Pediatr Surg Int (2002) 18: 696–700
DOI 10.1007/s00383-002-0794-3

ORIGINAL ARTICLE

Abdurrahman Önen · Ali İhsan Dokucu
Murat Kemal Çiğdem · Hayrettin Öztürk · Selçuk Otçu
Selçuk Yücesan

Factors effecting morbidity in typhoid intestinal perforation in children

Accepted: 13 December 2001 / Published online: 20 December 2002

Abstract To determine the factors affecting morbidity in patients with typhoid intestinal perforation (TIP), 42 patients who had been operated upon for TIP between 1990 and 2000 were reviewed. The average age was 10.4 years, the male-to-female ratio 2.5/1. The mean interval from admission to operation was 6 h. Twenty-three children had multiple perforations. Primary closure (PC) was performed in 55% of the patients, ileostomy in 26%, and resection with anastomosis (RA) in 19%. Parenteral nutrition (PN) was available for 22 patients for an average of 9 days. Postoperative complications occurred more commonly in patients with delayed admission and/or severe peritonitis. Hospitalization was shorter and the postoperative complication rate lower in patients who received PN and in those who underwent ileostomy. None of the patients developed an enterocutaneous fistula. The 2 deaths (4.8%) resulted from overwhelming sepsis. The most significant factors affecting morbidity were prolongation of perforation-operation interval and severe peritonitis. No operative procedure is likely to be the best in all cases; therapy should be individualized. Ileostomy appears to be an effective procedure, particularly in patients with severe abdominal contamination and delayed presentation. The use of PN in addition to standard medical and surgical therapy in patients with TIP may be beneficial.

Keywords Typhoid perforation · Children · Parenteral nutrition

A. Önen (✉) · A.İ. Dokucu · M.K. Çiğdem · H. Öztürk · S. Otçu
S. Yücesan
Department of Pediatric Surgery,
Medical Faculty of Dicle University, Diyarbakır, Turkey
E-mail: aonenmd@yahoo.com
Tel.: +90 412 2488495
Fax: +90 412 2488440

A. Önen
Department of Pediatric Surgery, Medical Faculty
of Dicle University, 21280 Diyarbakir, Türkiye

Introduction

The mortality of typhoid intestinal perforation (TIP) has decreased slightly over the last decade. With an estimated annual incidence of 0.54%, typhoid fever (TF) is still a serious global health problem that usually occurs due to inadequate environmental sanitation in those developing countries with the fewest resources available for effective treatment [18, 20, 22, 23, 26]. TIP is the most frequent and serious complication of TF [1, 2, 25, 26]; the incidence has been reported to be between 0.8% and 18% [14, 16, 21]. Reported mortality of TIP ranges between 5.2% and 60% [1, 20, 22, 23, 26].

The morbidity and mortality of TIP remain unacceptably high. They are influenced by the high incidence of postoperative complications, especially continuing peritonitis and septicemia in the postoperative period. The most serious complication is enterocutaneous fistula, the most frequent wound infection. There is no general agreement about the operative procedure of choice, and other factors that may affect morbidity are still controversial. We reviewed our patients with TIP to determine the factors that effect morbidity.

Patients and methods

The medical records of 42 patients who were operated upon for TIP between 1990 and 2000 were reviewed. Age, sex, clinical features, preoperative investigations, and preoperative and operative treatments were reviewed. The effects of age, parenteral nutrition (PN), perforation-operation interval, number of perforations, severity of peritonitis, and operative procedures on outcome were evaluated. The diagnosis of TIP following TF was established by history and clinical and radiologic examinations and confirmed intraoperatively by the typical findings of antimesenteric perforations of the ileum and/or isolation of *Solmonella typhi*, a positive Widal test, or pathologic examination. The investigations usually included a plain erect abdominal X-ray film, hemoglobin level, and leukocyte count (WBC).

All cases were admitted as emergencies and received surgical treatment after adequate urine output was established. Abdominal exploration was conducted through a right lower transverse incision. Single perforations were debrided and a two-layered primary

bowel closure (PC) was performed, usually combined with suturing of areas of apparent impending perforation. Multiple debridements and two-layered closures were utilized when multiple wide-apart perforations were present. Areas of incipient perforation were also debrided and closed. Resection and anastomosis (RA) was performed for multiple perforations close together after assuring that the abdomen was not severely contaminated. An ileostomy was performed when multiple perforations with severe peritoneal contamination were present. The peritoneal cavity was thoroughly irrigated with warm saline and drained in all cases. Wherever possible, tissue was obtained for histopathologic examination. All abdominal incisions were sutured closed primarily.

Postoperatively, the patients received IV fluids, antibiotics, blood transfusions, and other supportive measures. In all cases chloramphenicol, clindamycin and ampicillin were administered parenterally for at least 7 days following operation. After resolution of the paralytic ileus, treatment was continued with oral trimethoprim-sulfamethoxazole and chloramphenicol for a further week. Oral intake was resumed following resolution of the ileus. PN was calculated as follows: 1 kcal/ml, protein 2.5 g/kg, fat 3.5 g/kg, and carbohydrate 7–12 g/kg. The lipid solution was administered separately, the proteins and carbohydrates together. Nutrition was applied continuously via an infusion pump through a peripheral vein.

The Mann-Whitney *U* test, Fischer's exact test, and chi-square test were used for statistical analyses. A value of P less than 0.05 was accepted as significant.

Results

Patients were aged between 4 and 14 years (mean 10.4). There were 30 boys and 12 girls (2.5:1). Of the 42 patients, 28 had received medical therapy for an average of 9 days at other centers before admission to our clinic. The most common symptoms and findings were abdominal pain and generalized abdominal tenderness (Table 1). The median period between the first prodromal sign and the estimated perforation time was 14.8 days. The estimated time between perforation and surgery ranged from 1 to 7 days (average 2.8). WBC ranged from 3.2 to 18.7 $\times$ 10^9 ml. Radiologic examinations showed a pneumoperitoneum in 29 (69%) patients. A Widal agglutination test was performed in 31 cases, and significant titers were seen in only 15 (47%). The other children had typical operative findings of antimesenteric perforation of the terminal ileum. Aggressive fluid and electrolyte replacement was done in all cases and blood transfusions were administered to 13 patients (31%) who had severe anemia and/or hypovolemia. The average time required for preoperative resuscitation was 6 h (range 2–9 h), during which IV crystalloid was used to establish urine output and correct fluid and electrolyte imbalance, and antibiotics were administered.

Operative findings included severe peritoneal contamination in 19 (45.2%) patients, moderate in 15, and mild in 8. Perforations were located 5 to 80 cm from the ileocecal valve (mean 28 cm). Solitary perforations (n = 19) occurred on the antimesenteric side of the distal ileum and were well-circumscribed. Twenty-three children had multiple perforations; 10 had two, 7 had three, 5 had four, and 1 had five. The most frequently performed operative procedure was PC (55%). Pathologic examination confirmed the diagnosis of TIP in all cases. PN was provided to 22 (52%) patients for an average of 9 days (range 8–12).

Table 1 Symptoms and signs of patients with typhoid intestinal perforation at admission

Symptom/sign	No. of patients (%)
Abdominal pain	42 (100)
Abdominal tenderness	42 (100)
Fever	36 (86)
Lack of appetite	31 (74)
Vomiting	28 (67)
Headache	21 (50)
Constipation	20 (48)
Diarrhea	12 (29)

The overall mean duration of hospitalization was 13.4 $\pm$ 3.3 days ($\pm$ 1SD, range 7–23). The paralytic ileus usually began to resolve around the 5th to 6th postoperative day (POD), but progress to a regular diet could not be achieved until the 7th to 8th POD (mean 7.6 $\pm$ 2.1). The average time for ileus resolution was 8.1 $\pm$ 2.1 days in the patients who received PN and 7.3 $\pm$ 1.9 days in those did not ($P > 0.05$). The most common postoperative complications were wound infection (WI), which occurred in 22 cases (52%), followed by wound dehiscence (WD) in 17 (40%) (Table 2). None of the patients developed an enterocutaneous fistula. Three children required a repeat laparotomy due to postoperative intestinal obstruction or abdominal-wall dehiscence. Several children had more than one complication.

The factors affecting morbidity in patients with TIP are shown in Table 2. The occurrence of WI and WD was significantly higher in patients older than 10 years and when the perforation-operation interval was longer than 48 h. Although no significant relation between the number of intestinal perforations and postoperative complications was seen, the severity of peritonitis was a significant factor affecting postoperative WI and WD. The mean duration of hospitalization in patients who received PN (10.3 $\pm$ 3.1 days) was significantly lower compared to those who did not (15.6 $\pm$ 3.5 days) ($P < 0.001$). In addition, WI, WD, and sepsis were seen significantly less often in patients who received PN. The mean duration of hospitalization for patients who underwent an ileostomy (8.09 $\pm$ 1.04 days) was significantly lower than in patients treated by RA (13.25 $\pm$ 1.83 days) or PC (14.34 $\pm$ 1.30 days) ($P < 0.001$ and $P < 0.001$, respectively). Comparing the operative procedures performed, the postoperative complication rate was significantly lower in patients with an ileostomy.

Two children (4.8%) died. Both deaths occurred in the first 96 postoperative hours as a result of septicemia in combination with one or more postoperative complications'. These 2 children were admitted more than 3 days after the onset of pain. Both had severe abdominal contamination; 1 had two perforations and the other had four. PC had been performed in one and RA in the

Table 2 Factors effecting morbidity in patients with typhoid intestinal perforation (*WI* wound infection, *WD* wound dehiscence, *S* sepsis, *AD* abdominal dehiscence, *Pn* pneumonia, *IA* intraabdominal abscess, *NS* not significant, *PC* primary closure, *RA* resection with anastomosis)

	WI* (n = 22) n (%)	*P*	WD (n = 17) n (%)	*P*	S (n = 4) n (%)	*P*	AD (n = 3) n (%)	*P*	Pn (n = 4) n (%)	*P*	IA (n = 2) n (%)	*P*
Age (years)												
< 10 (n = 20)	8 (40)		6 (30)		3 (15)		2 (10)		4 (20)		1 (5)	
> 10 (n = 22)	14 (63.7)	< 0.001	11 (50)	< 0.05	1 (4.5)	NS	1 (4.5)	NS	0 (0)	NS	1 (4.5)	NS
Parenteral nutrition												
+(n = 22)	7 (31.8)		5 (22.7)		0 (0)		0 (0)		1 (4.5)		1 (4.5)	
–(n = 20)	15 (75)	< 0.001	12 (60)	< 0.001	4 (20)	< 0.05	3 (15)	NS	3 (15)	NS	1 (5)	NS
Perforation-operation interval												
< 48 h (n = 17)	4 (23.5)		3 (17.6)		0 (0)		0 (0)		0 (0)		0 (0)	
> 48 h (n = 25)	18 (72)	< 0.001	14 (56)	< 0.05	4 (16)	NS	3 (12)	NS	4 (16)	NS	2 (8)	NS
Number of perforations												
One (n = 19)	8 (42.1)		6 (31.6)		1 (5.3)		1 (5.3)		2 (10.6)		1 (5.3)	
Multiple (n=23)	14 (60.9)	NS	11 (47.8)	NS	3 (13)	NS	2 (8.7)	NS	2 (8.7)	NS	1 (4.3)	NS
Severity of peritonitis												
Mild-moderate (n = 23)	7 (30.4)		4 (17.4)		1 (4.3)		1 (4.3)		2 (8.6)		0 (0)	
Severe (n = 19)	15 (78.9)	< 0.001	13 (68.4)	< 0.01	3 (15.8)	NS	2 (10.5)	NS	2 (10.5)	NS	2 (10.5)	NS
Operative procedures												
PC (n = 23)	15 (65.2)		11 (47.8)		1 (4.3)		1 (4.3)		1 (4.3)		1 (4.3)	
Ileostomy (n = 11)	2 (18.2)	< 0.05	2 (18.2)	NS	0 (0)		0 (0)	NS	0 (0)		0 (0)	NS
RA (n = 8)	5 (62.5)		4 (50)		3 (37.5)	< 0.05	2 (25)		3 (37.5)	< 0.05	1 (12.5)	

other. Neither of them received PN; no deaths occurred in the patients who received PN.

Discussion

Typhoid fever is endemic and sometimes locally epidemic in some regions of our country as well as some developing countries. Mortality is 15% in untreated cases and 1% after antibiotic therapy [19]. TIP is a severe complication of TF. These perforations are not comparable to localized intestinal perforations due to trauma, appendicitis, ulcer, etc. [5, 10, 11, 15, 19, 23]. TIP presents a challenge in that the perforations not only cause high mortality, but the development of the perforation is also unpredictable. Diagnosis is mainly based on a history of remittent fever with headache followed by abdominal pain and features of peritonitis [15, 26]. Contamination of water and food may be the main source of TF in children.

Reviewing 1,990 cases of TIP, van Basten and Stockenbrügger [26] found Widal test to be positive in 25%–75% of cases. Thus, this test seems to be less useful in the diagnosis of TIP. In our study, the Widal test was positive in 47% of cases. Butler et al. [7] reported 286 patients with a pneumoperitoneum among 622 patients with TIP (46%). In the present study, pneumoperitoneum was found in 69% of cases. The high incidence in our series may be due to the late presentation; a pneumoperitoneum may not be detected in the early stages of TIP. The presence of a pneumoperitoneum at admission leads us to consider the admission delayed. Investigations such as WBC, eosinophil counts, and the Widal test are of limited value [12, 26]. Positive findings may be helpful, but negative results cannot exclude the diagnosis.

TIP occurs mostly in males, commonly after the age of 4 years [1, 13, 15, 23]. As observed in other studies, we found a male tendency with a male:female ratio of 2.5:1. The phenomenon that boys are affected more often than girls is not well-understood. A possible explanation could be that boys spend more time in outdoors activities and more often eat outdoors compared to girls. It was reported that the perforation rate increases with increasing age, and was previously found to be 1.7%, 12.4%, and 29.3% in patients 1–4, 5–9, and 10–12 years old, respectively [5]. In contrast, TIP was found in 47.6% and 52.4% of children 10 years or less and over 10 years, respectively, in our series. WI and WD were more frequent in patients older than 10 years. The lower morbidity in the younger children in our series may be related to the higher healing capacity in the younger child's rapidly-growing body.

Surgery is the accepted standard treatment of TIP. The operative procedure of choice, however, is still debated. PC, RA, and ileostomy are the generally described methods [5, 10, 11, 16, 23]. Numerous factors may be relevant in selecting the proper treatment. The type of surgery performed may have some bearing on the prognosis. Debridement and PC has been successfully used in many series [11, 20, 22, 23]. Chouhau and Pande [9], however, reported 58.7% mortality in 81 patients, most of whom were treated with PC. RA has also been recommended [5, 6, 24]. Tube ileostomy has been advocated to reduce the incidence of postoperative fistula formation [14]. Maloney [17] and Chambers [8]

successfully treated TIP patients with tube ileostomy via the perforation.

Early surgical intervention should include the choice of a prompt surgical technique that will permit easy and quick recovery, because these patients are usually severely ill. Our data support, but do not prove, that the best policy seems to be debridement and PC for single perforations, with resection reserved for multiple perforations in a short segment of bowel. We performed an ileostomy in cases with multiple perforations that had severe abdominal contamination. However, the operative technique of choice differs from patient to patient, and the outcome may be worsened by the employment of inappropriate procedures. In our experience, an ileostomy minimizes the need for reoperations on ischemic, inflamed, edematous intestine and also shortens the period of paralytic ileus. A short hospitalization and low postoperative complication rate are additional advantages of ileostomy. The disadvantage is the necessity of a second operation.

In general, children with TIP are severely catabolic at the time of admission. The TF-induced hypermetabolic state combined with a prolonged period of postoperative paralytic ileus enhances negative nitrogen balance [18]. PN has been suggested to improve the outcome in patients with TIP [20]. Akgün et al. [3] concluded that all patients with TIP should receive PN for a period of at least 10 days. In an attempt to improve their nutritional status, we used PN for an average period of 9 days in 22 patients with TIP. Since 1990, our goal is to use PN to shorten the duration and severity of postoperative sepsis. Because of the shorter hospitalizations and better postoperative outcome in our patients receiving PN, it might be beneficial to use PN routinely in patients with TIP. On the other hand, the use of PN requires technological equipment and experienced personnel, and is thus not available worldwide.

TIP is a severe complication of TF that may be fatal [11, 12, 16]. Although the outcome is better in patients with a single perforation and worse in those with multiple perforations [13], our series showed no significant relation between postoperative complications and the number of intestinal perforations. Delay between perforation and operation has long been recognized to be of major importance for the prognosis [2, 12, 25, 26]. In our series, the patients who underwent operation soon after the intestinal perforation, particularly within the first 48 h, had a better prognosis. One reason for delayed presentation of TIP in our region is that patients are first seen by general practitioners and are not referred for specialist care until much later. Unfortunately, 40% of our patients were operated upon after 48 h following perforation. The patients with severe peritonitis had a high postoperative complication rate.

The most frequent postoperative complication of TIP is WI and the most severe is enterocutaneous fistula [1, 11, 12, 18, 26]. Fecal fistula (FF) is a catastrophic complication, and significantly increases mortality to up to 67% [2, 20, 21]. A FF may require re-operation and the use of techniques such as exteriorization of the ileal loop and PN [25]. The main causes are reported to be the presence of a negative nitrogen balance and improper healing of the anastomotic line [10]. As cited above, none of the patients in our series had a FF. It may be speculated that this was because we used PN in over one-half of cases and chose an ileostomy in patients with severe peritonitis and multiple perforations associated with intestinal ischemia. We believe the treatment of choice for TIP is surgery, and the sooner this is done, the greater the chance of survival. Several postoperative complications, particularly enterocutaneous fistula, may increase mortality in patients with TIP, who are usually debilitated, dehydrated, and anemic preoperatively [21]. In the present series the mortality was 4.8%, which is relatively low compared with other series.

We conclude that: (1) the most significant factors affecting morbidity are prolongation of the perforation-operation interval and severe peritonitis; (2) the Widal test seems ineffective in establishing the diagnosis of TIP as one-half of cases can be missed; (3) younger children (< 10 years) are likely to have lower morbidity; (4) no operative procedure seems to be the best; treatment should be individualized. An ileostomy appears to be effective, particularly in patients with severe abdominal contamination and delayed presentation; and [5] PN reduces postoperative complications and its use in addition to standard medical and surgical therapy in patients with TIP may be beneficial. Significant improvement in survival of TF will depend not only on better perioperative management, but also on its prevention by providing safe drinking water and improving sanitation.

References

1. Abantanga FA (1997) Complications of typhoid perforation of the ileum in children after surgery. East Afr Med 74: 800–802
2. Abantanga FA, Wiafe-Addai BB (1998) Postoperative complications after surgery for typhoid perforation in children in Ghana. Pediatr Surg Int 14: 55–58
3. Akgün Y, Bac B, Boylu S, et al (1995) Typhoid enteric perforation. Br J Surg 82: 1512–1515
4. Ameh EA (1999) Typhoid ileal perforation in children: a scourge in developing countries. Ann Trop Paediatr 19: 267–272
5. Ameh EA, Dogo PM, Attah MM, Nmadu PT (1997) Comparison of three operations for typhoid perforation. Br J Surg 84: 558–559
6. Athie CG, Guizar CB, Alcantara AV, et al (1998) Twenty-five years of experience in the surgical treatment of perforation of the ileum caused by *Salmonella typhi* at the General Hospital of Mexico City, Mexico. Surgery 123: 632–636
7. Butler T, Knight J, Nath SK (1985) Typhoid fever complicated by intestinal perforation: a persisting fatal disease requiring surgical management. Rev Infect Dis 7: 244–256
8. Chambers CE (1972) Perforation of the ileum. Arch Surg 105: 550–552
9. Chouhau MK, Pande SK (1982) Typhoid enteric perforation. Br J Surg 69: 173–175
10. Eggleston FC, Santoshi B (1981) Typhoid perforation: choice of operation. Br J Surg 68: 341–342

11. Gibney EJ (1989) Typhoid perforation. Br J Surg 76: 887–889
12. Gupta V, Gupta SK, Shukla VK, et al (1994) Perforated typhoid enteritis in children. Postgrad Med J 70: 19–22
13. Kayabalı I, Gökçora IH, Kayabalı M (1990) A contemporary evaluation of enteric perforations in typhoid fever: analysis of 257 cases. Int Surg 75: 96–100
14. Kizilcan F, Tanyel FC, Büyükpamukçu N, Hiçsönmez A (1993) Complications of typhoid fever requiring laparotomy during childhood. J Pediatr Surg 28: 1490–1493
15. Levy RD, Degiannis E, Saadia R (1996) Management of intestinal typhoid perforation. S Afr J Surg 34: 138–140
16. Lizarralde EA (1981) Typhoid perforation of the ileum in children. J Pediatr Surg 16: 1012–1015
17. Maloney CT (1971) Surgical treatment of typhoid perforation of ileum. NY State J Med 71: 663–664
18. Merier DE, Tarpley JL (1998) Typhoid intestinal perforations in Nigerian children. World J Surg 22: 319–323
19. Merier DE, Imediegwu OO, Tarpley JL (1989) Perforated typhoid enteritis: operative experience with 108 cases. Am J Surg 157: 423–427
20. Mock CN, Amaral J, Visser LE (1992) Improvement in survival from typhoid ileal perforation. Ann Surg 215: 244–248
21. Nguyen VS (1994) Typhus perforation in the tropics apropos of 83 cases (abstract). J Chir (Paris) 131: 90–95
22. Noorani MA, Sial I, Mal V (1997) Typhoid perforation of small bowel: a study of 72 cases. J R Coll Surg Edinb 42: 274–276
23. Santillana M (1991) Surgical complications of typhoid fever: enteric perforation. World J Surg 15: 170–175
24. Shah AA, Wani KA, Wazir BS (1999) The ideal treatment of the typhoid enteric perforation – resection anastomosis. Int Surg 84: 35–38
25. Talwar S, Sharma RK, Prasad P (1997) Typhoid enteric perforation. Aust NZJ Surg 67: 351–353
26. Van Basten JP, Stockenbrügger R (1994) Typhoid perforation: a review of the literature since 1960. Trop Geogr Med 46: 336–339