Neonatal gastrointestinal perforation

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SUMMARY: Asabe K, Oka Y, Kai H, Shirakusa T. Neonatal gastrointestinal perforation. Turk J Pediatr 2009; 51: 264-270.

Infants, especially extremely low birth weight infants (ELBWIs, birth weight <1,000 g) continue to have a high mortality after gastrointestinal (GI) perforation. In Japan, the overall mortality rate for neonates under 30 days having GI perforation was 31.6% in 20031. From 1974 to 2003, 34 cases of GI perforation in neonates were treated surgically in Fukuoka University Hospital. The overall mortality rate was 50% (17 of 34). Etiologies included necrotizing enterocolitis (NEC) (35.3%), meconium peritonitis (25%), idiopathic (25%), and gastric perforation (11.8%). The present series was divided into four groups: survival and non-survival neonates of the early (1974 to 1997) and recent (1998 to 2004) periods. Several prognostic factors of neonatal GI perforation were compared between several groups. The gestational week (GW) at birth, birth weight (BW) and weight at operation were significantly lower for non-surviving neonates in the recent period compared with the other three groups. Although a real improvement in surgical outcome was noted with improved neonatal intensive care management, the mortality rate was still high, especially in extremely premature cases under both 1,000 g and 29 GWs. The vast majority of these extremely premature babies thus comprised the NEC patients. It is therefore necessary to substantially improve the medical treatment level for such premature babies.

Key words: gastrointestinal perforation, necrotizing enterocolitis, low birth weight infant.

Despite the recently improved neonatal intensive management, such as ventilator management, availability of antibiotics and other medicines, and operative and anesthetic techniques, gastrointestinal (GI) perforation during the neonatal period is still a major problem for pediatric surgeons[2-4]. The purpose of the present study was to clarify the factors that influence the prognosis of neonatal GI perforation.

Material and Methods

A retrospective chart review was done of all cases of neonatal GI perforations at Fukuoka University Hospital during the past 31 years (from 1974 to 2004) and it included 34 infants. Pertinent information included sex, gestational week (GW) at birth, birth weight (BW), Apgar score, age at presentation, etiology and site of perforation, weight at operation, type of surgery performed, outcome, and pre- or post-operative hemanalysis (blood gas pH, base excess, values of leukocyte, thrombocyte, and C-reactive protein). To study the effect of recent advances in perinatal and perioperative care on the outcome of these infants, the series was divided into an early group (before establishment of the tertiary maternity and perinatal care center of Fukuoka prefectural area: 1974 to 1997) and a recent group (1998 to 2004). There were four groups: surviving neonates in the early period (n=7), non-surviving neonates in the early period (n=10), surviving neonates in the recent period (n=10), and non-surviving neonates in the recent period (n=7). Statistical differences between several groups were determined by Tukey-Kramer post-hoc test. A value of $p<0.05$ was considered to be statistically significant.

Results

There were 7 survivors and 10 non-survivors in the early period (total 17 neonates), whereas there were 10 survivors and 7 non-survivors in the recent period (total 17 neonates). The

study population included 23 boys (67.6%) and 11 girls (32.4%), with a sex distribution (male: female) of about 2: 1. The survival rate of males was 56.5% (13 of 23) and of females was 36.4% (4 of 11) (Table I).

Twelve patients had necrotizing enterocolitis (NEC), which represents about one-third of all the investigated patients. The etiologies of non-NEC-related perforations included meconium peritonitis (6), idiopathic (6), gastric perforation (4), strangulated ileus (3; 1 postoperative state of congenital diaphragmatic hernia, 1 mesenteric hernia, 1 midgut volvulus), intestinal atresia (2), and meconium ileus (1). The overall mortality for the entire group was 50% (17 of 34 patients). The highest mortality was observed in patients with NEC, with death occurring in 10 (83.3%) of 12 babies (Tables II and VI). The mortality rate of non-NEC patients was 31.8% (7 of 22), 3 of which occurred in 4 patients with gastric perforation (Table VI).

The site of GI perforation was gastric in 4 cases, duodenal in 1, small bowel in 24, colon in 3, and rectum in 2. Survival rates were 25% (1 of 4), 0% (0 of 1), 50% (12 of 24), 66.7% (2 of 3), and 100% (2 of 2) (Table III). The prognosis of upper GI perforation was worse than that of lower GI perforation.

The GW of almost all patients in the early period (15 of 17) was more than 30. The mortality rate of that period was high regardless of GW. In the recent period, the GW of all death cases was under 29 GWs (Table IV).

Regarding the relationship between BW and prognosis, the mortality rate was high regardless of BW in the early period. In the

Table I. Gender and Prognosis of Neonatal GI Perforation

	Early period (n=17)		Recent period (n=17)		Whole period (n=34)		
Gender	Survivor	Non-survivor	Survivor	Non-survivor	Survivor	Non-survivor	Total
Male	6	7	7	3	13	10	23
Female	1	3	3	4	4	7	11
Total	7	10	10	7	17	17	34

Table II. Cause and Prognosis of Neonatal GI Perforation

	Early period (n=17)		Recent period (n=17)		Whole period (n=34)		
	Survivor	Non-survivor	Survivor	Non-survivor	Survivor	Non-survivor	Total
NEC	1	4	1	6	2	10	12
Meconium peritonitis	1	1	3	1	4	2	6
Idiopathic	3	1	2	0	5	1	6
Gastric perforation	1	3	0	0	1	3	4
Strangulated ileus	0	1	2	0	2	1	3
Intestinal atresia	1	0	1	0	2	0	2
Meconium ileus	0	0	1	0	1	0	1
Total	7	10	10	7	17	17	34

NEC: Necrotizing enterocolitis.

Table III. Site and Prognosis of Neonatal GI Perforation

	Early period (n=17)		Recent period (n=17)		Whole period (n=34)		
	Survivor	Non-survivor	Survivor	Non-survivor	Survivor	Non-survivor	Total
Stomach	1	3	0	0	1	3	4
Duodenum	0	1	0	0	0	1	1
Small intestine	5	6	7	6	12	12	24
Colon	1	0	1	1	2	1	3
Rectum	0	0	2	0	2	0	2
Total	7	10	10	7	17	17	34

Table IV. Gestational Week and Prognosis of Neonatal GI Perforation

Gestational week (wk)	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40
Early period			○	●					○	○	●	○	○	●				○	○
									●	●	●	●						●	
									●		●								
Recent period	●			○	○		○	●			○		○	○		○			○
				●	●			●						○		○			
				●															
				●															

○: Survivor, ●: Non-Survivor.

Table V. Birth Weight and Prognosis of Neonatal GI Perforation

	Early period	Recent period
Extremely low birth weight infant		
~1000 g	○○●	○○●●●●●●
Very low birth weight infant		
1000 g~1500 g	○●	○
Low birth weight infant		
1500 g~2000 g	○●●●●●	○○●
2000 g~2500 g	○●●	○○○
Full weight infant		
2500 g~	○○●	○○

○: Survivor, ●: Non-Survivor.

Table VI. Gestational Week and Birth Weight of Neonatal GI Perforation

	Early period	Recent period	Whole period
Nec			
No.	5	7	12
Gestatinal week (wk)	30.6±0.3	25.1±1.6*	27.4±3.0*
Birth weight (g)	1621±166	708±143*	1089±475*
Mortalitiy rate (%)	80.0	85.7	83.3
Non-NEC			
No.	12	10	22
Gestatinal week (wk)	32.6±5.1	33.3±4.2*	30.6±0.3*
Birth weight (g)	2003±791	2029±661*	1621±166*
Mortality rate (%)	50.0	10.0	31.8

NCE: Necrotizing enterocolitis *: $p<0.001$ (NEC versus No-NEC).

Table VII. Prognostic Factors of Neonatal GI Perforation

	Early period (n=17)		Recent period (n=17)	
	Survivors (n=7)	Non-survivors (n=10)	Survivors (n=10)	Non-survivors (n=7)
Gestational week (wk)	33.4 ± 4.9[d]	30.9 ± 2.7[c]	38.1 ± 4.7[c]	26.1 ± 2.2
Birth weight (g)	1906 ± 871[d]	1880 ± 534[c]	1908 ± 784[c]	819 ± 320
Apgar score				
1 min	7.0 ± 1.8[b,c]	5.3 ± 3.1	4.4 ± 2.6	3.1 ± 2.2
5 min	8.7 ± 1.2	5.8 ± 2.4	6.3 ± 2.5	5.4 ± 2.6
Pe-ope blood gas pH	7.295 ± 0.081	7.308 ± 0.007	7.302 ± 0.148	7.225 ± 0.224
Pre-ope blood gas BE (mEq/L)	-4.0 ± 3.6	-8.2 ± 6.8	-3.6 ± 4.8	-10.8 ± 11.2
Pe-ope WBC	12329 ± 9032	9733 ± 9141	20130 ± 18656	24614 ± 16875
Pre-ope PLT ($x10^4/mm^3$)	20.5 ± 13.4	23.5 ± 13.5	20.6 ± 11.7	13.1 ± 13.5
Pre-ope CRP (mg/dl)	3.5 ± 2.9	4.8 ± 5.6	5.4 ± 5.9	2.0 ± 1.6
Age at presentation (d)	4.9 ± 6.8	9.8 ± 10.2	7.8 ± 8.2	8.4 ± 4.8
Weight at operation (g)	1841 ± 928[d]	1684 ± 525[d]	1859 ± 837[c]	781 ± 241
Post-ope blood pH	7.483 ± 0.058[b]	7.440 ± 0.112	7.348 ± 0.126	7.225 ± 0.258
Post-ope blood gas BE (mEq/L)	-1.6 ± 4.6	2.2 ± 7.0	-2.6 ± 3.3	-10.4 ± 9.4
Post-ope WBC	10400 ± 5217[a]	3450 ± 1582[b]	20270 ± 17602	20750 ± 15343
Post-ope PLT ($x10^4/m^3$)	12.7 ± 8.2	9.0 ± 3.9	16.9 ± 10.2	14.6 ± 14.0
Post-ope CRP (mg/dl)	6.9 ± 2.5	17.9 ± 4.6	6.4 ± 5.3	1.6 ± 0.9

a: $p<0.01$ (compared with non-survivors of early period). b: $p<0.05$ (compared with survivors of recent period).
c: $p<0.01$ (compared with non-survivors of recent period). b: $p<0.05$ compared with non-suvivors of recent period).

recent period, the mortality rate of extremely low BW infants (ELBWIs, BW <1,000 g) was 75% (6 of 8). However, the mortality rate of higher BW infants (more than 1,000 g) was 11.1% (1 of 9) (Table V).

There was no difference in the mortality of NEC patients between the early period (80%) and the recent period (85.7%). However, there was a decrease in mortality of non-NEC patients between the early period (50%) and the recent period (10%). In the early period, GW and BW were not significantly different between the NEC patients and the non-NEC patients. On the other hand, GW and BW of the NEC patients were significantly lower than those of non-NEC patients in the recent period ($p<0.001$). Therefore, those of the NEC patients were also significantly lower than of non-NEC patients in the whole period (Table VI).

A comparison of several prognostic factors of neonatal GI perforation of survivors and non-survivors in both early and recent periods is shown in Table VII. GW, BW, and weight at operation were significantly lower for non-survival neonates in the recent period compared with the other three groups (both survival and non-survival neonates in early period, and survival neonates in the recent period). The number of pre-operative leukocytes was significantly higher for the non-survival neonates in the recent period compared with both survival and non-survival neonates in the early period. Apgar score and post-operative base excess were also lower for non-survival neonates in the recent period compared with survival neonates in the early period (Table VII).

Discussion

According to the national survey on neonatal surgery in 2003 by the Committee on Academic Survey and Advanced Medical Science of the Japanese Society of Pediatric Surgeons[1], there has been a large increase in the number of operations performed on neonates, from 662 cases in 1964 to 3,709 cases in 2003. Those 3,709 cases included ano-rectal malformation (369 cases; 9.9%), intestinal atresia (293 cases; 7.9%), hyperpyloric stenosis (205 cases; 5.5%), diaphragmatic hernia (189 cases; 5.1%), tracheoesophageal fistula and Hirschsprung disease (each 172 cases; 4.6%), malrotation (115 cases; 3.1%), GI perforation (114 cases; 3.1%), and so on. However, mortality of GI perforation (31.6%) accounted for the worst of those disorders that needed surgical treatment in the newborn period. The overall mortality rate of neonatal GI perforation in this series was 50%. There has been a significant reduction in mortality from the early period to the recent period (from 58.8% to 41.2%). The surgical outcome in the early period did not differ regardless of BW and GW. However, surgical outcome in the recent period has improved as a result of the improvement in neonatal intensive management. The trend toward better survival is more pronounced for infants with low BW and early GW, so that the mortality gap between small and immature babies and neonates with normal BW and term has narrowed in the recent period[4], excluding the premature babies under both 1,000 g and 29 GWs (Tables IV and V). However, St-Vil et al.4 reported that GW appeared to be of less prognostic importance than BW.

In this series, the rate of low birth weight infants (LBWIs) was not significantly different between the early period and the recent period (82.4% and 88.2%). However, the rates of very low BW infants (VLBWIs) were 29.4% and 52.9%, and totally 41.2%. Those of ELBWLs were 17.6% and 47.1%, totally 32.4%. The rate of LBWIs, especially of VLBWI and ELBWI, in neonatal GI perforation was higher than that of other institutions[2-5].

In this series, the survival rate of males was higher than that of females (Table I), but the reason for this was unclear. If enough cases were studied, the survival rates could be expected to be the same between genders. A larger volume study is needed to confirm the results.

Of our 34 patients, the predominant cause of perforation was NEC (Table II). Some investigators[4,5] have found an increasing incidence of NEC perforation as more LBWIs survive as a result of improved perinatal care. Indeed, NEC was the underlying etiology in 41.2% of all cases in the recent period, up from 29.4% in the early period. These infants were significantly smaller and more premature than the non-NEC group, and had a poorer prognosis; 83.3% of all deaths in this series occurred in children with NEC (Table VI).

According to the national survey on neonatal surgery up to 1983, the most commonly perforated site was the stomach (from 50% to 75%) followed by small intestine and colon.

However, the small intestine became the most frequent site (about 50%) after 1988, followed by the stomach and colon[1,6-11]. The most common site of GI perforation in our series was also the small intestine (24 cases) (Table III).

According to the national survey on neonatal surgery in 2003, the sites of mortality were as follows: stomach in 42.9%, small intestine in 50% and colon in 33.3%[1]. In our series, the mortality site was stomach in 75%, small intestine (including 1 duodenal case) in 52%, and colon (including 2 rectal cases) in 20%. Particularly notable, four gastric perforation cases were in the early period, and only one case survived (Table III). The survival rate was similar to that of the national survey in the same period (from 49.5% to 69.5%)[7,8].

There were some cases of mortality unrelated to GW and BW in the early period. However, in the recent period, the GW of all non-surviving cases was under 29, and the mortality rate was 75% (6 of 8) (Table IV). Nakamura et al.[3] revealed there was no survival for those under 25 GWs, and the mortality rate was 84.6% (11 of 13) under 30 GWs. Akatsuka et al.[12] also reported that the mortality rate of premature babies under 28 GWs was 80.0% (4 of 5). These results were similar to those of the present study.

Death was not related to BW in the early period. However, almost all death cases were ELBWIs (BW <1,000) in the recent period (Table V). The vast majority of these extremely premature babies thus comprised the NEC patients. Nakamura et al.[3] reported the highest mortality rate in VLBWIs. Shinohara et al.[13] and Uceda et al.[14] also had high mortality rate in ELBWIs.

With regard to the prognostic factors in both the early and recent periods, GW, BW, and weight at operation were significantly lower in non-survival neonates in the recent period compared with the other three groups (Table VII), meaning that the non-survival neonates in the recent period were extremely premature and LBW.

The national survey on neonatal surgery in Japan showed that surgical outcome for premature babies weighting less than 2,500 g at birth was still undesirable, though that for mature babies with good weight had improved immensely. However, compared to 1973, when 19% of all babies having surgery were premature and over half died, with a mortality rate of 51%, in 2003, the mortality rate was 16% even though the proportion of premature babies had increased to 28%. Over this time, there was a real improvement in surgical outcome[15] with the recently improved neonatal intensive management. At the present time, neonatal GI perforation is still a major problem for pediatric surgeons in our institution, especially premature babies under both 1,000 g and 29 GWs. The proportion of extremely premature babies has gradually increased in recent years. It is therefore necessary to substantially improve the level of medical treatment for such immature babies.

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