

# Peritoneal Drainage as Definitive Therapy in Neonates with Necrotizing Enterocolitis Irrespective of Weight and Gestational Age

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**Objective:** To evaluate efficacy of peritoneal drainage(PD) in neonates with necrotizing enterocolitis (NEC) having pneumoperitoneum or peritonitis as a definitive tool of management irrespective of weight and gestational age(GA).

**Design:**Prospective analysis of 12 cases. **Place and duration:**This study was conducted in 2 hospital in Taif Saudi Arabia from December 2002 to September 2005.

**Subject and Methods:** All neonates diagnosed as NEC with pneumoperitoneum or peritonitis were included in this study irrespective of weight and GA and peritoneal drainage was performed as a primary tool of management. **Results:**Peritoneal drainage was performed in 15 patients, but 3 of them were excluded as the cause of pneumoperitoneum and peritonitis were other than NEC.Out of 12 neonates 89% improved after PD,only 1(8%) needed surgery.Overall survival was 75%.Main cause of mortality was a second attack of NEC and sepsis. **Conclusion:** PD is an effective way of treating neonates with NEC irrespective of weight and GA. PD not only stabilizez the neonates rather proves to be a definite treatment for the sick premature babies who can not tolerate general anesthesia and surgical stress.Mortality rate is high with second attack of NEC.

**Key Words:** Necrotizing Enterocolitis, Peritoneal Drainage, Primary Peritoneal drainage, Pneumoperitoneum, Premature

NEC is a disease of paradoxes. It usually occurs in prematures but may occur in full terms It usually occurs on tenth day of life but may affect on first day, several weeks or even months after birth. It frequently appears sporadically but can present endemically. It usually affects bottle fed but may involve breast fed babies<sup>1</sup>. Nec is one of the most common life threatening gastrointestinal emergency in the neonatal period, occurring in 1% to 5% of all neonatal intensive care (NICU) admissions<sup>2</sup>. Approximately 90% of neonates developing NEC are premature<sup>3</sup>. Multiple etiologies including perinatal hypoxia, indomethacin treatment, congenital heart disease, major congenital anomalies, polycythemia and pre-eclampsia and top of them early enteral feeding are linked with NEC<sup>4,5,6</sup>. It is an acquired disease producing inflammation and necrosis of the mucosal and submucosal layers of gastrointestinal tract and often leading to perforation. It is considered the most common gastrointestinal emergency seen in NICU with mortality rate of 10% to 50% increasing to 70% for infants with extensive disease<sup>7</sup>. For infants who survive after an attack of NEC, complications like stricture, short gut syndrome, sepsis and total parenteral nutrition related problems increase their morbidity. Although with refinement in aenesthesia techniques and NICU care survival is increased but mortality and morbidity for these vulnerable infants remains high, when the neonate is extremely low birth weight less than 1000 grams the chances of survival may be as low as 20%<sup>8,9</sup>. Eight years back Ein et al<sup>10</sup> introduced PD as a primary tool to stabilize the premature babies with intestinal perforation due to NEC before laparotomy. But in the later years a no. of studies proved that PD can be used as a definitive therapy for management of neonates with pneumoperitoneum and peritonitis due to NEC<sup>11,12</sup>. Survival with PD has been

found to be comparable with immediate laparotomy and upto two third of neonates have survived with no further treatment<sup>11</sup>. From Dec.2002 to Sep.2005, 15 neonates under went PD but 12 were the real cases of NEC. The aim of study was to evaluate the results of PD in cases of NEC irrespective of gestational age and weight and to compare the results with international results.

## Materials and Methods

From December 2002 to september 2005 we performed PD in 15 cases in two hospitals ,namely King Abdul Aziz Specialist Hospital and Al Hada Armed Forces Hospital Taif,K.S.A. All neonates with pneumoperitoneum and peritonitis due to NEC irrespective of weight and GA were included for PD. 3 patients were excluded from the study because, the cause of pneumoperitoneum and peritonitis was not NEC.Diagnosis was based on clinical, biochemical and radiological findings according to Bell staging criteria.<sup>13</sup> Parents were educated about the disease ,the possible management including PD and possible complications and outcome.

P.D. was performed under local anesthesia with aseptic technique at bed side in NICU. Small incision was placed on the right or left side of the lower quadrant of abdominal wall.(the right side was usually the site of choice).A 6-8 F catheter was inserted carefully 2-3 cm. in the peritoneal cavity and fluid was collected for cell count and culture sensitivity. Catheter was fixed at skin and the end left free in a collection bag. Saline lavage of the peritoneal cavity was done twice till the drainage became clear. The infant was placed on bowel rest, broad spectrum antibiotics were administered and TPN was initiated. The drain was left in place for 10 to 20 days to allow drainage of additional contaminated material.For a second attack of NEC an additional drain was placed on the opposite side.

When drainage was minimum and patient recovered clinically, drain was removed and oral feeding was started gradually. The clinical course was followed closely. Hemodynamic stability, better oxygenation and absence of clinical deterioration were signs of improvement. Decrease in abdominal distension, decrease in tenderness and settling of abdominal wall cellulites were the earliest signs of improvement(24-48).Afterward intestinal obstruction, metabolic acidosis, white cell count abnormalities, thrombocytopenia and elevated C-reactive protein levels recovered more slowly (48-96).In cases of pneumoperitoneum, free air disappeared soon after PD along with return to normal distribution of gas patten with the passage of time. Laparotomy was planned for the cases who continued to deteriorate despite PD or there were features of obstruction with improvement in clinical and biochemical findings. Contrast study was performed in all patients before discharge.

### Results:

12 patients were diagnosed as cases of NEC. Hemodynamic instability 10(83%),lethargy 9(75%), vomiting 7(58%) and abdominal distension 10(83%) were the most common clinical features while thrombocytopenia 10(83%) and metabolic acidosis 9(75%) were the common biochemical findings. Regarding radiological picture pneumoperitoneum 8(66%) and bowel distension 7(58%) were at the top. Table 1 shows clinical, biochemical and radiological findings.

Table 2 shows gestational age (mean 30 weeks), weight at the time of birth (mean1384 grams), APGAR score at minute 5 (mean 7.1) and post natal age at the time of PD (mean 15 days).

Table 1 shows clinical, biochemical and radiological findings

Clinical	Biochemical	Radiological
Lethargy and Refusal to feed 9 (75%)	Neutropenia 8(66%)< 4000/mm <sup>3</sup>	Bowel distension 7(56%)
Vomiting 7(56%)	Thrombocytopenia 10(83%)<150000/mm <sup>3</sup>	Pneumoperitoneum 8(66%)
Diarrhea 4(33%)	Metabolic Acidosis 9(75%)	Pneumointestinalis 3(25%)
Progressive distension 10(83%)	Elevated CRP 8(66%)	Portal vein gas 1(8%)
Bleeding/Rectum 5(40%)	-	-
Hemodynamic instability 10(83%)	-	-
Peritonitis 4(33%)	-	-

Table 2 shows GA, weight at birth, APGAR score at minute 5, and age at the time of PD

Case	G.A in days	Weight in grams	APGAR score	Age at PD
1	27	700	6	13(days)
2	31	1350	8	24
3	36	2100	9	9
4	29	1225	7	20
5	25	950	5	14
6	27	880	7	11
7	38	2355	9	24
8	29	1350	7	13
9	28	1050	5	8 and 29
10	33	1800	8	10
11	37	2200	9	21
12	24	650	6	15

Mean GA 30 weeks, weight 1384 grams, Apgar score 7 and age at PD 15 days

Peritoneal drainage was started at 8-24 days(mean 15). 11(91%) of 12 showed initial improvement after PD while 1(8%) of 12 continued to deteriorate and under went laparotomy after 72 hours of PD. Resection of gangrenous bowel with primary jejunocolic anastomosis done. 1(8%) of 12 under went delayed surgery due to partial obstruction which proved to be stricture of distal ileum. 8(66%) of 12 survived after PD while only 1(8%) needed surgery. Survival after PD only was 66% while overall survival after PD and surgery was 75%. Those who recovered, gradual feeding was started between 16 to 25days after start of PD. Total hospital stay for those who survived ranged from 40-75days. 3(25%) of 12 died .2(16%) of them experienced a second attack of NEC and went into sepsis while 1(8%) died due to respiratory failure. Table 3 shows the relevant results.

Table 4 shows details of those 3 patients who died. Weight of 1<sup>st</sup> patient was 700grams, GA 27 weeks and age at 1<sup>st</sup> PD was 13 days. Baby got a second attack of NEC on day 32, PD was repeated but died due to sepsis 24 days after 1<sup>st</sup> PD. Weight of 2<sup>nd</sup> patient was 1050 grams, GA 28 weeks and age at 1<sup>st</sup> PD was 8 days. This baby also got a 2<sup>nd</sup> attack of NEC and died on day 28 after 1st PD. Weight of 3rd patient was 1225 grams, GA 29weeks and age at PD was 20 days. This was a case of Edward syndrome and microcephely and died due to respiratory failure on day 41 after PD.

During the course of treatment 5(41%) developed chest infection due to long term ventilation and 1(8%) of them went into respiratory failure and died. 4(33%) developed cholestatic jaundice, 2(16%) of them went into sepsis and second attack of NEC and died while 2(16%) improved and were discharged home

Table 3 shows improvement and survival after PD and ultimate survival

Age at peritoneal drainage	15 days(8-24)
Improvement after PD	11/12 (91%)
PD followed by early surgery	1/12(8%)
PD followed by delayed surgery (due to stricture)	12(8%)
Survival after PD only	8/12(66%)
Overall survival after PD and surgery	9/12(75%)
Start of feeding after PD(days)	16-25
Total hospital stay (days)	40-75

Table 4 shows details of those 3 patients who died

	Case 1	Case 2	Case 3
Weight	700gms	1050gms	1225gms
GA	27 wks	28 wks	29wks
Age at 1 <sup>st</sup> PD	13 days	8 days	20 days
Age at 2 <sup>nd</sup> PD	32 days	29 days	-
Improvement after PD	Yes	Yes	Yes
Days between PD and death	24 days	28 days	41 days
Cause of death	2 <sup>nd</sup> attack of NEC+ Respiratory failure	2 <sup>nd</sup> attack of NEC + Sepsis	Edward syndrome + Sepsis

Abbreviations: wks, Weeks, gms, Gram

**Discussion:**

Necrotizing enterocolitis(NEC) is the most common gastrointestinal emergency in neonates. It is a disease of unknown etiology with multifactorial pathogenesis. A unifying hypothesis that may explain NEC is hypoperfusion in an immature gut as a result of a perinatal insult, either antenatal and or postnatal. The circulatory changes are associated with mucosal injury, intestinal organisms and milk breaching the mucosal barrier, as well as a complex interaction of inflammatory cascade as a response to the injury. The newborn intestine has a low vascular resistance<sup>15</sup>, and the mechanism of gut injury may be related to decreased ability of the immature gut to regulate blood flow. The incidence of NEC is reported between 0.3 to 3/1000 live births<sup>14</sup>. The risk of developing NEC is inversely related to GA at birth with the extremely premature infants at greatest risk<sup>16</sup>. It is estimated 10% of very low birth weight infants develop NEC.<sup>14,16</sup> But 10% of full term infants also develop NEC<sup>17</sup>.

Insertion of peritoneal drains at bed side was developed as a palliative procedure to decrease surgical morbidity and mortality in infants weighing less than 1000 grams<sup>2,9</sup>. In addition to the inherent disadvantage of extreme prematurity compounded by critical illness, the success of surgical intervention is further decreased by stresses of transfer to the operating room and placement under general anesthesia.<sup>18</sup> because of small size of the very low birth weight(VLBW) infant, the creation of bowel anastomosis and or stomas without injury to friable tissue and the liver is difficult.<sup>18</sup> It is estimated that survival of infants less than 1000 grams who under go surgical intervention to treat NEC is just over 20%<sup>2,9</sup>. It is for the reason that the use of bed side peritoneal drains was initiated for the treatment of perforated NEC. The purpose of peritoneal drains is to decompress the peritoneal cavity

of gas, necrotic debris and stool while avoiding the inherent risk associated with traditional treatment with NEC.

A prospective study was carried out on 15 patients in Taif region ,KSA.3 of 15 were excluded from study because the cause of perforation and peritonitis were other than NEC, So 12 patients were main stay of study. 8(66%) were having pneumoperitoneum while 4(33%) presented with peritonitis. Similar study was carried out by Xavier Demestre et al<sup>19</sup> in which they analysed 47 patients after PD.

11 of 12 of our patients were premature. mean GA was 30 weeks while mean weight 1384 grams and Apgar score was 7 at birth. Lessin et al<sup>20</sup> carried out PD on 9 patients, most of them were premature and low birth. Azaro et al<sup>21</sup> and Morgan et al<sup>22</sup> also showed that most of their patients with NEC were premature and low birth weight.

According to Kanto et al<sup>23</sup> NEC is commonly heralded by non specific clinical findings that simply represent physiological instability. Lethargy, temperature instability and hemodynamic instability were present in 10 (83%) of our 12 patients. Our 10(83%) patients were having progressive distention, 7(58%) vomiting, 5(41%) bleeding per rectum and 4(33%) diarrhea. The results almost mimic with the study conducted by O,Neil<sup>24</sup>. 70% of his patients presented with abdominal distention, 70% with vomiting 26% with diarrhea and 59% with bleeding per rectum. Of our 12 patients biochemical study showed neutropenia in 8(66%), thrombocytopenia in 10 (83%), metabolic acidosis in 9(75%), and elevated C-reactive proteins in 8(66%). A study conducted by Hunter et al showed that 87% of patients with NEC had platelet count less than 150,000 cell/mm<sup>3,25</sup>. Issacs D et al are of the opinion that C reactive protein is elevated in almost all

patients of NEC<sup>26</sup>. Radiologically speaking 7(58%) of our patients had bowel distention, 8(66%) pneumoperitoneum, 3(25%) pneumointestinalis and 1(8%) portal vein gas. Daneman A et al studied 47 patients, bowel distention was present in 55 % cases while pneumointestinalis was present in 14 % of cases<sup>27</sup>. Portal vein gas is not very common, once present it is of poor prognosis. According to Kosloske AM portal vein gas is present in only 9-20% of cases<sup>28</sup>.

In our series of 12 cases, 11(91%) improved after PD irrespective of GA and weight at birth because weight of 3 neonates was less than 1000 grams. This is the population with the highest neonatal mortality risk<sup>12</sup>. Roven et al<sup>29</sup> also reported a 100% improvement after PD. 1(8%) patient did not improve after PD, so early surgery was performed. According to Rowe MI et al<sup>30</sup> early laparotomy has high mortality in NEC and results into massive resection of gut and bad prognosis. But our patient survived as the necrosis was segmental and massive resection was not needed. 1(8%) of 12 patients went under delayed surgery due to stricture of distal ileum and repeated presentation with partial obstruction. The most common complication of PD placement reported is stricture formation<sup>9</sup>. But it is not like that in our study because only one patient developed stricture. In our series of 12 cases, over all survival after PD only was 8(66%). Survival after PD has been reported to be between 27% and 100%,<sup>10, 31</sup>, although in most series it is around 60%. Cass et al<sup>32</sup> mentioned 90% survival after PD. Over all survival after PD and surgery in our series was 9(75%).

3(25%) neonates died. 1st patient died on day 24 after PD. His weight at birth was 700 grams and GA 27 weeks. From the beginning he was in respiratory distress and ventilated. He got a second attack of NEC on day 15 after 1<sup>st</sup> PD and ultimately died of respiratory failure. But after 1<sup>st</sup> PD this patient showed remarkable improvement. 2nd patient was also low birth weight and premature and died on day 28 after 1<sup>st</sup> PD due to 2<sup>nd</sup> attack of NEC and sepsis but this patient also improved after PD. 3<sup>rd</sup> patient was also premature and low birth weight. This patient was having many other problems i.e Edward syndrome, respiratory distress and sepsis, He died on day 41 after PD but improved regarding NEC.

In our series of 12 patients, 5(41%) got some complications i.e, chest infection, respiratory failure, cholestatic jaundice and sepsis. Patients with respiratory failure and sepsis died while others could come out of their problems during treatment. For those who survived, total hospital stay ranged between 40-75 days.

Another important thing to mention in our study is that, out of 12, we performed PD on 4(33%) patients with peritonitis with out evidence of perforation. Kazez et al<sup>33</sup> showed that intestinal distension increases the damaging effect of hypoxia-reoxygenation on the gut. Therefore we performed PD when abdominal distension appeared and peritoneal fluid increased on radiological examination

suggesting advanced NEC. According to a study published by Cass DL et al,<sup>32</sup> PD can be performed to alleviate respiratory distress in non perforated NEC. The infants in this report experienced respiratory decompression requiring maximum ventilator support as a result of significant abdominal distention caused by NEC. After peritoneal drains were placed, there was significant improvement in ventilation, acid base status and urine output.

#### Conclusion:

Peritoneal drains improve outcome in case of perforated or non perforated NEC irrespective of weight at birth and gestational age and most of the patients do not need any other therapy i.e, laparotomy. In cases which do not respond surgery can be performed after initial trial of PD. PD not only stabilizes the neonates rather proves to be a definite treatment for the sick premature babies who can not tolerate general anesthesia and surgical stress. Mortality rate is high with second attack of NEC.

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