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Original Article

Outcomes of Surgical Management for Necrotizing Enterocolitis: an 11-year Experience

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Abstract

Background: Necrotizing enterocolitis (NEC) is a serious disease in neonates and requires surgical treatment in cases with complications. The purpose of this study was to review outcomes of NEC patients treated by various procedures during an 11-year period.

Patients and Methods: A retrospective cohort study of patients with NEC treated at Khon Kaen Hospital between January 2009 and December 2019 was conducted. Medical records of patients were abstracted for clinical characteristics and presentations, laboratory findings, radiologic studies and results of treatment.

Results: Seventy-three NEC patients (40 males and 33 females) was available for the study. Sixty-one cases (84%) were managed by medical treatment and 12 cases (16.4%) required surgery because of complications due to intestinal perforation and peritonitis. Of the 12 surgical NEC, 10 cases (83%) were premature (median gestational age, 29 weeks) and 10 were low birth weight infants (median birth weight, 1263 grams). Nine cases (75%) had a serious condition treated by primary peritoneal drainage (PPD) and 4 cases survived (44%). Three cases underwent primary exploratory laparotomy (PEL) – 2 had necrotic bowel resection with enterostomy, and one had primary anastomosis – and only one survived. The overall mortality of surgical NEC was 60% (7 of 12 cases), and the mortality rate of medical NEC was 12% (7 of 61 cases).

Conclusion: NEC patients with serious complications including intestinal perforation and peritonitis require surgical treatment. PPD was done more common than PEL because of severely – ill patients with extremely and very low birth weight. The overall mortality of surgical NEC remains high, at 50%.

Keywords: Necrotizing enterocolitis, Primary peritoneal drainage, Primary exploratory laparotomy, Necrotic bowel resection, Enterostomy

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Introduction

Necrotizing enterocolitis (NEC) is the most common gastrointestinal surgical condition leading to death in neonates with prematurity and low birth weight. This condition is an acquired disorder of the intestines, commonly found in infants born before 36 weeks of gestation.[1,2] NEC is a severe inflammation of all layers of the gastrointestinal wall, which can lead to ischemic necrosis.[3-6] In 1978 Bell[6] categorized NEC into three-stages for the purposes of diagnosis and treatment. The Bell staging criteria have been modified by Kliegman[7] in 1987 (Table 1). Although most patients with NEC improve with medical treatment, some cases require surgical management. The best surgical procedure for advanced diseases with extensive intestinal necrosis and perforation remains controversial. We reviewed our experience of treating NEC during an 11-year period at a tertiary hospital in the Northeastern Thailand.

Patients and Methods

The present retrospective cohort study was conducted at the Department of Surgery, Khon Kaen Hospital (KKH). The study was approved by the Hospital's Ethics Committee. All patients with NEC who were admitted to KKH between January 2009 to December 2019 were identified from the electronic medical records, using ICD-10 Code 77.9. Patients who had incomplete medical record data were excluded. Data collected included clinical characteristics, presentation, laboratory and radiologic findings, and results of the treatment. The outcomes of survivors were finalized on December 31, 2020. Data were analyzed using the software STATA version 11.0 (Stata Corp, College Station, TX, USA). Differences between categorical variables were evaluated by Chi-square or Fisher's exact test, and between continuous variables by Wilcoxon rank-sum or Kruskal – Willis test. *P*-values less than 0.05 were considered statistically significant.

Table 1 Modified Bell staging criteria for necrotizing enterocolitis[8]

Stage*	Clinical findings	Abdominal findings	Roentgenographic findings
I A	Temperature instability, apnea, bradycardia, lethargy	Gastric retention, gastric distention, heme-positive stool	Normal or intestinal dilatation, mildileus
I B	Temperature instability, apnea, bradycardia, lethargy	Grossly bloody stool	Normal or intestinal dilatation, mildileus
II A	Temperature instability, apnea, bradycardia, lethargy	Moderate abdominal distention, bloody stool, absent bowel sound	Intestinal dilatation, ileus, pneumatosis intestinalis
II B	Temperature instability, apnea, bradycardia, lethargy, metabolic acidosis, thrombocytopenia	Moderate abdominal distention, bloody stool,absent bowel sound, definite tenderness with or without cellulitis or right lower quadrant mass	Intestinal dilatation, ileus, pneumatosis intestinalis, portal vein gas
III A	Temperature instability, bradycardia, lethargy metabolic acidosis, thrombocytopenia, hypotension, apnea combined respiratory and metabolic acidosis, DIC, neutropenia, oliguria	Marked abdominal distention, bloody stool, absent bowel sound, marked tenderness with or without cellulitis or right lower quadrant mass, signs of peritonitis	Intestinal dilatation, ± pneumatosis intestinalis, ± portal vein gas, ascites
III B	Temperature instability, bradycardia, lethargy metabolic acidosis, thrombocytopenia, hypotension, apnea combined respiratory and metabolic acidosis, DIC, neutropenia, oliguria	Marked abdominal distention, bloody stool, absent bowel sound, marked tenderness with or without cellulitis or right lower quadrant mass, signs of peritonitis	Intestinal dilatation, ± pneumatosis intestinalis, ± portal vein gas, ascites, pneumoperitoneum

* IA, IB = suspected NEC,
II A = definite NEC, mildly ill; II B = definite NEC, moderately ill,
III A = advanced NEC, severely ill, intact bowel; III B = advanced NEC, severely ill, bowel perforation

Results

Ninety-seven NEC patients were admitted at KKH during the study period. Only 73 patients had complete records. There were 40 boys and 33 girls. Of the 73 patients, the median gestational age (GA) was 31.5 weeks (range, 24 to 41 weeks) and the median birth weight (BW) was 1,510 grams (range, 620 to 3,390 grams). Thirty-six patients (49%) were classified as having very low birth weight (VLBW), and 13 (18%) were classified as having extremely low birth weight (ELBW). The median onset time of NEC was 11 days (range, 2 to 43 days). Sixty-one cases (84%) were categorized as Bell stages I and II, and medically treated. The remaining 12 cases (16%) were classified as advanced NEC (Bell stage III) and required surgical treatment. Patient characteristics in both medical and surgical treatment groups were similar (Table 2).

Patients in the surgical treatment group had more severe symptoms than those in the medical treatment group, which included significantly more frequent lethargy and abdominal erythema ($p < 0.05$). Presence of leukocytosis white blood cell (> 10,000/mm^3), or neutropenia (absolute neutrophil count < 1,500/mm^3) or thrombocytopenia (platelet < 150,000/mm^3) was not significantly different between the medical and surgical groups (see Table 3). On radiographic examination, there was greater degree of intestinal dilatation in patients in the medical treatment group, while pneumoperitoneum, an indication for surgery, was found in 10 of the 12 (83%) patients in the surgery group (see Figure 1).

The 61 patients with stages I and II NEC were conservatively treated by NPO, nasogastric or orogastric intubation, antibiotics, and total parenteral nutrition.

Table 2 Comparison of clinical characteristics of patients with NEC (n = 73) between those undergoing medical treatment (n = 61) and those undergoing surgical treatment (n = 12)

Clinical Characteristics	Medical NEC (n = 61)	Surgical NEC (n = 12)	*P*-value
Gender			
Male (no.): Female (no.)	33 : 28	7 : 5	0.788
Gestational age (weeks)			
Median (range)	32 (29.3 to 37.0)	29.1 (26.0 to 35.5)	0.091
< 28 (no.)	9	5	
28-32 (no.)	24	3	
32-36 (no.)	12	2	
> 36 (no.)	16	2	
Prematurity: no. (%)	45 (74)	10 (83)	0.384
Maturity: no. (%)	16 (26)	2 (17)	
Birth weight (grams)			
Median (range)	1,520 (620 to 3,390)	1,260.5 (720 to 3,350)	0.190
< 1,000 *: no. (%)	8 (13)	5 (42)	
1,000-1,500 **: no. (%)	21 (34)	2 (17)	
1,500-2,000: no. (%)	11 (18)	2 (17)	
2,000-2,500: no. (%)	6 (10)	1 (9)	
> 2,500: no. (%)	15 (24)	2 (17)	
Low birth weight	46 (76)	10 (83)	0.490
Normal birth weight	15 (24)	2 (17)	
Age at onset of symptoms (days)			
Median (range)	13 (2 to 44)	9.5 (3 to 45)	0.704
Risk factors: no. (%)			
Birth asphyxia	52 (80)	12 (100)	0.204
Congenital heart disease (PDA)	9 (15)	4 (33)	0.132
Previous sepsis	49 (80)	10 (83)	0.585
Administration of NSAID	3 (5)	3 (25)	0.052

* < 1,000 grams = extremely low birth weight; 1,000-1,500 grams = very low birth weight; no. = number

Table 3 Comparisons of symptoms, laboratory and radiologic findings between NEC patients undergoing medical and those undergoing surgical treatment

	Medical NEC (n = 61)	Surgical NEC (n = 12)	*P*-value
Symptom: no. (%)			
Hypothermia	29 (48)	9 (75)	0.116
Fever	25 (41)	6 (50)	0.751
Bradycardia	16 (26)	4 (33)	0.725
Lethargy	17 (28)	8 (67)	0.017
Apnea	28 (43)	5 (42)	0.999
Hypotension (shock)	36 (59)	9 (75)	0.350
Pregarvage residuals	36 (59)	7 (58)	0.999
Grossly bloody stool	9 (15)	1 (8)	0.999
Abdominal distension	52 (85)	12 (100)	0.339
Abdominal erythema	7 (12)	8 (67)	0.001
Laboratory findings			
Hemoglobin (gm/dL)			
Mean ± sd	14.1 ± 3.13	12.8 ± 3.94	0.666
White blood cell count (cell/mm3)			
Median (range)	11,500 (2,000 to 39,600)	21,485 (6,100 to 46,800)	0.052
Neutropenia*: no. (%)	61 (100)	12 (100)	NA
Thrombocytopenia**: no. (%)	11 (18.0)	5 (41.7)	0.120
Radiographic findings: no. (%)			
Intestinal dilatation	52 (85)	6 (50)	0.013
Ascites	3 (5)	2 (17)	0.187
Pneumatosis intestinalis	10 (16)	2 (17)	0.999
Pneumoperitoneum	0	10 (83)	0.001

* absolute neutrophil count < 1,500/mm^3; ** platelet count < 150,00/mm^3; no. = number; sd = standard deviation

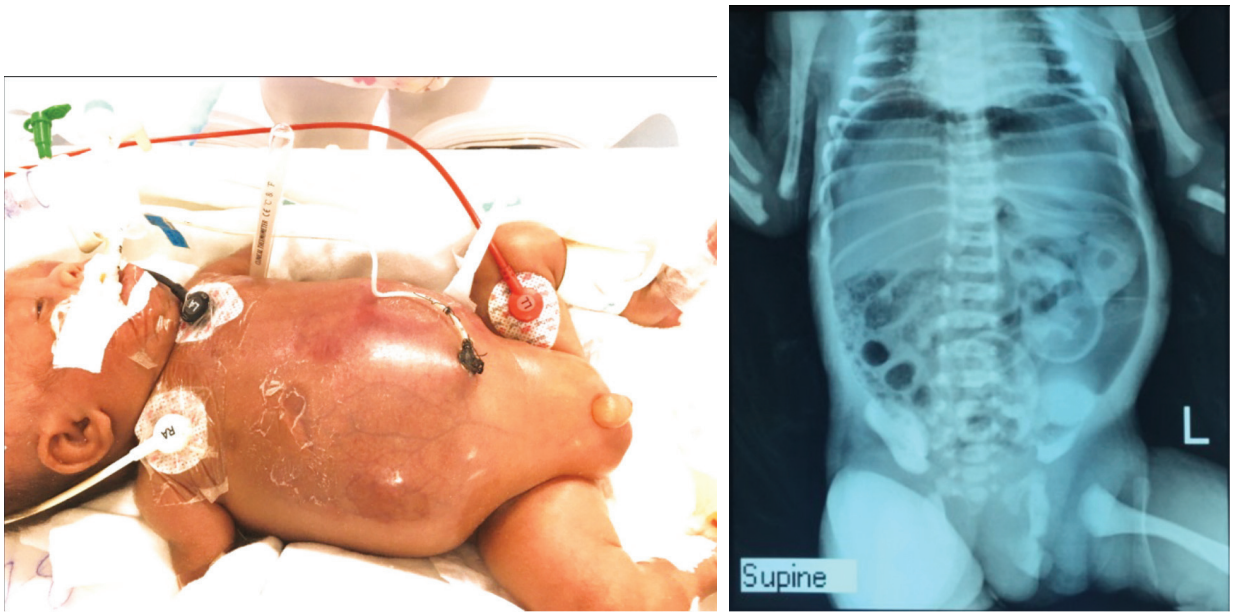

Figure 1 A very low birth weight infant with signs of peritonitis (abdominal distension, erythema and guarding) and abdominal film showing free air in the abdomen (pneumoperitoneum)

Table 4 Clinical characteristics, operative procedures and outcomes of NEC patients undergoing surgery

Case No.	GA (weeks)	BW (grams)	Age at operation (days)	Symptomatologes and indications for surgery	Operative procedures*	Results
1.	25	770	6	• Birth asphyxia, pneumonia • Bowel perforation	PPD	• Survived • Umbilical hernia • Delayed development
2.	28	990	7	• Birth asphyxia, ET-intubation • Bowel perforation	PPD	• Survived • Later Dx Hirschsprung's disease and treatment by Soave pull-through operation • Patho; Absence of ganglion cells in the rectum • Lysis of adhesion due to postop. obstruction • Doing well
3.	27	890	8	• Birth asphyxia, ET-intubation, PDA, jaundice platelet 5400/mm^3 • Signs of peritonitis	PPD	Survived • Lost to follow-up
4.	24	720	8	• Birth asphyxia, ET-intubation, abnormal color of abdomen • Bowel perforation	PPD	Dead
5.	30	1600	10	• Respiratory distress, septicemia, shock, abnormal color of abdomen, platelet 52000/mm^3 • Bowel perforation	PPD	Dead
6.	39	3350	11	• Sepsis, PDA, got NSAID, platelet 20000/mm^3 • Bowel perforation	PPD	Dead
7.	29	1085	11	• Birth asphyxia, ET-intubation, lethargy,sepsis • Bowel perforation	PPD+EL, NBR and primary anastomosis	Dead
8.	35	1755	9	• Birth asphyxia, ET-intubation, lethargy,sepsis, platelet 36000/mm^3 • Signs of peritonitis Bowel perforation	PPD+EL, NBR and enterostomy	• Survived • Lost to follow-up after closure of enterostomy 8 months
9.	30	1600	10	• Birth asphyxia, sepsis • Bowel perforation	PPD+EL, NBR and enterostomy	Dead
10.	37	2090	22	• Birth asphyxia, sepsis, shock • Bowel perforation	PPD+EL, NBR and enterostomy	Dead
11.	29	1440	19	• Twins, birth asphyxia, ET atbirth, lethargy, sepsis, • Signs of peritonitis	PEL, NBR and enterostomy	• Survived • Lost to follow-up after closure of enterostomy 3 months
12.	35	2660	3	• Birth asphyxia,abnormal color abdomen • Bowel perforation	PPD+EL, NBR and enterostomy	Dead

PPD (6)	Survived 3	Dead 3
PPD+EL, NBR and enterostomy (3)	Survived 1	Dead 2
PEL, NRB and enterostomy /anastomosis (3)	Survived 1	Dead 2

* Abbreviation: PPD = primary peritoneal drainage, EL = exploratory laparotomy, PEL = primary exploratory laparotomy, NBR = necrotic bowel resection

Fifty-four patients (89%) survived and 7 (11%) died due to respiratory distress, persistent pulmonary hypertension and septicemia. Five patients with respiratory distress were intubated since birth. The 12 patients with advanced NEC required surgical intervention. Indications for surgery included intestinal perforation in 10 (83%) and obvious peritonitis (abdominal erythema and guarding) in the remaining 2 patients. Nine of the 12 cases (75%), who were severely ill, underwent primary peritoneal drainage (PPD) or bedside peritoneal drainage (BPD) in the Neonatal Intensive Care Unit (NICU) under local anesthesia (Figure 2). Six patients underwent PPD and 3 (50%) survived. Three patients initially underwent PPD and later required exploratory laparotomy because of complications, and one (33%) survived (Table 4). The remaining 3 patients with advanced NEC underwent primary exploratory laparotomy (PEL), bowel resection and enterostomy (Figure 3). Two patients died, while one survived and later underwent closure of the enterostomy. Causes of death in the surgical NEC group included severe sepsis, respiratory failure and congestive heart failure, in the presence of congenital heart diseases and extensive intestinal necrosis. The overall survival rate of advanced NEC in the present study was 42% and mortality rate was 58%.

Figure 2 Primary peritoneal drainage by placement of Penrose drains at both sides of lower abdomen; done under local anesthesia

Discussion

At present, the incidence of NEC is increasing. The Increasing NEC incidence relates to decreasing birth weight and gestational age.[9,10] Worldwide, the incidence of NEC is approximately 1 to 3 per 1,000 live births, and over 90% of cases are seen in infants with body weight less than 1,500 grams and gestational age less than 32 weeks.[2,6,9] The incidence of NEC seen at Queen Sirikit National Institute of Child Heath was 1.04 per 1,000 live births in the period between 1993-1994, which increased to 2.7 per 1,000 live births at Rajavithi Hospital in 2004.[11,12] The Ministry of Public Health of Thailand reported the incidence of NEC as 3.7 to 11 per 1,000 live births, using data of all hospitals in the country.[13] The increasing NEC incidence may be partly explained by the increasing frequency of teenage pregnancy, which

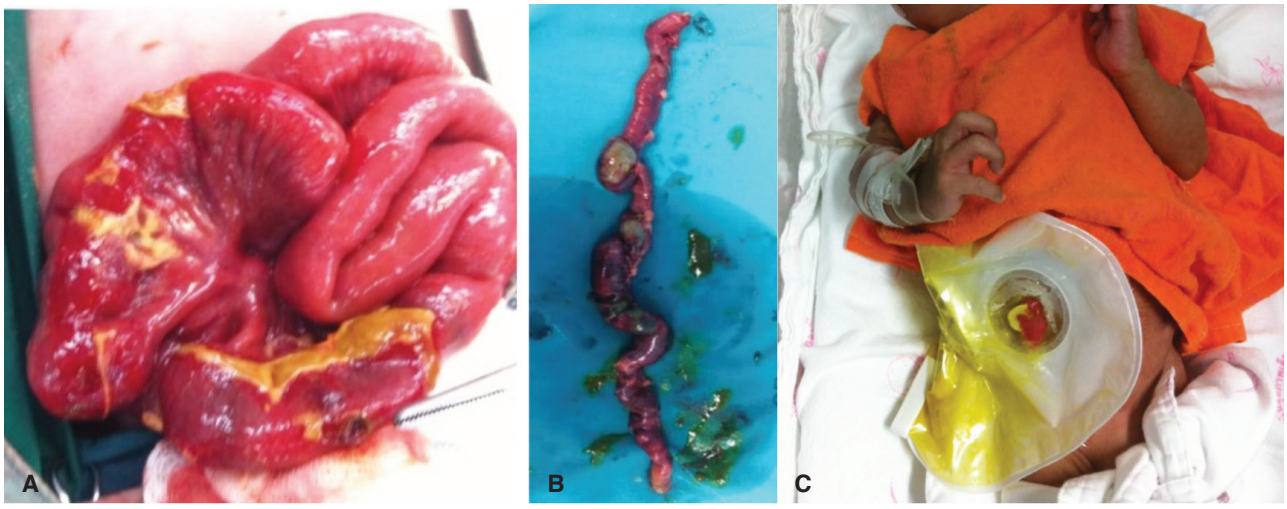

Figure 3 Primary exploratory laparotomy in a premature infant: bowel necrosis and perforation (A); segmental resection of necrotic bowel (B); and creation of a stoma or enterostomy (C)

is a risk factor for premature deliveries and VLBW or ELBW babies.[11,12] Most NEC patients seen at KKH, especially those with severe conditions, were transferred from the other provinces.

In the present study, NEC occurred slightly more frequently in the male than in the female (1.2:1). The majority occurred in premature infants (75%) and in those with VLBW and ELBW, which constituted 50% of the cases. These findings were similar to those of previous reports.[6,11-13] We also found that major risks for NEC included birth asphyxia, sepsis, patent ductus arteriosus (PDA) and administration of non-steroid anti-inflammatory drugs (NSAID) for closure of PDA.

The Bell staging criteria[6,7] for the diagnosis and management of NEC is the international standard. The majority of NEC patients categorized as having stages I and II disease are usually conservatively or medically treated, whereas the minority with stage III or advanced NEC require surgical treatment. In general, 20% to 50% of NEC patients will require surgery.[14-16] In the present study, 16% of NEC patients were surgically treated. There is some controversy regarding the timing of and decision-making during surgery, and the various surgical procedures. The absolute indication for surgery is evidence of pneumoperitoneum detected by abdominal x-rays which indicates intestinal perforation.[17,18] Signs of peritonitis, intestinal obstruction (fixed bowel loops from abdominal imaging due to non-movable necrotic bowels), palpable abdominal mass and clinical deterioration (failure of medical treatment) are relative indications for surgery. Decision making and timing of surgery will depend on the surgeon and his or her experience.[19] In the present study, NEC patients required surgery due to evidence of intestinal perforation in 10 cases and due to signs of peritonitis in 2 cases.

Primary exploratory laparotomy with resection of necrotic bowel, while trying to preserve as much viable intestine as possible, and the creation of a stoma or enterostomy, is the traditional operation of choice.[19] Closure of the enterostomy should be done after 3 months to ensure complete resolution of the inflammatory process.[17-19] Prior to the enterostomy closure, colonic or small bowel strictures should be excluded with a barium or other contrast study, administered through the enterostomy.[18] Bowel resection with primary anastomosis is not generally recommended as the process of ischemic necrosis might be ongoing, with a high risk of anastomotic leakage.[6] Primary intestinal anastomosis is acceptable in cases of focal NEC, and intestinal perforation and necrosis at the upper jejunum. We have seen one patient with jejunal perforation close to the duodenojejunal junction. It was necessary to perform segmental jejunal resection and primary anastomosis in order to avoid high-output enterostomy. This patient died due to severe sepsis, but without evidence of anastomotic leakage (Table 4, patient no.7).

Primary peritoneal drainage (PPD), recommended by Ein in 1977,[20] is an alternative surgical procedure for advanced NEC. It is suitable for severely ill VLBW and ELBW infants with clinical instability, unable to be transferred to the operating room or unable to tolerate general anesthesia. This procedure can be done in the NICU or ordinary neonatal ward, as a bed-side peritoneal drainage.[14,20,21-23] PPD can reduce pneumoperitoneum and bowel inflammation.[14,20,21-23] The survival rate of patients with advanced NEC treated by PPD is approximately 30%,[14,20,21] similar to that of the present study. Currently, PPD is a standard procedure for advanced NEC.[22] Other operative procedures, such as the "patch, drain and wait technique" proposed by Moore in 1989,[23] and the "clip-and-drop-back technique" proposed by Voughan in 1996,[24] are suitable for NEC with multi segmental necrosis. We have no experience with these operative interventions.

The outcome of surgery for NEC is not entirely satisfactory compared with the outcome of medical treatment. Medical treatment of NEC carries a mortality of about 20%, whereas the mortality of surgical treatment is probably in excess of 35% and may be as high as 50%.[10,16,25-27] In the present study the mortality in the medical treatment group was 12% and the mortality in the surgical treatment group was 60%. For the survivors of surgical treatment, some degree of neurodevelopmental impairment, delayed growth development, adhesive small bowel obstruction and intestinal failure may occur.[22] These survivors should be followed in the long-term in order to detect and treat these problems.

The present study has some limitations. Data collection might be unreliable or incomplete due to loss of documentation after a long period of time, such as information on as laboratory findings, radiographic imagings, risk factors, or milk formula feeding after birth. These defects will be corrected by systematic planning of data gathering for a future prospective study.

Conclusion

Most patients with NEC can be managed by medical treatment. In the present study, the ratio of NEC patients managed by medical to surgical treatment was 5:1. Indications for surgery included intestinal perforation (83%) and peritonitis (17%). PPD was more common performed than PEL, at a ratio of 3:1, because of severely-ill patients with VLBW and ELBW. The overall mortality of surgical treatment for NEC patients remained high, at 50%.

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Conflict of Interest

None

Funding

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บทคัดย่อ ผลของการรักษาโดยการผ่าตัดภาวะลำไส้เน่าในเด็กทารก: ประสบการณ์ในระยะเวลา 11 ปี

สิทธิโชค เล่าหะวิลัย พบ.[1], เทติยา วิริไฟ พบ.[1], เบญจพร ศิลารักษ์ ภบ.[2]

[1]กลุ่มงานศัลยกรรม โรงพยาบาลขอนแก่น

[2]กลุ่มงานเภสัชกรรมโรงพยาบาลขอนแก่น

ความเป็นมา: ลำไส้อักเสบรุนแรงจนเกิดการลำไส้เน่าในเด็กทารก (necrotizing enterocolitis – NEC) เป็นโรคที่มีอาการรุนแรงมากและต้องการการรักษาโดยการผ่าตัดในผู้ป่วยบางรายที่มีภาวะแทรกซ้อน วัตถุประสงค์ของการศึกษาครั้งนี้ เพื่อทบทวนผลการรักษาผู้ป่วยโรคนี้ที่รักษาโดยการผ่าตัดชนิดต่างๆ ในช่วงระยะเวลา 11 ปี

วัสดุและวิธีการศึกษา: เป็นการศึกษาย้อนหลังในผู้ป่วย NEC ที่รับการรักษาในโรงพยาบาลขอนแก่นตั้งแต่เดือนมกราคม 2552 ถึง เดือนธันวาคม 2562 ข้อมูลผู้ป่วย NEC ถูกนำมาวิเคราะห์เกี่ยวกับข้อมูลทั่วไป ลักษณะทางคลินิก ผลการตรวจทางห้องปฏิบัติการ ภาพถ่ายรังสี และผลการรักษา

ผลการศึกษา: ผู้ป่วย NEC ที่นำมาทำการศึกษาทั้งสิ้น 73 ราย เป็นเพศชาย 40 ราย เพศหญิง 33 ราย ผู้ป่วย 61 ราย (ร้อยละ 84) ได้รับการรักษาโดยการใช้ยาและ 12 ราย (ร้อยละ 16) ได้รับการรักษาโดยการผ่าตัดเพราะมีภาวะแทรกซ้อนจากลำไส้ทะลุและเยื่อบุช่องท้องอักเสบ ในผู้ป่วย NEC 12 รายที่ได้รับการผ่าตัด 10 ราย (ร้อยละ 83) เป็นเด็กที่คลอดก่อนกำหนด (ค่ามัธยฐานของอายุครรภ์มารดา 29 สัปดาห์) และ 10 รายเป็นทารกน้ำหนักแรกเกิดน้อยกว่าปกติ (ค่ามัธยฐานของน้ำหนักแรกเกิด 1,263 กรัม) ผู้ป่วย 9 ราย (ร้อยละ 75) ที่มีอาการหนักมาก ได้รับการรักษาโดยการใส่ท่อระบายน้ำออกจากช่องท้องและมีชีวิตรอด 4 ราย (ร้อยละ 44) ผู้ป่วยอีก 3 ราย ได้รับการรักษาโดยการผ่าตัดเปิดหน้าท้อง ตัดเอาลำไส้เน่าออก พร้อมทั้งเปิดลำไส้ไว้หน้าท้องเป็นทวารเทียม (2 ราย) และเย็บต่อลำไส้ในครั้งเดียว (1 ราย) มีเพียงผู้ป่วย 1 รายที่ผ่าตัดเปิดหน้าท้องมีชีวิตรอด อัตราการเสียชีวิตทั้งหมดในผู้ป่วย NEC ที่ผ่าตัดคือร้อยละ 60 (7 ใน 12 ราย) เปรียบเทียบอัตราการเสียชีวิตร้อยละ 12 (7 ใน 61 ราย) ในผู้ป่วยที่ได้รับการรักษาโดยการใช้ยา

สรุปผลการศึกษา: ผู้ป่วย NEC ที่มีภาวะแทรกซ้อนรุนแรงต้องการรักษาโดยการผ่าตัด จากข้อบ่งชี้มีการทะลุของลำไส้และเยื่อบุช่องท้องอักเสบ การผ่าตัดใส่ท่อระบายน้ำออกจากช่องท้องได้รับการทำมากกว่าการผ่าตัดเปิดหน้าท้อง เพราะเหตุที่ผู้ป่วยมีอาการหนักมากและมีน้ำหนักน้อยมากอัตราการเสียชีวิตในผู้ป่วย NEC ที่ผ่าตัดยังคงสูงถึงร้อยละ 50