

Pattern of Presentation and Management of Typhoid Intestinal Perforation in Sagamu, South-West Nigeria: a 15 year Study

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Abstract

Background: Mortality from typhoid intestinal perforation remains high in the West African sub-region.

The aim of this retrospective analysis was to assess the presentation pattern, mode of therapy and outcome of cases diagnosed and treated as typhoid intestinal perforation at Olabisi Onabanjo University Teaching Hospital, Sagamu, between January 1990 and December 2004.

Methods: Complete records of 105 adult patients were studied.

Results: The male to female ratio was 2:1. The mean age was 27 years.

Prior to arrival in our hospital, all the patients were on various combinations of antibiotics. Twenty-seven (26%) patients had been hospitalized elsewhere during the current illness.

Chloramphenicol was the drug of first choice in the first ten years (phase 1). It was replaced with ciprofloxacin in the subsequent five years (phase 2).

Blood culture was positive for salmonella organisms in 5(4%) patients. Resistance to chloramphenicol was found in three (60%) out of these five positive cultures.

All patients had laparotomy after resuscitation.

There were 112 perforations, mostly in the ileum and jejunum. Perforations were single in one hundred and one patients and multiple in four patients. Single perforations were treated by two-layered closure, multiple perforations by primary resection and anastomosis.

Fifty-five (52.4%) patients developed complications.

Fourteen (13.3%) patients died. There was a slight drop in mortality (8.8 %) in phase 2. Deaths were due to septicaemia in 8(57%) patients.

Conclusion: The pattern of presentation and outcome of management of typhoid intestinal perforation are similar to what is observed in other centres in our local environment. However the drop in mortality rate in the last 5 years of the study and the finding of strains of salmonella typhi resistant to chloramphenicol require further evaluation.

Key words: typhoid intestinal perforation, ciprofloxacin, chloramphenicol, operative management.

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INTRODUCTION

Salmonella typhi infection continues to be a significant problem world wide. According to a global estimate, there are approximately 10 million new cases of typhoid fever each year and a conservative estimate of 600,000 deaths¹. Intestinal perforation remains the most lethal of all complications². In developing nations, patients often present late with generalized peritonitis.

Previous reports record mortality in double digits ranging from 22%³ to 13.8%⁴. Persistent septicaemia and intestinal fistulae accounted for most deaths.^{2,5}

However mortalities ranging from 7%⁶ to 0%^{7,8} have been reported from some institutions where quinolones and third generation cephalosporin (ceftriaxone) were used as first line drugs with parenteral nutritional support.

The purpose of this study was to review the pattern of presentation and outcome of management of typhoid intestinal perforation in Sagamu, South-West Nigeria over the last fifteen years. Generic ciprofloxacin became available in our hospital as first line drug for peritonitis suspected to be due to typhoid perforation from the year 2000.

Patients and Methods

Complete records of 105 patients with typhoid intestinal perforation managed at Olabisi Onabanjo University Teaching Hospital, Sagamu, between January 1990 and December 2004 formed the basis of the study. The demographic data, clinical features, investigations, surgical operations performed and management outcome were obtained from case notes, theatre and ward registers. In this study the diagnosis of typhoid intestinal perforation was based on clinical features as well as operative findings of oval perforation on the antimesenteric border of the jejunum or/and ileum, as well as between the taenia coli in the colon.

In eight cases, identified from the theatre and ward registers, the case notes were missing. They were therefore excluded from the study.

Patients who did not have laparotomy were also excluded.

All the included patients had laparotomy under general anaesthesia. They had pre-operative anaesthetic assessment using the American Society of Anaesthetists (ASA) pre-operative grading.

They were studied in two groups. Group A comprised 71 cases managed in phase 1 between Jan 1990 and December 1999, who received chloramphenicol as first line drug in addition to metronidazole and gentamicin. Group B comprised 34 patients who were managed between January 2000 and December 2004 and received ciprofloxacin as first line drug in addition to metronidazole.

Results

Demographic data

Group A. There were 46 males and 25 females giving a male: female ratio of 1.8:1. Their ages ranged from 16 yrs to 63 yrs with a mean age of 27.2 yrs.

Group B. There were 23 males and 11 females giving a male to female ratio of 2.1:1. Their ages ranged from 15 yrs to 72 yrs with a mean age of 26.5 yrs.

Over 60% of cases occurred in the dry season.

Clinical features Fever, headache, abdominal pain and tachypnoea were common to all patients. Other clinical features were vomiting, abdominal distension, dehydration and haematochezia. Table I

Prior to arrival in our hospital, all the patients were on various combinations of antibiotics such as ampicillin, ampicillin-cloxacillin combination and chloramphenicol.

Twenty-seven (26%) patients had been hospitalized elsewhere during the current illness.

Investigations Widal test was done once and only in 11(10%) patients. The titres had a range of 1 in 40 to 1 in 160 dilution against the "O" antigen.

Blood culture was done in 34 (30%) patients and was positive in 5 (4%) patients. The organism was sensitive to ciprofloxacin in all the five cases and resistant to chloramphenicol in three.

All the patients had plain abdominal X-rays. Pneumoperitoneum was present in 39 (37%) patients.

Anesthetist's assessment

All the patients had a pre-operative anaesthetic assessment using the American Society of Anaesthetists (ASA) pre-operative grading. The distribution is as shown in Table II. Over 62% were ASA III & IV.

Operative findings

There were 112 perforations. One hundred and five (94%) perforations were in the ileum, 5 (4%) in the jejunum and two (2%) in the caecum/ascending colon. Perforations were single in one hundred and one patients and multiple in four patients. At laparotomy, single perforations were treated by two-layered closure (101 patients), multiple perforations by primary resection and anastomosis (3 patients) and a limited right hemicolectomy was performed in one patient who had massive haematochezia in addition to ileal perforations. Faecal peritonitis was present in 18% of cases. Copious lavage of the peritoneal cavity with warm normal saline was done in all cases.

Five patients had re-exploration for suspected intraperitoneal abscess. Scanty amount of pus was found in two of them. The five patients died.

Mortality

There were 14(13.3%) deaths, eleven patients died in Group A (15.5%) and three patients died in Group B (8.8%).

Eight of the patients died of uncontrolled sepsis between the 5th and 11th postoperative days. Five of these were re explored for suspected intraperitoneal abscess. Two patients died of multiple organ failure on the 3rd and 4th post-operative days, and four patients died from persistent enterocutaneous fistula 24th, 33rd, 37th and 56th postoperative days. All the deaths were in patient with ASA grades IV (7 deaths) and V (4 deaths).

Complications

Fifty-five (52.4%) patients developed complications. The complications are as shown in Table 3. The common complications were surgical wound infection, empyema thoracis, burst abdomen and enterocutaneous fistula.

Duration of hospital stay

Mean duration of hospital stay was 18 days in group A and 12 days in group B.

Cost of treatment.

In the 1990's the total cost of treatment of one patient ranged between ₦4000 and ₦5000 (75-100 US dollars) while from 2000 it increased to between ₦15000 and ₦45000 (100-300 US dollars).

Table I

Clinical features of the patients

| Parameter | Group A | | Group B | |
|----------------------|-------------------------|------|-----------------------|------|
| | No of patients N = (71) | % | No of patients n = 34 | % |
| Fever | 71 | 100 | 34 | 100 |
| Headache | 71 | 100 | 34 | 100 |
| Abdominal pain | 71 | 100 | 34 | 100 |
| Vomiting | 52 | 73.2 | 27 | 79.4 |
| Abdominal distension | 68 | 95.8 | 31 | 91.2 |
| Haematochezia | 15 | 21.1 | 6 | 17.6 |
| Tachypnoea | 71 | 100 | 34 | 100 |
| Pallor | 9 | 12.7 | 3 | 8.8 |
| Dehydration | 65 | 91.5 | 29 | 85.3 |

Table II

Anesthetists' assessment

| ASA | GROUP A | | GROUP B | |
|-------|---------|------|---------|------|
| | No | % | No | % |
| I | 6 | 8.5 | 3 | 8.8 |
| II | 14 | 19.7 | 6 | 17.7 |
| III | 22 | 31.0 | 15 | 44.1 |
| IV | 24 | 33.8 | 7 | 20.6 |
| V | 5 | 7 | 3 | 8.8 |
| Total | 71 | 100 | 34 | 100 |

Table III

Complications in the patients

| | Group A | | Group B | |
|---------------------------------|---------------|------|---------------|------|
| | No of patient | % | No of patient | % |
| Surgical site infection | 28 | 39.4 | 10 | 29.4 |
| Empyema thoracis | 26 | 36.6 | 5 | 14.7 |
| Burst abdomen | 3 | 4.2 | 1 | 2.9 |
| Enterocutaneous fistula | 7 | 10 | 2 | 5.9 |
| Adhesive intestinal obstruction | 9 | 12.6 | 3 | 8.8 |
| Incisional hernia | 5 | 7 | 3 | 8.8 |

Discussion

Typhoid intestinal perforation remains a scourge of emerging nations, with mortality remaining in double digits over the past quarter of a century.

The mean age of the patients was 27yrs with a male to female ratio of about 2:1. These are young people who go out to work to earn a living and are likely to eat outside their homes, thereby being exposed to food contaminated with salmonella typhi.² The age and sex distribution is comparable to reports by other authors.¹⁻⁵

In this study, though the disease occurred throughout the year, it peaked at the end of the dry season, when water is scarce and the concentration of organism per unit volume is expectedly high. The infective dose of salmonella typhi has been put at between 1×10^3 to 1×10^6 organisms¹.

Common clinical features were fever, abdominal pain, abdominal tenderness and tachypnoea. A high incidence of chest infection was found in this study and studies by previous authors^{1,2,5}.

The risk of multidrug resistant salmonella infection is high in our group of patients because all of them were on antibiotics (usually ampicillin or chloramphenicol) at presentation. The development of intestinal perforation while on these drugs would suggest either inadequate dosage or impotent drug. Chloramphenicol resistant

salmonella typhi was first discovered in 1950 but became a significant problem in 1972 with outbreaks in Mexico, India, Thailand and Vietnam.¹ In this study the organisms in three out of the five positive blood cultures were resistant to chloramphenicol. Prospective studies are needed in our environment, to evaluate the significance of this finding. Multi drug resistant salmonella typhi represents a significant obstacle to control of the disease.

Prolonged perforation-surgery interval is associated with poor prognosis. In this study the timing of perforation was not recorded, but over 26% of our patients were transferred from another hospital. The perforation-surgery interval is likely to be close to 72hrs in most cases and this may partly account for the high mortality and complication rates found in this study.

Surgical operations performed included mainly simple closure of single perforation and peritoneal lavage with warm normal saline. In one patient with massive haematochezia and multiple ileal perforations, a limited right hemicolectomy was done. Three other patients with multiple perforations had segmental resection and anastomosis. No patient in this series required ileostomy. Simple procedures that achieve effective closure of the perforation have been reported to be associated with better survival.^{4,5}

In this study Widal test was done in 10% of cases but the result neither influenced diagnosis nor management. Blood culture was positive in 4 % (5 patients) of cases. The organism was sensitive to ciprofloxacin in all the five cases and resistant to chloramphenicol in three. This low yield on culture may be related to the fact that all the patients were on antibiotic therapy prior to presentation. Bone marrow culture was not available to our patients. Bone marrow has an estimated concentration of 10 bacteria per ml marrow (ten times that in blood), giving a better yield on culture even in patients on antibiotics¹.

In this study, some differences were noted between Group A (that received chloramphenicol) and Group B (recipients of ciprofloxacin) in terms of mortality, morbidity and duration of hospital stay. Eleven (15.5%) deaths occurred in Group A while three (8.8%) patients died in group B.

This however did not reach statistical significance ($0.10 > p > 0.05$).

Possible reasons for these apparent differences may include improvement in anaesthesia, pre and postoperative care or the introduction of a more effective drug. This would require further evaluation.

Post operative sepsis is commonly reported as a cause of significant mortality and morbidity.^{2,3,4,5} Eight of them

died from uncontrolled septicaemia between the 5th and 11th day post operation. Five of these were re-explored between the 3rd and 5th day post operation for suspected intraperitoneal abscess in view of persistent pyrexia. Scanty amount of pus was found in two of them. This suggests that the persistent pyrexia after surgery was not due to an abscess but uncontrolled septicaemia. Deaths in these five patients were due to uncontrolled septicaemia and the stress of the 2nd exploration. Effective use of ultrasonography to exclude an intra-abdominal abscess would have made the 2nd exploration unnecessary. Finding of scanty pus on re-exploration in typhoid intestinal perforation was also reported by Saxe et al².

Chatterjee H et al⁶ reported a significant improvement in mortality rate from 17.7% to 7% when ciprofloxacin replaced chloramphenicol as drug of first choice. On the other hand mortality remained between 22% and 24% in over two decades at another centre where chloramphenicol remained the drug of choice.³ A mortality of 0% was reported in typhoid colonic perforation due to a combination of early surgical intervention, use of effective antibiotics (ciprofloxacin or ceftriaxone) and parenteral nutritional support.^{7,8}

In places where quinolone resistance is rare the fluoroquinolones are the current treatment of choice. They are rapidly effective even with short courses and cure rate exceeds 96%.^{1,9,10,11.}

The main concern had been the cost of the drug. In this study the cost of treatment increased five-fold when ciprofloxacin was used as first line drug. This high cost may be a barrier to effective treatment in poor patients.

The other concern is the potential for the emergence of resistance if ciprofloxacin is widely used. An epidemic of ciprofloxacin-resistant salmonella typhi was reported in 1998 in Tajikistan.^{10.}

In conclusion, the pattern of presentation and outcome of management of typhoid intestinal perforation found in this study are similar to what is observed in other centres in our local environment. However the drop in mortality rate in the last 5 years of the study and the finding of strains of salmonella typhi resistant to chloramphenicol require further evaluation.

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