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Long term outcome of preterm infants with isolated intestinal perforation: A comparison between primary anastomosis and ileostomy

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ABSTRACT

Aim of the study: Management of isolated intestinal perforation (IIP) poses a challenge for the pediatric surgeon. Intestinal resection and primary anastomosis is considered to be as good as the classical approach, namely, intestinal diversion by ileostomy. However, few reports compare primary anastomosis and ileostomy as IIP treatment. In our institution we favored primary anastomosis as first line treatment whenever patient's condition permitted. Our purpose is to retrospectively compare the outcomes of preterm infants treated with primary anastomosis or ileostomy during a laparotomy in which an IIP was found.
Method: We identified all newborns who had abdominal operations for IIP from 2000 through 2013. Patients with extensive necrotizing entorocolitis and comorbidities were excluded, as well as those who died in the first 24 h. Demographics, type of treatment and complications were reviewed. Major complications included the need for an urgent reoperation, development of late NEC and death.
Results: Twenty-three patients with a median gestational age (GA) of 27 weeks and median birth weight (BW) of 883 g had receive two types of treatment: group I included 9 patients who had intestinal resection of the affected bowel and ileostomy; group PA consisted of 14 patients who had intestinal resection and primary anastomosis. The decision to perform PA or I was based on the surgeon's judgment, in the absence of a specific protocol. There were no significant differences in GA and BW between both groups. Overall mortality was 30.4%. However mortality was restricted to group PA ($n = 7$ cases; 50%) ($p = 0.019$). Most major complications occurred in group PA (71% vs. 11%, $p = 0.029$). There were six cases of late NEC, all in group PA ($p = 0.048$), and four of those patients died. Other than the type of treatment, no differences could be identified between both groups.
Conclusion: Preterm newborns with IIP are at a higher risk for developing life-threatening complications if treated with primary anastomosis than with ileostomy.

Isolated intestinal perforation (IIP) and necrotizing enterocolitis (NEC) are the two most common causes of neonatal intestinal perforation [1]. IIP, also known as focal, idiopathic or spontaneous intestinal perforation, has been widely described to represent a different clinical entity from NEC [2–3]. It occurs mostly in the very-low birth weight infant, with a reported incidence of up to 1:5000 live newborns [4]. Unlike NEC, IIP characteristically involves a limited intestinal segment, usually in the distal ileum, sparing the remaining bowel [5]. A congenital defect of the muscular layer of the intestine has been suggested to be a major contributing factor in IIP [6]. Several antenatal and postnatal predisposing factors have also been suggested, including infection [7–9], drugs such as indomethacine and steroids [10–12], enteral feedings and sustained CPAP. Nevertheless, its pathophysiology remains unclear and there is still discussion whether IIP belongs to the NEC spectrum [13]. Recent series report mortality to be 35–47%, and subsequent long-term intestinal morbidity as high as 53% [5,14–15].

As happens in NEC, the appropriate treatment for IIP remains controversial. Although some advocate for drainage alone, others recommend laparotomy with intestinal resection and primary anastomosis or ileostomy [16,17].

The unfavorable outcome of some patients with IIP treated in our institution led us to review our experience. The aim of this study is to compare the long term outcome of patients who underwent intestinal resection for IIP, followed by primary anastomosis or ileostomy.

1. Patients and methods

We identified all newborns who had abdominal operations for a single intestinal perforation from 2000 through 2013. Approval was obtained from our institutional ethics board.

We included preterm babies (younger than 37 weeks of gestation) undergoing laparotomy for intestinal perforation whose surgical

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findings were a small and single ileal perforation. We excluded patients with evidence of extensive NEC and patients who underwent intestinal resection larger than 10 cm. Patients with other diagnoses such as intestinal atresia or meconium ileus and patients with non-ileal isolated perforations were excluded too. We also excluded patients deceased during laparotomy or in the first 24 h postoperatively because early mortality may reflect the severity of the preoperative status more than the benefits of a specific surgical technique.

Two groups were defined according to their primary treatment:

- Group PA: Patients who had a limited ileal resection and a primary anastomosis.
- Group I: Patients who had a limited ileal resection and ileostomy.

The staff surgeon decided at the time of laparotomy on the ultimate treatment, depending on the bowel appearance, the degree of peritoneal soiling, the baby global status and personal preference.

Data were collected on the following variables:

a) Demographics: gestational age, birth weight and gender.
b) Age at laparotomy.
c) Comorbidities.
d) Peritoneal soiling.
e) Inotropic drugs.
f) Duration of surgery.
g) Mortality and the cause of death.
h) Major complications:
   a. Leading to death.
   b. Leading to an urgent surgery.
   c. NEC development.
i) Minor complications:
   a. Managed conservatively.
   b. Leading to an elective surgery.

Reversal of ileostomy was not considered a complication, as it is inherent to the ileostomy procedure.

The statistical analysis was performed with the Statistical Package for the Social Sciences (SPSS), 22.0 version (SPSS, Inc., Chicago, IL, USA). Normality of the variables was tested with Shapiro–Wilk test. Chi square and Fisher F tests were used to compare qualitative variables between both groups. Mann–Whitney test was used to compare the quantitative variables. The association between demographic factors, comorbidities and type of primary treatment, and outcome was also analyzed. A p-value <0.05 was considered statistically significant.

2. Results

Twenty-three patients with IIP met the inclusion criteria. Median gestational age was 27 weeks ($\pm$2.3 gw, rank 24–32). Median birth weight was 883 g ($\pm$238 g, rank 550–1620). There were 13 boys and 10 girls. Median age at surgery was 7.7 days ($\pm$5.4, rank 2–22). The median follow-up was 3.3 years (25 days–15 years). All surviving patients had at least one year follow-up.

Laparotomy was performed in all cases following adequate resuscitation. No patient had a peritoneal drain inserted prior to surgery. Fourteen patients had a primary anastomosis (group PA) and nine had ileostomy (group I).

Table 1 shows the results for each patient and their follow-up.

Variable comparison between groups PA and I is shown in Table 2. Both groups had similar pretreatment characteristics ($p > 0.05$). Duration of surgery, peritoneal soiling and need of inotropic drugs were not statistically different in both groups ($p > 0.05$). The only significant risk factor has been the type of primary treatment (ileostomy or primary anastomosis). No other variable (gestational age, birth weight, age at laparotomy, comorbidities, use of inotropic drugs or peritoneal soiling) was predictive of major complications or death.

Overall survival was 70%. Mortality in group PA was 50% whereas there were no deaths in group I ($p = 0.019$). Half (47.8%) of the patients presented at least one major complication including intestinal obstruction ($n = 6$), anastomotic stricture ($n = 6$) and NEC ($n = 6$). Ten patients (71.4%) in group PA underwent an urgent reoperation, whereas only one patient in group I had a major complication (intestinal obstruction) ($p = 0.029$). Six patients suffered a subsequent NEC, all of them in group PA (PA = 42.96% vs I = 0%, $p = 0.048$), of whom four patients died (66%). NEC developed not sooner than 30 days after the previous IIP event. Two patients in group I required elective surgery: one for an incisional hernia and the other for a prolapsing ileostomy.

3. Discussion

The appropriate treatment of IIP remains controversial: a straightforward intestinal resection, with either primary anastomosis or ileostomy, has been thought to be a too aggressive treatment for these low birth weight infants [14–15,16–21]. Some authors have suggested that peritoneal drainage could offer a definitive treatment, making abdominal surgery unnecessary [16–17]. However, the majority of reported cases had a subsequent laparotomy following drainage [14,19–21]. In this series, peritoneal drainage has not been used as a primary treatment for IIP.

Concerning the surgical treatment, it has been widely published that primary anastomosis is at least as good as ileostomy in neonatal intestinal perforation (caused by IIP or NEC) [22–23]. Ileostomy also carries some additional morbidity related to stoma management and subsequent surgical closure. Primary anastomosis is thus widely accepted by pediatric surgeons under favorable circumstances (healthy appearance of the remaining intestine, well controlled soiling without generalized peritonitis, patient in acceptable hemodynamic condition) [24]. However, there are no reports comparing primary anastomosis and ileostomy in IIP alone [25–27].

We mainly based patient selection on surgical findings as described in the surgical report. We have arbitrarily selected only patients who underwent ileal resection smaller than 10 cm, in which the rest of the bowel was normal. With this criterion we tried to avoid the presumable overlapping with NEC [22–23]. Even if any cases of NEC have inadvertently entered the study, those must be very limited NECs and the same treatment would be applied. Furthermore, no patient in this series had an early NEC (the earliest was 31 days after the IIP event). Pathology reports were not able to discriminate IIP from NEC in these patients with very short ileal involvement.

Outcomes from the excluded patients were also reviewed. There were no demographics or outcome differences between excluded patients treated with ileostomy or primary anastomosis (data not shown). This is a retrospective, nonrandomized study and has obvious limitations. Our preference was to offer a primary anastomosis to infants when bowel and child's condition permitted and the surgeon's experience warranted a good result. It has been striking that severity parameters such as the presence of peritoneal soiling and the need of inotropic drugs have been similar in both treatment groups. Although no significant differences in the duration of surgery were revealed between groups, ileostomy tended to take longer than primary anastomosis. This fact may reflect that the peritoneal condition and soiling were worse in group I patients than in those of group PA, as it took longer to perform a presumable faster procedure. To our surprise, the infants whom we thought had the highest risk for problems did have a better outcome.

Some complications such as bowel adhesions appeared in both groups. Adhesions are probably related to peritonitis and to surgical manipulation, and both groups were at risk. The rest of the major complications occurred only after primary anastomosis: anastomotic strictures, lactobezoar and NEC. In fact, none of the deaths was owing to an anastomosis leak or early reoperation. In this scenario, NEC resulted to the ultimate cause of death in the majority of patients who developed it (4 out 6 patients).