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ORIGINAL ARTICLE

Efficacy of Peritoneal Drainage for Focal Intestinal Perforation

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ABSTRACT

Objective: Focal intestinal perforation (FIP), which is characterized by the lack of inflammatory infiltration peripheral to the perforation, develops with few premonitory symptoms. The treatment typically involves laparotomy for drainage or percutaneous drain insertion. We retrospectively investigated the efficacy and risks associated with laparotomy-assisted drainage and peritoneal drainage (PD) for FIP. **Study Design:** This was a retrospective, comparative study. **Results:** We retrospectively evaluated seven infants with FIP who were admitted to the neonatal intensive care unit between April 2007 and March 2017. Five infants were administered indomethacin and six were administered steroids. The PD group had significantly higher birth weight, higher C-reactive protein (CRP) levels, and shorter operating times. In addition, they gained weight postoperatively but often required adjuvant therapy for bowel function. There was no significant difference between the groups regarding the time to post-operative full feeding, and all infants showed improved physical appearance. **Conclusions:** PD under local anesthesia can be considered for treating infants with FIP who have elevated CRP levels and poor general condition. We think management of this condition is still challenging in our experience, and it is necessary to continue in the future.

Key words: C-reactive protein; Extremely low birth weight infant; Focal intestinal perforation; Peritoneal drainage

INTRODUCTION

With recent advances in perinatal care, there has been an increase in the number of low birth weight infants who suffer from neonatal diseases. Due to their prematurity, extremely low birth weight infants (ELBWIs) have a particularly high incidence of complications that are known to affect their lifetime prognosis. Gastrointestinal perforation is one such complication. In Japan, the mortality rate of neonates with gastrointestinal perforation was 18.9% in 2013, exceeding the rate of 16.9% in 2008, which is said to be due to increased birth and survival rates of ELBWIs, coupled with a simultaneous increase in the incidence of gastrointestinal perforation [1].

Gastrointestinal perforations that occur during the neonatal period include necrotizing enterocolitis (NEC) and focal intestinal perforation (FIP) without necrotic changes [2]. FIP is alternatively called as intestinal perforation, local intestinal perforation, isolated intestinal perforation [3,4], or spontaneous intestinal perforation [5].

NEC is presumed to cause intestinal necrosis when a pathogen enters the intestinal tract and triggers an excessive immune response because of the prematurity of the neonate's intestinal structure and intestinal immunity and proliferation of abnormal intestinal flora [6]. Pathologically, FIP is characterized by loss of muscle layer without inflammation or ischemia. In addition, due to the intestinal prematurity of neonates, the administration of steroids or indomethacin (e.g., for patent ductus arteriosus repair) is indicated when *Candida* or *Staphylococcus epidermidis* is the causative pathogen [7].

Early treatment for gastrointestinal perforation includes peritoneal drainage (PD) surgery and drainage with laparotomy; however, indications for these

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procedures and their therapeutic effects are not completely known. Ein et al. first reported PD surgery for NEC in 1977 [8], and various reports have been published since then, including subsequent treatment plans [9-11]. Cass et al. had reported on PD surgery for FIP in 2000 [12].

We therefore conducted a retrospective comparative investigation of the efficacy and risks of drainage with laparotomy versus PD for early treatment of infants with FIP who were hospitalized in our neonatal intensive care unit (NICU) between April 2007 and March 2017. For PD performed in our hospital, indwelling Penrose drains were inserted at two sites (the foramen of Winslow and pouch of Douglas) under local anesthesia supplemented with neuroleptanalgesia in NICU.

MATERIALS AND METHODS

A total of 1737 infants were admitted to our NICU from April 2007 to March 2017. In this study, we included 102 ELBWIs among the 1560 infants with complete medical records, including sex, gestational age, birth weight, and 5-min Apgar score. FIP diagnosis was based on the infant's clinical course and plain radiographic findings. In total, seven (6.8%) of 102 ELBWIs had FIP and were included in the study. We investigated the following characteristics in these seven infants with FIP (Figure 1): Sex, gestational age, birth weight, 5-min Apgar score, indomethacin administration, steroid administration, day of onset of gastrointestinal perforation, white blood cell count and C-reactive protein (CRP) level at onset, blood gas pH, operating time, time to post-operative full feeding, use of adjuvants for bowel function, and treatment outcomes.

Moreover, we consulted with pediatric department about the general condition before treatment and decided it. The criteria of the poor general condition were infant's appearance, work of breathing, and circulation to skin.

RESULTS

Table 1 summarizes ELBWIs who developed FIP, whereas Table 2 summarizes patient characteristics. The infants included four boys and three girls. The median gestational age was 25.2 weeks (24.1–28.6 weeks), mean birth weight was 767 g (660–965 g), mean 5-min Apgar score was 8 (5–9), and there was one case of maternal transport. Overall, indomethacin was administered to 71.4% of the infants and steroids to 85.7%. Six infants received pre-operative enteral nutrition. The median time to onset of gastrointestinal perforation was 5 days (3–8 days) after birth. All infants had abdominal distension, but none had bloody feces. The median white blood cell count was 14.0 μL^{-1} (4.7–32.1 μL^{-1}), median CRP was 0.64 mg/dl

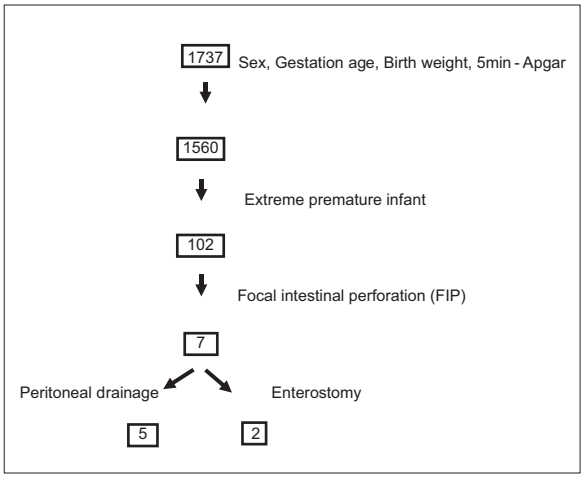

Figure 1: Study design (April 2007–March 2017)

Table 1: Summary of extremely low birth weight infants who developed focal intestinal perforation

M: F	4:3
Mean gestation period, weeks	25.2 (24.1–28.6)
Mean birth weight, grams	767.0 (660–965)
Mean 5 min-Apgar	8 (5–9)
Received indomethacin	5 (71.4%)
Steroids	6 (85.7%)
Mean day of life at perforation	5.0 (3–8)
Mean WBC, 1000 μL^{-1}	14.0 (4.7–32.1)
Mean CRP, mg*dL^{-1}	0.6 (0.3–1.1)
Mean pH	7.3 (7.2–7.40)
Mean operation time, mins	36 (15–106)
Mean day of full feeding after post-operation	28 (24–38)
Defecation adjuvant	4 (57.1%)

(0.3–1.1 mg/dl), and median pH was 7.31 (7.21–7.39). The CRP levels were higher in the PD group than in the laparotomy and enterostomy (Lap+Ent) group. The median operating time was 36 min (15–106 min); five infants underwent PD for the first surgery, and two underwent laparotomy and enterostomy. The PD group had shorter operating times. The ascites culture of one infant showed *Alcaligenes xylosoxidans* and *Burkholderia cepacia*.

The median time to full feeding was 28 days (24–38 days), with no significant difference between the PD and Lap+Ent groups during the post-operative

Table 2: Details of the extremely low birth weight infants who developed focal intestinal perforation

A: Pre-operative conditions									
Case	Sex	Gestation period	Birth weight (g)	5 min-Apgar	Maternal transport	Received indomethacin	Steroids	Day of enteral/trophic feeds started	Day of life at perforation
1	M	25W4D	785	7	No	Yes	Yes	2	5
2	F	27W1D	965	8	No	No	Yes	No	8
3	F	28W6D	795	8	No	Yes	Yes	1	4
4	M	24W6D	710	8	No	Yes	Yes	2	8
5	M	25W1D	767	9	Yes	Yes	Yes	1	4
6	F	25W2D	660	8	No	Yes	No	2	3
7	M	24W1D	692	5	No	No	Yes	4	7

B: Surgery Case								
	Clinical abdominal distension	Blood stools	WBC (1000 μL^{-1})	CRP ($mg*dl^{-1}$)	ph	Operation	Operation time, mins	Abdominal dropsy culture
1	Yes	No	16.0	0.90	7.35	PD*	20	No
2	Yes	No	20.3	1.10	7.39	PD*	36	Alcaligenes xylosoxidans
								Burkholderia cepacia
3	Yes	No	5.7	0.30	7.31	PD*	15	No
4	Yes	No	32.1	0.38	7.21	PD*	20	No
5	Yes	No	14.0	0.38	7.24	PD*	40	No
6	Yes	No	4.7	0.30	7.36	Enterostomy	80	No
7	Yes	No	12.4	0.30	7.23	Enterostomy	106	No
*PD: Peritoneal drainage								

C: Post-operative conditions and outcomes					
Case	Day of full feeding after post-operation	Daikenchuto	Glycerin enema	Reoperation	Alive or dead
1	26	Yes	Yes	No	Alive
2	24	No	No	No	Alive
3	28	Yes	Yes	Yes, enterostomy	Alive
4	30	Yes	Yes	No	Dead
5	38	Yes	Yes	No	Alive
6	29	No	No	No	Alive
7	25	No	No	No	Alive

clinical course. All four infants requiring Daikenchuto for the purpose of improving gastrointestinal motility or enemas as adjuvant treatment for post-operative bowel function belonged to the PD group. One infant transitioned from PD to Lap+Ent group. One infant in the PD group died 6 months after the surgery because of respiratory failure due to chronic lung disease.

We compared post-operative weight gain in the PD and Lap+Ent groups; at both 1 and 3 months post-operatively, the PD group showed better weight gain than that by the Lap+Ent group (Figure 2).

DISCUSSION

The incidence of FIP in ELBWIs weighing <1000 g at birth is <3–7% [5,13,14]. In our hospital, the incidence of FIP in ELBWIs was 6.8%, which was comparable to the reported rate [5,13,14]. In contrast to the reported gestational age (26.9 weeks) and birth weight (981 g) of ELBWIs with FIP [15], the gestational age was lesser (25.2 weeks) and birth weight was lower (767.0 g) in our hospital.

FIP in ELBWIs could be caused by maternal factors, including chorioamnionitis [16], but factors associated with infant prematurity must also be considered. According to Stavel et al., although there was a correlation between FIP and indomethacin administration, there was no correlation between FIP and early enteral nutrition [17]. In addition, five of the seven infants (71.4%) in our study developed FIP following indomethacin administration, and one infant who did not receive enteral nutrition developed FIP (Figure 2). Steroid administration is known to be markedly effective in ELBWIs with late-onset circulatory collapse, which is common in patients with chronic lung disease [18]. Hence, steroids are often administered from birth. In our study, six of the seven infants (85.7%) were administered steroids (Figure 2) and subsequently developed FIP. Based on these results, one of the causes of FIP could be reduced blood flow to the intestinal mucosa due to indomethacin administration and damage to the intestinal mucosa due to steroid administration. Consequently, it is vital to continue investigation of this condition as few ELBWIs have FIP.

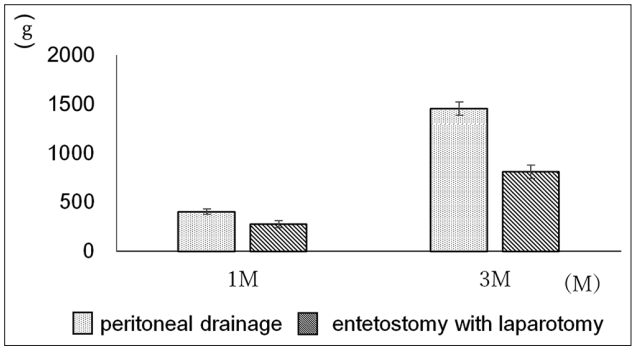

Figure 2: Comparison of post-operative weight gain in the peritoneal drainage group and the enterostomy with laparotomy group

Laparotomy has been the conventional treatment for gastrointestinal perforation in ELBWIs, but PD surgery for NEC was reported in 1977 [8]. Furthermore, there was a report in 2000 on PD surgery for FIP [12]. Since then, PD has been preferred as the initial surgical procedure in smaller babies in unstable condition because the beliefs that these babies may not tolerate laparotomy, although the benefits of laparotomy procedures, including enterostomy, are still under discussion [19]. In a Japanese report, PD was performed in 15% of patients with FIP compared with enterostomy in 55%, which included 15% of those undergoing gastrointestinal resection and 8.2% undergoing simple perforation closure [15].

Some reports have shown no significant difference in the prognosis between PD and laparotomy as the initial surgery for gastrointestinal perforation [19]; however, those who undergo PD sometimes require post-operative laparotomy. Moreover, there is no significant difference in the time to post-operative full feeding between PD and laparotomy as the initial surgery for gastrointestinal perforation [20]. In our study, 71.4% of infants with FIP underwent PD, which was higher than the normal proportion. One infant in the PD group who could not tolerate post-operative enteral nutrition underwent Lap+Ent. Hence, post-operative laparotomy may be sometimes required after initial PD.

We found no significant difference in the time to post-operative full feeding between the PD and Lap+Ent groups, which was consistent with previously reported findings. There were more ELBWIs with FIP in the PD group in our hospital because when the general condition of an infant is determined to be poor based on an elevated CRP level following perforation, and PD is the first surgical option due to the shorter operating time and low level of invasiveness. This study showed that PD is a valid option because of the lack of differences between the two procedures.

A Japanese study reported that the mortality rate of infants with FIP was 20.6% [15]. To date, all but one of the seven infants in our study have survived. The infant who did not survive died due to acute exacerbation of chronic lung disease at 6 months of age, indicating that there was no difference in the prognosis for the two surgical techniques. Postoperatively, the PD group gained weight more rapidly. Although there was no difference between the groups for initiating oral feeding in our study, the Lap+Ent group had an intestinal fistula, which is thought to create mal-

absorption issues, including post-operative diarrhea, short bowel syndrome, and not absorbed nutrition in the anal digestive tract.

More infants in the PD group required post-operative adjuvants for bowel function (Table 2), which was possibly due to tissue, such as omentum, attaching to the perforation during the healing process after PD [21], with the adhesion possibly impeding enterokinesis.

The limitation of this study was the small number of patients. Hence, further investigation on PD for treating FIP is warranted.

CONCLUSION

PD is effective for treating FIP in LBWIs. We found no significant difference between the PD and Lap+Ent groups regarding the time to post-operative full feeding. PD under local anesthesia supplemented with neuroleptanalgesia can be used because it is less invasive and has a shorter operating time compared with Lap+Ent. Therefore, when an infant's general condition is poor, and the CRP level is elevated after perforation, it is considered to be an effective method for improving the condition of such infants. We think that management of this condition is still challenging in our experience, and it is necessary to continue in the future.

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