (1–2 weeks old) who did not receive blood transfusion. Mally et al. reported a relationship between late-onset NEC in 17 stable, growing PTNBs and elective transfusion to treat anemia due to prematurity.[11] In this study, the onset of symptoms was late in 60% of NBs, all of whom received transfusions 12–72 h before symptom onset.

The most frequent symptoms were abdominal distension and gastric residue (all cases), which confirmed the findings by Vieira, who considered these symptoms predictive of NEC.[12] When diagnostic methods were performed, they were seen to be effective to confirm enterocolitis, particularly abdominal X-ray, which was performed in the entire sample and indicated positivity.

CONCLUSION

Few strategies have been shown to be effective in preventing NEC; all attempts to minimize the frequency and severity of the disease address the eradication of causal risk factors. These preventative measures include early initiation of enteral nutrition, preferably exclusively using breastmilk, with progression to a careful diet, as well as adopting measures for infection control and prophylactic measures, antibiotic therapy, parenteral nutrition, and use of probiotics. As for NEC associated with transfusion, some practices are being followed such as diet retention from 4 h before the transfusion until 4 h after completion. However, the data must be carefully interpreted since this study was retrospective and is therefore susceptible to bias and the confounding variable effect.

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