EFFICACY OF CIPROFLOXACIN AND CEFOTAXIME IN PATIENTS WITH CIRRHOSIS LIVER PRESENTING WITH SPONTANEOUS BACTERIAL PERITONITIS TO A TERTIARY CARE HOSPITAL

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ABSTRACT

Objectives: To compare the efficacy of Ciprofloxacin and Cefotaxime in Cirrhosis Liver patients with spontaneous bacterial peritonitis (SBP)

Materials and Methods: This prospective, comparative, single center study was conducted in the Department of Medicine, Khyber Teaching Hospital Peshawar from 1st October 2017 to 31st December 2018. A total of 300 admitted patients having Cirrhosis Liver with SBP were included in this study. The patients were randomized into Group A and Group B. Group A was treated with intravenous Ciprofloxacin and Group B was treated with intravenous Cefotaxime given twice daily for a period of 5 days. Diagnostic peritoneal paracentesis was done before the start of the treatment and repeated after 5 days therapy. Patients who were either non cirrhotic or had secondary bacterial peritonitis were excluded from the study.

Results: A total of 300 cirrhosis liver patients with SBP were studied in two equal randomized groups. Out of these 168 were male and 132 were female. The mean age of patients in study was 51.14±11.9 years. The age ranged between 15-75 years. In Group A, 82% responded to ciprofloxacin and in group B, 86% responded to cefotaxime.

Conclusion: Both intravenous ciprofloxacin and cefotaxime are effective in treating spontaneous bacterial peritonitis in patients with cirrhosis liver.

Key Words: Ciprofloxacin, Cefotaxime, Spontaneous bacterial peritonitis, Efficacy

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INTRODUCTION

Conn and Fessel defined spontaneous bacterial peritonitis (SBP) in 1971 as a syndrome manifested as infected ascitic fluid in patients with decompensated hepatic cirrhosis [1]. SBP is an infection of previously sterile ascitic fluid and the source of infection is not clearly identifiable but the infecting organisms usually belong to normal intestinal flora [2, 3]. SBP can occur in both adults and children and is a well-recognized complication of cirrhosis of liver [4].

The mechanism for bacterial inoculation of ascites has been a subject of great debate since Harold Conn [1] who first described it, but evidence suggests that bacterial infection of ascitic fluid from intestine or hollow organ lumen occurs through transmural migration (bacterial translocation) and/or hematogenous route in combination with an impaired immune system[1]. The theory of bacterial translocation is supported by frequent isolation of enterotoxin from ascitic fluid [5-8].

Bacterial infection of ascitic fluid is a common complication of decompensated cirrhosis. Its incidence is about 10-27% at the time of admission or after hospitalization [9-11]. Gram negative aerobic organisms are responsible in 75% of SBP cases, of which Klebsiella pneumonia organism accounts for 50% of these. Gram positive aerobic organisms are also responsible in minority, of which Streptococcus pneumoniae or Streptococcus Viridans group are the commonest [12, 13]. As ascitic fluid is a high oxygen tension media so anaerobic bacteria are very rarely isolated in SBP. In most of cases only one infecting organism is isolated (92%) though polymicrobial isolation has also

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been reported [14].

To establish the diagnosis of SBP ascitic fluid analysis obtained through paracentesis of peritoneal cavity is mandatory. In the microbial analysis total neutrophil count is the most valuable test to make the presumptive diagnosis of SBP. Usually a total neutrophil count in excess of 250 cells/mm^3 points towards a diagnosis of SBP and is considered valid evidence for the start of antibiotic treatment in symptomatic patients [15].

As untreated, SBP can be fatal, starting empiric antibiotic therapy well in time improves the overall survival rates in patients. But despite timely treatment the mortality rate is about 10-30% and the survivors have a high chance of reinfection [16, 17].

Broad spectrum intravenous antibiotics having good coverage against gram negative aerobic organisms should be used as soon as SBP is diagnosed. SBP is usually treated with third generation cephalosporin but cefotaxime is the best choice which is given for 5 days. These drugs are highly efficacious and have no nephrotoxity and resolution is obtained in 80-90% of cases [18, 19].

Quinolones are used as alternative drugs in place of cephalosporins. The two mostly used quinolones are ciprofloxacin and ofloxacin. The pharmaceutical advantage for the prescribing physician is that both intravenous and oral preparations are available for both the categories of drugs. Studies have clearly shown that both quinolones and cefotaxime have comparable results and have no difference in resolution rate [20, 21].

The current study was aimed at comparing intravenous cefotaxime with intravenous ciprofloxacin in terms of resolution of infection and overall efficacy of treatment. This study would also help us understand the emergence of resistance against these two groups of antibiotics.

MATERIAL AND METHODS

This randomized non-blinded controlled trial was conducted in department of medicine, Khyber teaching hospital Peshawar (KTH) from 1st October 2017 to 31st December 2018. An Institutional ethical approval was granted for this research work through IREB of the institute. A total of 300 cases of decompensated cirrhosis liver with ascites who were admitted in the medical units in KTH were included in this study. Study population was 15 to 65 years old patients. Patients who had features of secondary peritonitis, those with ascites due to cardiac failure, renal failure or malnutrition, those currently using corticosteroids and a recent history of use of intravenous antibiotics in the last 7 days were excluded from the study, Additionally patients with normal ascitic fluid cytology or serum creatinine levels greater than 2 mg% or those patients who did not want to participate in trial were also excluded from the study.

A thorough history was taken and clinical examination of all patients was performed. All relevant laboratory investigations were performed in our local hospital laboratory under supervision of consultant pathologist. The diagnosis of SBP was established by ascitic fluid analysis before start of the study protocol. A total neutrophil count more than 250 cells/mm^3 in the setting of a transudative ascites with protein concentration less the 2.5 grams/dL was considered as suggestive of SBP. Moreover, Ascitic fluid culture was done in those cases who had not received antibiotics in the last 3 days (before hospital admission). However, culture was not considered essential for the diagnosis. All patients were randoy divided into two groups by lottery method, group A and group B. Each group comprised 150 participants. Group A was assigned to receive 2 gm intravenous cefotaxime twice a day and group B was assigned to receive 200 mg intravenous ciprofloxacin twice a day. Both groups received antibiotic therapy for a total period of 5 days. After 5 days of therapy, ascitic fluid paracentesis was re-performed and a neutrophil count less than 250/mm^3 along with absence of fever and abdominal pain was considered as a desirable outcomes.

All informations and demographic data like name, age, sex, address were recorded on pre designed proforma and analyzed using SPSS version 20. P value of < 0.05 was considered significant. The results were presented in form of tables or graphs.

RESULTS

Total 300 patients were enrolled in the study, out of which 168 were male and 132 were female. The mean age of patients was 51.14±11.9 years while age ranged between 15 and 75 years (Table 1).

The most common clinical presentations of patients were abdominal pain (77.7%) followed by abdom-

Table 1: Age of patients (Years)

Mean	51.14
Std. Deviation	11.95
Minimum	15.00
Maximum	75.00

Table 2: Response to treatment

Ciprofloxacin (Group A)		Frequency	Percent	p-Value
Response	Yes	123	82.0	0.9
	No	27	18.0	
	Total	150	100.0	
Cefotaxime (Group B)				
Response	Yes	129	86.0	
	No	21	14.0	
	Total	150	100.0	

Table 3: Neutrophil count in Ascitic fluid

Neutrophil Count (cells/ mm^3)	Frequency	Percent
250-350	49	16.3
351-450	56	18.7
451-550	65	21.7
551-650	56	18.7
651-750	37	12.3
>751	37	12.3
Total	300	100.0

Table 4: Age wise distribution of SBP

Age Range (Years)	Frequency	Percent
15-25	15	5.0
26-35	56	18.7
36-45	74	24.7
46-55	83	27.7
56-65	47	15.7
66-75	25	8.3
Total	300	100.0

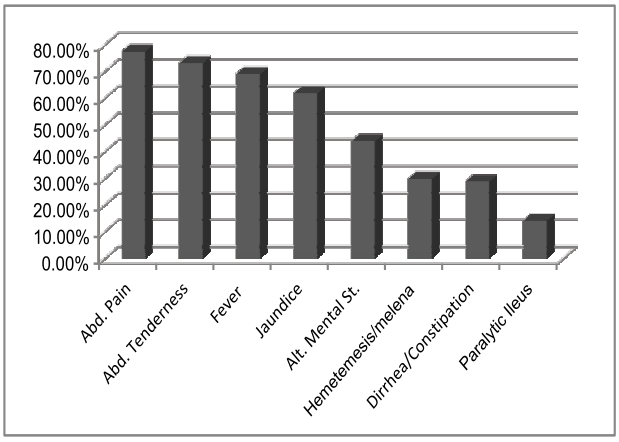

Fig 1: Clinical Presentation of SBP

inal tenderness (73.3%) and fever (69.3%) (Fig. 1).

Out of 150 patients with SBP in group A, 123 (82%) patients responded to 5 days' infusion of Ciprofloxacin compared with 129 (86%) patients who received 5 days infusion of Cefotaxime (P. value: 0.9).

Table 3 shows the results of ascitic fluid paracentesis. The results were further analyzed age wise and the age group found to be affected the most was 46-55 years (27.7%) followed by 36-45 years (24.7%) (Table 4).

DISCUSSION

Spontaneous bacterial peritonitis (SBP) is an acute bacterial infection of ascitic fluid in the absence of any identifiable secondary bacterial infectious cause. Patients with decompensated cirrhosis are at higher risk of developing spontaneous bacterial peritonitis. It is a serious and a common complication of End Stage Liver Disease (ESLD). Clinically among patients who present with spontaneous bacterial peritonitis, 70% of them are in Child-Pugh class C [22, 23]. Spontaneous bacterial peritonitis can occur in both children and adults. It can affect patients with cirrhosis due to any pathological cause and can occur as complication of Budd-Chiari syndrome.

We registered total of 300 patients in this study, dividing them into two equal groups randomly. The mean age of patients was 51 years in our study. Taskiran B reported mean age of 51 in a study comparing responses of Cefotaxime with Ofloxacin in SBP while Manohar TP reported mean age of 42 years which is less than our study [22- 24]. In a local study conducted by Imran M, the mean age was 52 years which correlates with our study [25]. These results from above and many other sources demonstrate that SBP mostly develops in age group between 40 to 50 years denoting the commonest age of decompensation in most patients with Cirrhosis Liver.

Scores of local and international studies have deliberated on the prevalence of SBP in cirrhotic patients and response it shows to the different treatment regimens. This study compared the efficacy of two well-known drugs, Ciprofloxacin (Quinolone) and Cefotaxime (3rd Generation Cephalosporin). The aim was to know whether the efficacy of both drugs is the same or any different as in recent past a decline was noted due to the emergence of multiple drug resistance. In this study we compared the efficacy of both the given drugs in diagnosed cases of SBP and found that both the drugs were quite effective i.e. Ciprofloxacin vs. Cefotaxime (82% vs. 86% with p-Value 0.09). Angeloni S also compared the efficacy of ciprofloxacin with cefotaxime however, his findings were that ciprofloxacin was more effective than cefotaxime in infection resolution (80% vs. 41%) [26]. In another study, oral ciprofloxacin was proved to be slightly more effective than cefotaxime (80% vs 76%) [27]. Terg R and Tuncer I in their studies reported infection resolution rate of 78.4% and 80% with ciprofloxacin and cefotaxime respectively [21-27]. These studies nearly correlate with our study. In a local study conducted by Ahmad M, quite high percentage of resistance was reported with sensitivity of 67% vs. 60% to ciprofloxacin and cefotaxime respectively [28]. A recent study conducted abroad by Yin HJ et al showed efficacy of 69% vs 76% to cefotaxime and ciprofloxacin respectively [29]. The results of this study are contradictory to our study. In a study conducted by Felisart J concluded that Cefotaxime was 85% effective in treatment of SBP [30]. A similar study was conducted on efficacy of cefotaxime by Runyon B and it revealed that it cured 91% of SBP patients [18]. A recent local study conducted by Sarwar S reported 86% efficacy to Cefotaxime which correlate with our study [31]. All these results reveal that both ciprofloxacin and cefotaxime are still effective in the treatment of SBP and there is no significant difference in the efficacy of these two medications.

Regarding the clinical presentation of patients included in study, 77.7% had abdominal pain, 73.3% had abdominal tenderness, 69.3% had fever, 62% had jaundice, 44% had altered mental status, 30% had hematemesis and melena, 29% had either diarrhea or constipation and 14.3% had paralytic ileus. Rashid A reported abdominal pain and tenderness in 78% of his population which is coinciding with our findings [32]. Different percentages of clinical signs and symptoms have been reported in other studies [22, 32- 34]. One study reported that 30% of patients with SBP were completely asymptomatic [33]. Another study conducted locally showed asymptomatic SBP in 7% of his studied population[32].

Regarding age wise distribution, 27.7% of patients were in age range of 46-55, 24.7% were in age range of 36-45 and 18.7% were in age range of 26-35. Nearly the same age wise distribution of patient has been reported by Ahmad M and Aziz A in their studies [28, 35,36].

Regarding the neutrophil count in ascitic fluid, 21.7% patients had 451-550/mm^3 and 18.7% had 351-450/mm^3 and 551-650/mm^3. Only 12% had neutrophil count more than 750. Aziz A has reported mean neutrophil count of 283± 305/mm^3 while a local study reported quite high mean neutrophil count (1760/mm^3) [35,37].

Both the ciprofloxacin and cefotaxime need more clinical applications in the setting of SBP and can serve as a lifesaving tool aimed at improving the outcome of this serious disease especially in our set up where meager health facilities and resources are available.

Being a single centered study with limited number of patients are the pertinent limitations of this study. A large cohort randomized multicenter clinical trial is the need of time for generalization and validation of these outcomes.

CONCLUSION

Both ciprofloxacin and cefotaxime are still very effective in resolution of infection in spontaneous bacterial peritonitis and there is no significant difference in the efficacy of these two drugs. Both are quite cost effective as compared to drugs like Imipenem or Tazobactum.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Khan Z:	Concept and critical review.
Rashid A:	Acquisition and proof reading.
Haider I:	Analysis and interpretation of data.
Suleman S:	Data collection and final approval.
Badshah A:	Critical Rewiew.
Khan I: :	Manuscript Writting.
Khan WM:	Final drafting, manuscript evaluation.
Din JU:	Overall supervision, manuscript evaluation.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.