

## RESEARCH ARTICLE

### A study on antimicrobial use in the management of duodenal perforation and its cost-effective analysis

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#### ABSTRACT

**Background:** Duodenal perforation is mostly seen in gastrointestinal perforation due to either disease or trauma, which forms nearly one-third of acute abdominal catastrophe. Although modern sophisticated gadgets are available in the diagnostic armamentarium, proper history elicitation, methodological physical examination, and sharp clinical observation play a major role in accurate diagnosis of acute abdominal conditions. In duodenal perforation, there is a sudden release of gastric contents into peritoneal cavity, which leads to a devastating sequence of events such as chemical and bacterial peritonitis, fluid and electrolyte imbalance, toxemia, septicemia, circulatory failure, and finally death. **Aims and Objectives:** The aim of this study was to evaluate the use of antibiotics in the management of duodenal perforation. This was a non-invasive prospective observational study. Seventy-nine patients with duodenal perforation undergoing elective and emergency surgery from the surgery wards were selected for the study on satisfying the inclusion criteria. **Materials and Methods:** The study method involves the selection of patients based on the inclusion and exclusion criteria, to record the prescribing pattern of antibiotics in the post-operative wards of surgery, to find the effectiveness of the antibiotics prescribed in relation to the number of hospital days, and to analyze the cost-effectiveness using statistical tool. This study was conducted from May 2018 to October 2018. **Results:** Data were collected from 79 patients. It was observed that the incidence of perforation was higher in males than females (7:1) in the age group of 31–40 years (28%) and mean Li-standard deviation is  $11.28 \pm 7.63$ . Pip/taz was most commonly prescribed (29 out of 79 cases). In terms of cost, on an average, pip/taz was found to involve highest amount. When the mean deviation of hospital stay was taken into account, piperacillin was at lower margin when compared with others ( $10.23 \pm 2.59$ ). The statistical analysis of hospital stay shows a significant difference between all three drugs Cefotaxime, ceftriaxone and cefixime ( $P \leq 0.017$ ,  $P \leq 0.0139$ , and  $P \leq 0.085$ , respectively). Thus, 26 patients out of 29 patients were successfully cured with pip/taz with a mean hospital stay of ( $10.23 \pm 2.59$ ) days and three patients were discharged against medical advice. We considered cost effective involved in the treatment with drugs as health-care cost in rupees and number of days taken to cure as clinical outcome. From this, we calculated average cost-effective ratio and the highest being pip/taz (109.29) when compared to cefotaxime (97.1). **Conclusions:** From our study, we conclude that piperacillin/tazobactam should be the choice of antimicrobials for this duodenal perforation.

**KEY WORDS:** Duodenal Perforation; Antimicrobial; Cost-Effective Analysis; Piperacillin/Tazobactam

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#### INTRODUCTION

Duodenal perforation is mostly seen in gastrointestinal perforation due to either disease or trauma,<sup>[1,2]</sup> which forms nearly one-third of acute abdominal catastrophe. Although modern sophisticated gadgets are available in the diagnostic armamentarium, proper history elicitation, methodological

National Journal of Physiology, Pharmacy and Pharmacology Online 2020. © 2020 Merughu Padma Latha, et al. This is an Open Access article distributed under the terms of the Creative Commons Attribution 4.0 International License (<http://creativecommons.org/licenses/by/4.0/>), allowing third parties to copy and redistribute the material in any medium or format and to remix, transform, and build upon the material for any purpose, even commercially, provided the original work is properly cited and states its license.

physical examination, and sharp clinical observation play a major role in accurate diagnosis of acute abdominal conditions. In duodenal perforation, there is a sudden release of gastric contents into peritoneal cavity, which leads to a devastating sequence of events such as chemical and bacterial peritonitis, fluid and electrolyte imbalance, toxemia, septicemia, circulatory failure, and finally death. The duodenum extends from pylorus to duodenojejunal flexure, lies above umbilicus opposite to vertebrae L1, L2, and L3 about 25 cm long C shaped, devoid of dorsal mesentery, divided into four parts: The first part of superior – 5 cm, the second part of descending – 7.5 cm, the third part of horizontal – 10 cm, and the fourth part of ascending – 2.5 cm.<sup>[3]</sup> Perforation due to any cause, there is a sudden spillage of intraluminal contents into the peritoneal cavity. This stage of perforation is sometimes sealed off by anatomical and physiological and pathological factors.

### Anatomical Factor

Excluding the subphrenic spaces, the greater sac of the peritoneum is divided into pelvis and peritoneal cavity proper. The latter is subdivided into supracolic and infracolic compartment by transverse colon and transverse mesocolon, which control the spread of infection from one to another. When supracolic compartment overflows, it crosses over the colon into infracolic compartment or by way to right paracolic gutter into the right iliac fossa and to the pelvis. The omentum which is otherwise called abdominal policeman covers the infected area and localizes the infection.

### Physiological and Pathological Factor

Clinical course is largely governed by the manner in which adhesion forms around the affected organ. In some cases, the perforation will be sealed by omentum, under surface of the liver and by a jejunal loop, inflamed peritoneum. Perforation of an ulcer is a rapid process, due to sudden sloughing of the unsupported portion on the floor of the ulcer, due to the impairment of blood supply by the endarteritis, the flow and action of the gastric contents, which reduces mucosal barrier. The margins of the ragged ulcer floor are digested resulting in a clear punched out hole. Immediately, after perforation gas and gastric juice escape into the peritoneal cavity following which chemical peritonitis develops causing sequestration of fluid in the third space, paralytic ileus ensues and adds on to hypovolemic shock. This sequence of events results in abdominal pain, distension, and impaired abdominal movements with respiratory complications. Types of perforation include subacute perforation, acute perforation, and chronic perforation.<sup>[4-6]</sup> Without surgical intervention, death is the risk of a fatal outcome which is increased with delays in diagnosis.<sup>[7,8]</sup>

## MATERIALS AND METHODS

### Place of Study

This study was conducted at the Department of Pediatrics, Rajah Muthiah Medical College and Hospital, Tamil Nadu, India, a 1610-bedded multispecialty tertiary care teaching hospital.

### Type of Study

This was a non-invasive prospective observational study.

### Sample Collection

Sample size: Seventy-nine patients.

### Sampling Methods

This was a consecutive sampling method.

### Inclusion Criteria

The following criteria were included in the study:

- Patients aged between 18 years and 80 years
- Patients with duodenal perforation undergoing elective and emergency surgery from the surgery wards
- Patients who were willing to cooperate.

### Exclusion Criteria

The following criteria were excluded from the study:

- Patients with significant hepatic and renal failure
- Pregnant women
- Patients who were not willing to cooperate
- Patients with gastric and intestinal perforation.

### Statistical Analysis

Data were presented in the form of statistical tables and charts. SPSS software version 20 was used for statistical analysis.

### Ethical Approval

Approval was taken from the Institutional Ethics Committee before commencement of the study.

## RESULTS

Prescribing pattern of antimicrobials is described in Tables 1 and 2. Cost analysis of antimicrobials is described in Tables 3 and 4. The mean deviation of hospital stay on an average was found to be less in the patients treated with pip/taz ( $10.23 \pm 2.59$ ) [Table 5]. Table 6 represents statistical significance of drugs in duration of stay in hospital. The

**Table 1: Prescribing pattern of antimicrobials**

Drug	Patients (%)
Pip/taz	29 (36.70)
Cefotaxime	22 (27.84)
Ceftriaxone	16 (20.25)
Cefixime	12 (15.18)

**Table 2: Prescribing pattern of the antimicrobials used for duodenal perforation**

Age	Pip/taz	Cefotaxime	Ceftriaxone	Cefixime
17–20	5	2	1	1
21–30	2	4	4	3
31–40	9	5	6	2
41–50	9	8	2	1
51–60	1	2	2	4
61–70	2	1	1	1
71–80	1	0	0	0

**Table 3: Mean cost of drugs**

Drug	Cost in Rs.
Pip/taz	2839
Cefotaxime	1940
Ceftriaxone	2200
Cefixime	1691

**Table 4: Cost assessment**

Drugs compared	P-value	Result
Pip/taz and cefotaxime	≤0.001	No significant difference
Pip/taz and ceftriaxone	≤0.001	No significant difference
Pip/taz and cefixime	≤0.019	Significant difference

**Table 5: Duration of hospitalization**

Drug	Mean duration of hospital stay (days)
Pip/taz	10.23±2.59
Cefotaxime	13.6±5.47
Ceftriaxone	11.75±2.51
Cefixime	12.9±3.84

significant difference was found with pip/taz and cefotaxime; pip/taz and ceftriaxone; and pip/taz and cefixime. Out of 79 patients admitted, 6 patients were discharged against medical advice and 26 were cured from pip/taz [Table 7]. Patient versus cost versus days analysis is presented in Table 8.

## DISCUSSION

Data were collected from 79 patients. It was observed that the incidence of perforation was higher in males than

**Table 6: Duration of hospitalization: Statistical significance**

Drugs compared	P-value	Result
Pip/taz and cefotaxime	≤0.017	Significant difference
Pip/taz and ceftriaxone	≤0.0139	Significant difference
Pip/taz and cefixime	≤0.0851	Significant difference

**Table 7: Tabulation of number of patients recovered**

Result	Cured (%)	AMA (%)
Pip/taz	26 (32.9)	3 (3.1)
Cefotaxime	20 (25.3)	2 (2.5)
Ceftriaxone	16 (20.2)	0 (0)
Cefixime	11 (13.9)	1 (1.2)

**Table 8: Patient versus cost versus days analysis**

Drug	Patient %	Cost %	Days %
Pip/taz	36	32.7	21.1
Cefotaxime	27	22.5	28
Ceftriaxone	20	25.3	24.2
Cefixime	15	19.7	26.6

females (7:1) in the age group of 31–40 years (28%) and mean Li-standard deviation is  $11.28 \pm 7.63$ . The seasonal incidence of the disease was found to be much high in the month of January about 9 to 11%. The patients who had undergone surgery were subjected to heavy manual work as their occupation in the past with the staple diet being rice. As the part of the management of duodenal perforation, antibiotics play a major role. Our study revealed that pip/taz was prescribed in 29 patients out of 79 (36.07%). The maximum number of patients belonged to the age group of 31–40 and 41–50 years with 9 patients in each group. In terms of cost, on an average, pip/taz was found to involve highest amount (in terms of money) Rs. 2839. We used unpaired “t”-test as suitable statically tool for the assessment of cost of antibiotics prescribed. It was found that pip/taz was compared to cefotaxime and ceftriaxone. Then, it was no significant difference,  $P \leq 0.001$  while cefixime had a significant difference,  $P \leq 0.019$ . When the mean deviation of hospital stay was taken into account, piperacillin was at lower margin when compared with others ( $10.23 \pm 2.59$ ). The statistical analysis of hospital stay shows a significant difference between all three drugs Cefotaxime, ceftriaxone and cefixime ( $P \leq 0.017$ ,  $P \leq 0.0139$ , and  $P \leq 0.085$ , respectively). Thus, 26 patients out of 29 patients were successfully cured with pip / taz with a mean hospital stay of ( $10,23 \pm 2,59$ ) days and three patients were discharged against medical advice. We considered cost effective involved in the treatment with drugs as health care cost in rupees and number of days taken to cure as clinical outcome. From this, we calculated average cost-effective ratio and the highest being pip/taz (109.29) when compared to cefotaxime (97.1).

The study conducted by Punamiya *et al.*<sup>[9]</sup> has got piperacillin-tazobactam (51%) and cefotaxime (49%) as highly sensitive drugs. In a study by Gangalaxmi *et al.*,<sup>[10]</sup> 28.5% were cured by pip/taz and 26.4% of patients were cured by cefotaxime, respectively.

Since this is a retrospective review and vulnerable to poor record-keeping as noted in the incomplete data in 8% of the total patients managed, as they were discharged against medical advice.

According to our study results, antimicrobial option of therapy for duodenal perforation by piperacillin/tazobactam (pip/taz) is more effective compared to others.

## CONCLUSIONS

From this study, we finally report that antimicrobial of choice of the treatment of duodenal perforation being pip/taz with the best treatment alternative cefotaxime. Cost-effective analysis is a cost optimization process but not a cost reduction process. As the percentage of patients cured within fewer days hospitalization is 21.1%. From our study, piperacillin/tazobactam should be the choice of antimicrobials for this duodenal perforation.

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