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Original Research Article

COMPARING THE EFFICACY OF INTRAVENOUS CIPROFLOXACIN AND CEFTAZIDIME FOR TREATING SPONTANEOUS BACTERIAL PERITONITIS IN LIVER CIRRHOSIS PATIENTS

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Abstract: *The aim of current analysis was to compare the efficacy of intravenous ciprofloxacin and ceftazidime for treating spontaneous bacterial peritonitis (SBP) in patients with liver cirrhosis. A retrospective study was conducted in the Medicine Department of SIMS, Lahore, from September 2021-September 2022. The study selected 110 cirrhosis patients with SBP were included in the study and were divided into two groups, A and B. Group A (n=55) was administered ciprofloxacin intravenously, and group B (n=55) was administered ceftazidime intravenously. The patients diagnosed with type 1 hepatorenal syndrome were treated with albumin and terlipressin daily. The clinical signs and causes of infection did not vary between both groups. The infection was resolved in 50 patients (90.9%) ceftazidime patients and in 51 patients (93%) ciprofloxacin patients. Out of 17 patients who developed, 10 patients (58.8%) completely recovered after terlipressin and albumin treatment, 1 (5.8%) showed partial response, and 6 (35.3%) did not respond. Switch therapy with ciprofloxacin and ceftazidime is equally effective in treating spontaneous bacterial peritonitis in cirrhotic patients with ascites*.

Keywords: Spontaneous bacterial peritonitis, switch therapy, liver cirrhosis, ascites

Introduction

Spontaneous bacterial peritonitis is a common condition that develops in 10-30% of patients diagnosed with cirrhosis with ascites (Marciano et al., 2019). The recommended antibiotic treatment for spontaneous bacterial peritonitis patients is IV- 3rd generation cephalosporin (Bacha et al., 2022). Research has shown that administering antibiotics intravenously and then oral switch therapy shows positive results (Khan et al., 2022). Terg et al. reported the excellent effectiveness of ciprofloxacin switch therapy for the treatment of mild and severe spontaneous bacterial peritonitis(Terg et al., 2000). Similarly, Navasa et al. also showed that when ofloxacin was orally administered in patients with uncomplicated spontaneous bacterial peritonitis, it showed similar results to the administration of cefotaxime intravenously (Navasa et al., 1996). In another study, oral administration of ciprofloxacin was proved to be similarly effective for spontaneous bacterial peritonitis as cefotaxime and ceftriaxone (Khan et al., 2021). However, no study has yet been conducted in Pakistan to compare the efficacy of ciprofloxacin switch therapy and 3rd generation cephalosporin. The advantages to switching therapy including reduced hospital stay, are only a hypothesis up till now.

Type 1 hepatorenal syndrome occurs in 1/3rd of the patients diagnosed with cirrhosis with ascites and spontaneous bacterial peritonitis. Hence, SBP is a major risk factor for type 1 HRS caused by arterial blood infection. Administration of albumin intravenously with antibiotics can prevent this syndrome. Studies have shown excellent results of vasoconstrictors like midodrine, ornipressin, and terlipressin when administered with IV albumin (Gonzalez and Velez, 2022). But the effect of this treatment on HRS caused by spontaneous bacterial peritonitis is still unknown. This study aims to compare the efficacy of intravenous switch therapy of ciprofloxacin and ceftazidime for treating SBP and test the effectiveness of terlipressin and albumin for the treatment of SPB-induced HRS.

Methodology

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A retrospective study was conducted in the Medicine Department of SIMS, Lahore, from September 2021-September 2022. We selected 110 cirrhosis patients with spontaneous bacterial peritonitis who were included in the study and were divided into groups, A and B, with 55 patients each. The patients who had undergone an antibiotic course within 30 days before the study, were > 18 years and <75 years, were allergic to quinolones or β-lactam antibiotics, were diagnosed with any bacterial or fungal infection or organic nephropathy, or had any evidence of GI bleeding, cardiac failure, shock, dehydration, extrahepatic neoplasia or hepatocellular carcinoma were excluded from the study. All the patients gave informed consent to participate in the research. The ethical board of the hospital approved the study.

All the patients were physically examined, and routine tests, chest and abdominal radiography, and abdominal ultrasonography were performed before the procedure. Ascitic fluid (60 ml) and blood (20 ml) was collected for culture along with urine culture and fresh urine sediment. Ascitic fluid PMN cell count and culture were performed on the 2nd day and 7th day after treatment initiation. 10 ml of ascetic fluid was injected into the two blood culture bottles. These tests were performed as outpatients those who did not complete antibiotic treatment in the out-patients department. IV ceftazidime was administered after every 24 hours with respect to the respective creatinine levels: 2g twice a day (less than 1.5 mg/dL), 1g twice a day (1.5-2.5 mg/dL), 1g (more than 2.5 mg/dL). Intravenous ciprofloxacin was administered after every 24 hours at 200 mg bd for 2.5mg/dL serum creatinine and 200 mg for creatinine more than 2.5 mg/dL. An oral dose was administered after the intravenous dose if the patients did not show any clinical signs of infection and the PMN count had reduced to more than 50% of the initial level in the blood and ascitic fluid. Oral ciprofloxacin was administered at 500 mg bd for 2.5mg/dL creatinine and 250mgbd for creatinine more than 2.5 mg/dL. Both antibiotics were administered for 8 days, and the patients were reported free of infection when they showed no clinical signs, white blood cell count was average, PMN count was less than 250/mm^3 in the ascitic fluid, and ascitic fluid cultures came out negative. For the patients who were not treated with antibiotic treatment, their treatment was altered accordingly.

The patients who showed a progressive decline in renal function even after the infection was resolved had a creatinine level of 2.5 mg/dL with no effect of discontinuation of diuretics and volume expansion (1.5 liters isotonic saline), had less than 0.5g per day proteinuria and had a routine kidney ultrasound was diagnosed with Type 1 Hepatorenal syndrome. A central venous line, a urinary bladder catheter, and a peripheral intravenous catheter were inserted in these patients. Terlipressin was continuously administered intravenously at 2mg per day. The dose was increased by 2 mg after every 2 days if serum creatinine levels did not improve. Albumin was also administered at 20-40g per day to maintain central nervous pressure. This procedure was continued until HRS was reversed or for 15 days maximum. If the serum creatinine was less than 1.5 mg/dL after the treatment, it was a complete response; if it was more significant than 1.5 mg/dL, it was regarded as a partial response. No diuretics were administered during this treatment; they were given after the complete or partial response. A 3-month follow-up was done in all patients or until liver transplantation or death.

All the data were analyzed by SPSS version 22 and were presented as mean± standard deviation. Chi-squared test was performed to compare results in both groups. Categorical data were evaluated using Fisher's exact test, and t-test evaluated the continuous data. A univariate analysis was performed to identify factors influencing the follow-up survival in HRS patients. A p-value> 0.05 was significant.

Results

Cirrhosis was diagnosed in patients by performing a liver biopsy, ultrasonography, or by clinical data. Table I shows the data on antibiotic treatment in both groups. The clinical signs and causes of infection did not vary between both groups. The infection was resolved in 50 patients (90.9%) in group A and 51 patients (93%) in group B. The failure of infection resolution was due to the recurrence of infection, adverse effects, and superinfections.

The clinical outcome and complications after antibiotic treatment are shown in Table II. Out of 17 patients who developed, 10 patients (58.8%) completely recovered after terlipressin and albumin

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treatment, 1 (5.8%) showed partial response, and 6 (35.3%) did not respond to the treatment. Three types 1 hepatorenal syndrome patients died during the hospital stays. The PMN count in serum creatinine and blood ($p<0.001$), serum urea and total serum bilirubin ($p<0.0025$) and creatinine clearance ($p<0.01$) at admission was significantly related to in-hospital survival.

Table I: Comparative outcomes of antibiotic treatments

	Ceftazidime (n=55)	Ciprofloxacin (n=55)
Age	58 ± 0.9	59 ± 0.9
Sex	32/23	31/24
Cause of cirrhosis		
Virus related	44 (80%)	52 (94.5%)
Other causes	11 (20%)	3 (5.5%)
Clinical signs of SBP		
Fever	36 (65.4%)	35 (63.6%)
Abdominal pain	34 (61.8%)	33 (60%)
Ileus	6 (10.9%)	8 (14.5%)
Hepatic encephalopathy	21 (38.1%)	24 (43.6%)
Renal failure	25 (45.4%)	26 (47.3%)
Community-acquired	34 (61.8%)	37 (67.3%)
Cause of SBP		
Positive culture	30 (54.5%)	30 (54.5%)
Gram negative bacilli	28 (50.9%)	28 (50.9%)
Escherichia coli	21	24
Acinetobacter freundii	2	3
Pseudomonas aeruginosa	1	1
Gram negative cocci	1	1
In vitro susceptibility to the assigned antibiotic	29/30 (96.7%)	31/33 (93.9%)
Others	1	1
Laboratory features		
Polymorphonuclear leucocytes in peripheral blood (cells/mm3)	7299 ± 619	7698 ± 609
Polymorphonuclear leucocytes in ascitic fluid (cells/mm3)	1098 ± 137	949 ± 63
Hematocrit (%)	32 ± 0.4	33 ± 0.3
Bilirubin (mg/dL)	3.9 ± .2	4.2 ± .2
Albumin (g/dL)	1.2 ± 0.3	1.5 ± 0.2
Prothrombin activity (%)	45 ± 1.7	41 ± 1.2
Serum urea (mg/dL)	52 ± 3.8	51 ± 4.1
Serum creatinine (mg/dL)	0.9 ± .1	0.9 ± .1
Other features		
Child-Pugh classification (B/C)	10/43	8/50
Child-Pugh score	10 ± .1	10 ±.1
Model for end-stage liver disease score	18 ± .7	16 ±.7
Heart rate	79 ± 0.8	76 ± 0.7
Mean arterial pressure	88 ± 0.7	90 ± 0.8

* p=0.025

Table: II Outcome of antibiotic treatment

	Ceftazidime	Ciprofloxacin
Patients with complications	19 (34.5%)	13 (23.6%)
Renal failure	15 (27.3%)	12 (21.8%)
The onset of renal failure	6 (10.9%)	2 (3.6%)
Further impairment of pre-existing renal failure	8 (15.5%)	9 (16.3%)
Type 1 HRS	10 (18.1%)	7 (12.7%)
The peak value of serum urea (mg/dL)	77 ± 7.8	64 ± 4.5
The peak value of serum creatinine (mg/dL)	1.5 ± .1	1.3 ± .1
Peak reduction of creatinine clearance (mL/min)	43 ± 1.1	45 ± 1.2
Peak reduction of 24-h urine volume (mL)	968 ± 63	1029 ± 59
Peak reduction of 24-h urinary Na excretion (mmol)	41 ± 2.1	41 ± 2.8
Worsening of hepatic failure, n (%)	10 (18.2%)	4 (7.2%)
With hepatic encephalopathy, n (%)	8 (14.5%)	4 (7.2%)
Gastrointestinal bleeding, n (%)	2 (3.6%)	2 (3.6%)

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Deaths during hospitalization, n (%)	6 (10.9%)	4 (7.2%)
In-hospitalization mortality		
Type 1 hepatorenal syndrome	2	1
Multiple organ failure	1	1
End-stage liver disease	1	1
GI bleeding	1	1
Follow-up deaths, n (%)	11 (20%)	7 (12.7%)
Follow up deaths		
End-stage liver disease	2	1
GI bleeding	1	1
Type 1 hepatorenal syndrome	1	0
Pneumonia	0	1

Discussion

Navasa et al. reported that oral quinolinones and ofloxacin efficacy was the the same as 3rd generation cephalosporin for treating uncomplicated spontaneous bacterial peritonitis in patients with cirrhosis with ascites (Navasa et al., 1996). Terg et al. proved that oral administration and switch therapy of ciprofloxacin was equally effective in treating SBP (Terg et al., 2000). Therefore, it was concluded that SPB patients were safe to be discharged before the completion of antibiotic treatment, and the treatment could be completed at home by orally administrating the antibiotics. However, this was just a hypothesis that was never tested until now. In this study, we administered ciprofloxacin and ceftazidime intravenously, followed by their oral administration for treating SPB in patients with cirrhosis with ascites. Our study proved the earlier hypothesis. However, the switch therapy with ciprofloxacin was more effective regarding short hospital stays which, in turn, reduced the treatment cost.

The hospital stay of patients treated with ceftazidime was similar to Yu-Jun et al. (Yu-Jun et al., 2020) and Marciano et al. (Marciano et al., 2019). The comparative results of both antibiotics concerning hospital stay and duration of treatments were similar to other studies (Abd-Elsalam et al., 2021; Mattos et al., 2020). The other noticeable point in our study is the in-hospital mortality which was surprisingly lower than in other studies (4.5%).

Renal failure is common in SBP and cirrhosis with ascites patients, with almost 1/3rd of those developing renal failure(Wakani et al., 2019). In these renal failure patients, most of them are diagnosed with type 1 HRS. In our study, 24.5% of patients had renal failure, and 15.4% developed type 1 HRS. 64.7% of these patients recovered by albumin and terlipressin treatment, where patients showing complete response had a low mortality rate than those showing partial or no response. This reduced the overall in-hospital mortality due to SBP as opposed to previous studies where renal failure was not a risk factor for death in SBP patients (Wong et al., 2021). The previous studies listed different causes of death in these patients (Sanglodkar et al., 2020), among which the severity of infection was found in our research. The in-hospital mortality in our study was similar to Alsyamy and his colleagues (Alsyamy et al., 2022). Although we did not use albumin to prevent type 1 HRS, albumin and trespressin are the best therapeutic options for its prevention.

Conclusion

Switch therapy with ciprofloxacin and ceftazidime is equally effective in treating spontaneous bacterial peritonitis in cirrhotic patients with ascites.

Conflict of interest

The authors declared absence of conflict of interest.

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