Analysis of Cases of Nerotizing Enterocolitis of the Sao Francisco Na Providencia de Deus University Hospital in the Period of January 2015 to October 2017

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Abstract

Necrotizing enterocolitis (CNS) 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 varying and progressive intensity, of a multifactorial pathology resulting from the interaction between the loss of the integrity of the intestinal mucosa and the host response to this damage. The present article is a retrospective, descriptive and observational 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 Providence of God, from January 2015 to October 2017. The various forms of clinical and evolutionary presentation of CNS were investigated and the factors associated with the disease were evaluated in order to seek greater knowledge about this pathology by professionals working in neonatal intensive care units, as well as the appropriate management of the patient in an attempt to reduce its incidence and associated complications. As for the prevention of CNS, few strategies have been proven effective, all attempts to minimize the frequency and severity of the disease were directed to the eradication of the risk factors concerned.

Keywords: Enterocolitis; Necrotizing; Infant; Premature Birth

Introduction

Necrotizing enterocolitis (CNS) is the most frequent surgical emergency in the neonatal period and with a high mortality rate [6]. It is a pathological clinical syndrome, characterized by gastrointestinal and systemic signs and symptoms of varying and progressive intensity. It is a multifactorial pathology resulting from the interaction between the loss of the integrity of the intestinal mucosa and the host response to this damage. The pathophysiological mechanism results from the lesion of the intestinal mucosa leading to ischemia and necrosis. It results from an inflammatory process that promotes intestinal vasoconstriction in response to inflammation, tissue ischemia, loss of mucosal integrity culminating in necrosis of the affected areas, with varying degrees of intestinal injury, allowing the passage of bacteria and toxins into the systemic circulation [1].

It most often affects preterm infants, especially those of very low weight. Its incidence is inversely proportional to gestational age, with a mortality rate ranging from 1% to 8%. It affects 5% to 10% of premature newborns (NB) and up to 7% of full-term newborns. This is due to the combination of the immaturity of the gastrointestinal mucosa associated with the immaturity of the immune system, which makes the preterm newborn (PTNB) more susceptible to the occurrence of this disease [8].

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The spectrum of ENC is broad and ranges from a light to fulminant frame. The onset of the clinic correlates inversely with gestational age, arising in the first days of life in preterm newborns and during the first weeks in large preterm infants. Diagnosis is based on clinical suspicion, supported by radiographs and laboratory tests. Among the gastrointestinal clinical signs, it can be verified the increase of abdominal circumference, abdominal distension, decrease of air-fluid noises, fecal alterations, hematochezia, erythema in the abdominal wall and palpable abdominal mass. Systemic clinical signs are characterized by respiratory failure, circulatory collapse, and decreased peripheral perfusion. Laboratory findings associated with CNS are leukocytosis, leukopenia, neutropenia, acute hematocrit drop, and especially thrombocytopenia [7].

Radiological signs included generalized intestinal distension, localized distension, intestinal pneumatosis, which can diffuse to the portal and pneumoperitoneum venous system [1].

Treatment is defined following bell classification stages, ranging from Ia to IIb [1,7].

In stage I, there is a suspicion of CNS:

- Ia: Signs of thermal instability, hypoactivity, apnea, increased gastric waste, vomiting, bloating and microscopic enterorrhagia.

In X-ray examination, distension of the loop and paralytic ileus can be found.

- IIb: the clinical and radiological signs are the same, but enterorrhagia is macroscopic.

In stage II the ECN is defined:

- IIa: Has in addition to the signs of IB, a decrease or absence of air-fluid noises and abdominal palpation pain. On X-ray, localized intestinal pneumatosis plus IIb signs can be found.

- IIb: signs of IIa, in addition to metabolic acidosis, leucopenia thrombocytopenia, signs of peritonitis, abdominal wall cellulitis, and palpable abdominal mass. On X-ray, pneumatosis in two to three abdominal quadrants, pneumoportogram and signs of ascites.

In stage III, it is advanced with high chances of surgical intervention:

- IIIa: no intestinal perforation, signs IIb, in addition to hypotension or signs of shock, mixed acidosis disseminated intravascular coagulation, multiple organ failure and worsening of abdominal distension. On X-ray there is increased ascites.

- IIIb: characterized by intestinal perforation and X-ray may present pneumoperitoneum, in addition to clinical and radiological signs equal to stage IIIa.

The general principles of treatment follow bowel rest, oral fasting, gastric decompression, parenteral nutrition, decreased aggression to the gastrointestinal tract, identification and therapy of the infectious process, control of multiple organ failure, identification and early correction of surgical complications. Antibiotic therapy ranges from 3 to 14 days, according to the stage of classification of the disease [1,6,8].

Although CNS is still one of the great challenges of neonatology, much knowledge has emerged to elucidate its etiopathogenesis, opening new perspectives for its management and prevention.
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Objectives of the Study

The objective of this work is to study the various forms of clinical presentation and evolutive presentation of CNS and to evaluate the factors associated with the disease, in order to seek greater knowledge in relation to this pathology by professionals working in neonatal intensive care units (NICU), as well as the appropriate management of the patient in an attempt to reduce its incidence and associated complications.

Methodology

This is a retrospective, descriptive and observational study in which the study population consisted of newborns admitted to nicu with perforated CNS diagnosed who were born at the São Francisco University Hospital in Providence of God, from January 2015 to October 2017.

Data collection was performed using a structured instrument, using medical records from the newborns admitted to the NICU sector, diagnosed with NEC and born at the São Francisco University Hospital in Providência de Deus, through research carried out at Ta-syRel system. All the medical records of NBs who, from the NICU records, were suspected of NEC were investigated. Cases of confirmed diagnoses of perforated NEC underwent the application of the instrument, with analysis of the records made by doctors and nurses in the medical records of each newborn, with a view to preparing the summary of each case. Through these data, manual tabulation of the results corresponding to the five newborns was performed. The tables were prepared by analyzing the data expressed as median, mean, standard deviation and frequency.

The literature review was conducted using publications from 2000 to 2017, selected in electronic databases and manual research, in databases such as US National Library of Medicine (PubMed), Scientific Eletronic Library Online (SCIELO), Index of Scientific and Technical Literature of Latin America and the Caribbean (LILACS), national clinical protocols, and book chapters. The descriptors used were necrotizing enterocolitis, risk factors, necrotizing enterocolitis, prematurity, complications of prematurity, intestinal perforation.

Results

The sample consisted of five newborns diagnosed with enterocolitis, who underwent a surgical procedure. The studied population had an average gestational age between 26 and 31 weeks and an Apgar score in the 5th minute of life between 9 and 10. Most newborns were classified as suitable for gestational age (AGA). The number of deaths was 80%, not necessarily due to the immediate disease (Table 1).

| Gestational age | 28,5 ± 1,87 |
|-----------------|-------------|
| Apgar no fifth minute | 9 ± 1 |
| AIG | 80% |
| PIG | 20% |
| Onset of symptoms | 9 ± 9,02 |
| Deaths | 80% |

Table 1: Population characterization (n = 5).

Data expressed in mean ± standard deviation or frequency (percentage). Small SGA for gestational age.

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As for the feeding of these newborns, all were fed with breast milk (SC) and infant formula (Table 2), with an average progression of the diet of 20 mL/kg/day. It is important to note that, for the first enteral feeding, everything that the NB received was considered, therefore, the mixed feeding, the one that the NB received breast milk or milk formula, means that it may have received in the same meal both a little each, or in different meals, each type of food.

| Parameter                                      | Value         |
|------------------------------------------------|---------------|
| Start of enteral feeding                       | 3 (2 - 4)     |
| Initial volume of whole feed (ml/kg/day)       | 15 (10 - 20)  |
| First feed with LM+ formula                   | 100%          |
| Diet progression                               | 20 ± 10       |
| ptNB who had contact with SCI in the first 14 days of life | 100%          |

**Table 2: Characterization of the first feeds.**  
Data expressed in median, mean ± standard deviation or frequency (percentage).

Among the associated pathologies, respiratory distress syndrome (RDS) was highlighted, being present in 80% of cases, followed by sepsis with 40% and asphyxia with 20%. In relation to other associated causes, it is noted that the entire population studied underwent umbilical catheterization, and 80% received red blood cell transfusion.

The clinical signs evidenced were in total abdominal distention and gastric waste, followed by a portion of bilious vomiting (60%), and some cases of apnea and thermal instability (20% each) (Table 3).

| Pathology                          | Frequency (%) |
|------------------------------------|---------------|
| Sepsis                             | 40            |
| SDR                                | 80            |
| Asphyxia                           | 20            |
| Umbilical catheterization          | 100           |
| Concentrated red blood cell transfusion | 80           |

**Table 3: Characterization of pathologies and other associated causes.**  
Data expressed in frequency (percentage).

As for diagnostic methods, the search for occult blood and reducing substances in the feces was not performed. The entire population studied was diagnosed and confirmed with X-rays of the simple abdomen, with only 40% confirmed with horizontal X-rays. Abdominal ultrasound was requested for 60% of the patients, but all were inconclusive (Table 4).

The medical treatment was performed, the dietary pause, parenteral nutrition and antibiotic therapy were included in 100% of the cases.

**Discussion**

The morbidity rate among very low birth weight newborns has decreased due to advances in perinatal care. However, this success of care allowed the appearance of serious pathologies, hitherto unknown. CNS is a pathology that arose with intensive care. It presents high rates of morbidity and mortality, with severe complications resulting from extensive intestinal necrosis.

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Table 4: Characterization of signs and symptoms and diagnostic methods.

Data expressed in frequency (percentage).

| Sign/Symptom                  | Percentage |
|-------------------------------|------------|
| Thermal instability           | 20%        |
| Bloating                      | 100%       |
| Gastric residue               | 100%       |
| Bilious vomiting              | 80%        |
| Apnea                         | 20%        |
| Rx simple abdomen             | 100%       |
| Rx horizontal rays            | 40%        |
| USG abdomen                    | 60%        |

It is known that it occurs in some intensive care units and is not observed in others. This suggests the possibility that iatrogenic factors linked to care contribute to its emergence.

Despite the limited sample size, the results were similar to those found in the literature. The importance of prematurity in the etiology of CNS is well known, being in this study, 100% premature.

Regarding Apgar indices, no risk factor was considered, and all newborns had a good Apgar index, which differs from Hackett, et al. who demonstrated that episodes of chronic fetal hypoxia, unapparent at birth, were subsequently associated with enterocolitis.

The onset of enteral feeding, the type of milk and the progression of breastfeeding are also risk factors implicated in the disease. A protective effect of human milk in relation to this disease is suggested due to the immunoglobulins and secretory IgA present. In this study, there does not seem to be a relationship between milk type and the mode of progression of enteral feeding and the severity of enterocolitis. All babies started enteral diets with trophic diets. The minimum enteral diet with slow progression is the most indicated to prevent the onset of CNS and is also shown to be optimal for maturation of the gastrointestinal system of the preterms, reduction of digestive intolerance, and shortening of weight recovery time. Studies suggest that the initial whole diet is up to a maximum of 28 ml/kg/day [4,5]. However, the sample was small in order to draw conclusions about this problem, as well as the non-differentiation of the exclusivity of diet with breast milk and infant formula and the diets, in their entirety, were considered mixed.

All factors that may cause repercussions in mesenteric circulation were considered to be at risk for the development of CNS and not all area likely to be corrected or avoided. Of the newborns affected by CNS, 80% had RDS, confirming the reports of Cunha and Pachi and Uras, who cited RDS as a risk factor for CNS. The findings showed that the umbilical catheterization performed in all newborns who presented CNS coincided with the reports of Santos, who cites this variable as a triggering factor due to the decrease in intestinal blood flow, with consequent local ischemia, and may progress to necrosis. In the population and studied, 100% of the NB underwent umbilical catheterization, none of them for a prolonged time (greater than 5 days) and only one NB, had the catheter during the presentation of symptoms, which makes it difficult or analysis of this problem.

Although intestinal bacterial colonization by potentially pathogenic microorganisms appears to be a risk factor for CNS, there was no evidence of any specific bacteria associated with the disease. Among the mechanisms of intestinal injury are the action of endotoxins on macrophages with the release of tumor necrosis factor, with increased platelet activation factor, resulting in vasoconstriction, ischemia and intestinal necrosis. In the study, 40% of the patients were diagnosed with sepsis during the presentation of symptoms, with introduction or exchange of antibiotic therapy as a form of prevention and treatment, however, it is not possible to identify what was the initial picture, whether the sepsis that led to CNS, or sepsis.

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It is worth mentioning the transfusion of red blood cell concentrate present in 80% of the NB. Several case reports and retrospective studies show that up to one third of all newborns who develop CNS may have received one or more transfusions within 24 to 72 hours prior to the onset of CNS, which corroborated or with this study. The population studied received concentrate 12 to 72 hours before the onset of symptoms. Since 2006, several retrospective studies have been published. Although these studies show difference in demographics, disease severity, incidence, several common elements have been seen, such as transfusion-associated enterocolitis is late onset at 2 to 5 weeks of postnatal age, while non-transfusion-related ones are generally younger (1 to 2 weeks). Mally, et al. reported a relationship between late-onset CNS in seventeen stable, growing premature neonates who were electively transfused for prematurity anemia. In this study, the onset of symptoms are late in 60% of newborns, all of whom were transfused 12 to 72 hours before the onset of the same.

The most frequent symptoms were in its entirety abdominal distension, and gastric residue, which confirmed the studies performed by Vieira, being considered a predictive factor for CNS. The diagnostic methods, when performed, were effective for the confirmation of enterocolitis, especially the X-ray of simple abdomen, which was performed throughout the population and suggestive of positivity in all of them [9-12].

Conclusion

In the prevention of CNS, few strategies have been proven effective, all attempts to minimize the frequency and severity of the disease are directed to the eradication of the risk factors concerned. Thus, the beginning of early enteral diet, preferably with exclusive breast milk, with careful diet progression, as well as adoption of infection control measures and prophylactic measures, antibiotic therapy, parenteral diet and use of probiotics, are measures that can help in the prevention of CNS. As for CNS associated with transfusion, some practices are being followed, such as diet retention from four hours before to four hours after completion of transfusion. However, there is a need for a cautious interpretation of the data, because the study was retrospective and therefore susceptible to bias and the effect of confounding variables.

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