ABSTRACT

Objectives: The aim of this study was to evaluate the effect of prenatal corticotherapy and neonatal outcome in newborns with necrotizing enterocolitis. Methods: This was a retrospective study evaluating 173 newborns diagnosed with necrotizing enterocolitis. Newborns were divided into two groups, with group 1 containing subjects who had received corticoids in the prenatal period, and group 2 with those who had not received the drug. The two groups were then compared according to perinatal parameters and clinical progression. Results: The mean birth weight was 1380.2 g for group 1 and 1279.5 g for group 2 (p > 0.05); mean gestational age was 32 weeks for group 1 and 33 weeks for group 2 (p > 0.05); 98.6% of the neonates in group 1 and 82.7% in group 2 were preterm (p = 0.001); mean time for symptom onset was 16 days for group 1 and 12 days for group 2 (p > 0.05). Upon diagnosis, 26.1% were Bell III in group 1 versus 27.9% in group 2 (p > 0.05); for Bell staging progression, 39.1% of the neonates in group 1, and 37.5% in group 2 were classified as Bell III (p > 0.05). The most often clinical complication in both groups was intestinal perforation. The mean hospital stay was 52 days in group 1 and 46 days in group 2 (p > 0.05). The mortality rate was 23.2% in group 1 and 20.2% in group 2 (p > 0.05). Conclusion: Prenatal corticotherapy was not associated with clinical outcome improvement in neonates with NEC.

Keywords: Enterocolitis, necrotizing; Prematurity; Adrenal cortex hormones/therapeutic use; Infant, premature

INTRODUCTION

Necrotizing enterocolitis (NEC) is an intestinal disease predominantly associated with prematurity and low birth weight. Age at onset of symptoms varies inversely with gestational age, where the more premature the infant, the later the chronological age for NEC onset. The disease affects approximately 10% of newborns weighing less than 1500 g, having a mortality rate as high as 54% in surgical cases, as well as presenting gastrointestinal sequelae, such as stenosis and short-bowel syndrome. The group at highest risk comprises neonates born at less than 28-week gestation and with birth weight lower than 1000 g.

The etiology of NEC involves four main factors: prematurity, intestinal hypoxia/ischemia, artificial enteral nutrition and intestinal bacterial colonization. Initial NEC symptoms are unspecific and variable, the most common findings being abdominal distension, gastric...
residues, bilious vomiting and traces of blood in faeces\(^7\). NEC cases are classified by Bell staging criteria\(^8\): Stage I for suspected cases, Stage II for proven cases and Stage III for neonates requiring operation.

The use of steroids in the antenatal period is known to accelerate maturation of the immature intestine, having been first observed in animal models\(^9\)\(^-\)\(^10\). However, its protective effect against the onset and development of NEC is not clearly understood in humans, considering a more mature mucous barrier would prevent the bacterial translocation involved in the pathogenesis of the illness\(^6\).

In this context, the objective of the present study was to evaluate the association between prenatal corticotherapy and postnatal outcome of newborns developing NEC, in a tertiary perinatal health care centre.

**METHODS**

A case-control study was conducted based on data collected from the medical records of 173 neonates who had presented a diagnosis of NEC, in the period spanning 1993 to 2003, and were admitted to the Neonatal Intensive Care Unit.

Two groups were compared: 1) neonates exposed to antenatal corticoids; 2) neonates not exposed to antenatal corticoids. The corticoid used was betamethasone 12 mg/d IM, twice with a 24-hour interval, at least 24 hours before delivery.

The two groups were compared according to the following parameters: newborn sex, birth weight, gestational age at delivery, prematurity, nutritional status, time between delivery and onset of NEC symptoms, Bell stage at diagnosis, Bell staging progression, clinical complication, length of hospital stay and mortality rate. Groups were also compared according to maternal age, parity, association with preeclampsia and delivery mode.

Gestational age was assessed by the last menstrual date, confirmed using ultrasound evaluation and the New Ballard method. Nutritional status was classified according to birth weight as: small (SGA) or adequate (AGA) for gestational age, in line with the curve proposed by Lubchenco et al.\(^11\) and Brenner et al.\(^12\). Bell staging criteria\(^6\) defined the NEC stage.

The Ethics Committee of our institution approved this study. The statistical analysis was performed with the Mann-Whitney non-parametric method for two variables, and Student’s \(t\) test, when variables accepted the normal value, with significant values for \(p < 0.05\).

**RESULTS**

One hundred and seventy-three newborns met the study entry criteria, comprising 69 (40%) newborns who had received antenatal steroids (group 1) and 104 (60%) who had not (group 2). Comparison of the two groups is shown in Table 1.

**Table 1. Perinatal parameters of newborns with necrotizing enterocolitis**

<table>
<thead>
<tr>
<th>Parameters used</th>
<th>Group 1 With corticoids (n = 69)</th>
<th>Group 2 Without corticoids (n = 104)</th>
<th>(p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (% female)</td>
<td>53.6</td>
<td>51</td>
<td>(p &gt; 0.05)</td>
</tr>
<tr>
<td>Mean birth weight (g)</td>
<td>1380.2</td>
<td>1279.5</td>
<td>(p &gt; 0.05)</td>
</tr>
<tr>
<td>Mean gestational age (weeks)</td>
<td>32</td>
<td>33</td>
<td>(p &gt; 0.05)</td>
</tr>
<tr>
<td>Prematurity (%)</td>
<td>98.6</td>
<td>82.7</td>
<td>(p = 0.001)</td>
</tr>
<tr>
<td>SGA (%)</td>
<td>45</td>
<td>50</td>
<td>(p &gt; 0.05)</td>
</tr>
<tr>
<td>Onset of symptoms (mean number of days)</td>
<td>16</td>
<td>12</td>
<td>(p &gt; 0.05)</td>
</tr>
<tr>
<td>Bell III at diagnosis (%)</td>
<td>26.1</td>
<td>27.9</td>
<td>(p &gt; 0.05)</td>
</tr>
<tr>
<td>Progression to Bell III (%)</td>
<td>39.1</td>
<td>37.5</td>
<td>(p &gt; 0.05)</td>
</tr>
<tr>
<td>Perforated bowel (%)</td>
<td>11.6</td>
<td>11.5</td>
<td>(p &gt; 0.05)</td>
</tr>
<tr>
<td>Mean hospital stay (days)</td>
<td>52</td>
<td>46</td>
<td>(p &gt; 0.05)</td>
</tr>
<tr>
<td>Mortality (%)</td>
<td>23.2</td>
<td>20.2</td>
<td>(p &gt; 0.05)</td>
</tr>
</tbody>
</table>

Population description: mean maternal age was 27.7 years for group 1, and 27.6 years for group 2 (\(p > 0.05\)). In relation to parity, 71% of patients in group 1 (49/69) and 62.5% of patients in group 2 (65/104) were multigravida (\(p > 0.05\)). In the first group, 72.5% (50/69) had a caesarean section versus 60.6% (63/104) in the second group, \(p > 0.05\). The frequency of preterm neonates in group 1 was 98.6% (68/69) and in group 2 was 82.7% (86/104).

Out of all newborns with NEC, the mean birth weight was 1380.2 g and 1279.5 g for groups 1 and 2, respectively. The mean age for onset of first symptoms was 26.1 and 27.9 days for groups 1 and 2, respectively. The most frequent clinical complication in both groups was bowel perforation, which occurred in 11.6% of neonates in group 1 (8/69), and 11.5% of neonates in group 2 (12/104).

Regarding Bell stage at diagnosis, 30.4% in group 1 were Bell I (21/69), 43.5% were Bell II (30/69) and 26.1% were Bell III (18/69), whilst in the second group, 29.8% (31/104) were Bell I, 42.3% were Bell II (44/104) and 27.9% were Bell III (29/104), with \(p > 0.05\).

**DISCUSSION**

NEC is a neonatal disease that affects mainly premature and very low birth weight infants\(^11\)\(^-\)\(^12\). In our study, we verified that the mean birth weight of neonates with NEC was similar to that described earlier by other authors\(^13\).
The disease is the most common surgical emergency in newborns and the most common cause of short bowel syndrome in infancy\textsuperscript{(14)}. A variable proportion of all affected neonates, 27-63\%, progress to surgical intervention\textsuperscript{(14)}. In our study, 38.2\% of infants diagnosed with NEC were surgically treated (Bell III).

The number of preterm neonates in groups 1 and 2 was as expected, since pregnant women who receive corticotherapy go into premature labour or require premature delivery, either for maternal or fetal reasons. The high number of caesarean sections was due to complexity of the cases referred to our Tertiary Center. The main indication for caesarean section was severe preeclampsia, followed by maternal diabetes and fetal distress.

Corticoids are known to accelerate maturation of the immature gut. The effect of prenatal administration of corticoids on morbidity and mortality of necrotizing enterocolitis was first examined in animal models. In these studies, a significantly improvement in both morbidity and mortality has been shown\textsuperscript{(9,10)}.

Studies have demonstrated that animal fetuses submitted to intrauterine administration of dexamethasone present a higher selective uptake of glucose and proline, evidencing increased enteral absorption capacity\textsuperscript{(9,15)}. In addition, the dexamethasone effect on the functional maturity of intestines also increases the differentiation of the brush border intestinal cells and generates precious lactase activity\textsuperscript{(44)}.

In humans, Bauer et al.\textsuperscript{(16)} showed a decreased incidence of NEC (p = 0.002) in infants treated with steroids. Nevertheless, it remains unclear whether antenatal steroid therapy in pregnant women can prevent the onset, or alleviate the clinical course of NEC.

In the present study, no statistical significance was observed regarding the effect of prenatal corticotherapy on clinical outcome of newborns affected by NEC. It is probable that, once NEC had set in, prenatal steroid therapy was unable to significantly influence severity, duration and progression of its clinical course. However, based on our study we are unable to comment on the possible mechanisms involved. Greater understanding of the molecular mechanism of NEC onset and progression can lead to new tools for its management and prophylaxis.

**CONCLUSION**

Prenatal corticotherapy was not associated with clinical outcome improvement in neonates with NEC in the studied population.

**REFERENCES**