OPEN ACCESS

Original Article

Comparative Efficacy of Intravenous Ciprofloxacin against Ceftriaxone in Spontaneous Bacterial Peritonitis Patients

Muhammad Imran Sheikh[1], Muhammad Usman Yaqub[1], Farhan Saeed[1], Asim Maqsood[1] and Muhammad Asad Raza[1]

[1]Department of General Medicine, Avicenna Medical College and Hospital, Lahore, Pakistan

ARTICLE INFO

ABSTRACT

Cirrhotic individuals with spontaneous bacterial peritonitis were treated empirically with ciprofloxacin or ceftriaxone. **Objective:** To compare the effectiveness of intravenous ciprofloxacin against ceftriaxone in cirrhotic patients who developed spontaneous bacterial peritonitis. **Methods:** This prospective interventional analysis was conducted at the Department of Medicine GHURKI Trust and Teaching Hospital, Lahore from Aug 2018 to 2023, and comprised 356 patients of spontaneous bacterial peritonitis. After getting informed written consent patients with ages 35-70 years were included. Equally divided cases into two groups, 178 patients in group I received intravenously ciprofloxacin 200mg and 178 patients in group II received intravenously ceftriaxone 1g for 6 days after every 12 hours. Post-treatment efficacy of both drugs was compared. **Results:** Patients under study had a mean age of 53.15 ± 11.67 years and had a body mass index of 24.8 ± 6.20 kg/m2. In group I efficacy was found in 142 (79.8%) and in group II effectiveness was found in 160 (89.9%) with p-value=0.002. We found a reduction in ascetic fluid polymorph nuclear count in both groups after 6 days with p<0.003. The frequency of complications in group II was higher found in 16 (8.9%) cases and in group I found in only 5 (2.8%) cases. 4 cases in group I and 2 cases in group II left against medical advice. The mortality rate was also non-significant among both groups. **Conclusion:** It was concluded that intravenous ciprofloxacin is equally efficacious as ceftriaxone in treating spontaneous bacterial peritonitis in cirrhotic individuals.

INTRODUCTION

A significant number of hospitalized cirrhotic patients with ascites develop spontaneous bacterial peritonitis (SBP), which is a potentially fatal complication [1, 2]. When treating SBP, third-generation cephalosporin administered intravenously is considered the therapy of choice [3]. Several trials have demonstrated that antibiotics administered intravenously first, with subsequent oral step-down dosing (switch treatment) work just as well [1]. This study did not compare ciprofloxacin switch therapy with an intravenous third-generation cephalosporin. Previous studies demonstrated that it is efficacious in treating both severe and simple SBP [4]. Researchers found that ofloxacin taken orally was just as effective as intravenous (IV) cefotaxime. However, they only ascertained those with simple SBP [5]. A further reduction in effective arterial blood volume as a result of the infection is believed to be the aetiology of type 1 HRS [6]. Administering intravenous albumin in conjunction with antibiotic therapy is an efficient means of preventing HRS. Vasoconstrictors such as Ornipressin, Terlipressin, Noradrenaline, or Midodrine [7]. Patients with cirrhosis who develop spontaneous bacterial peritonitis may not always need ceftazidime or ceftriaxone; ciprofloxacin may be an appropriate substitute. There was an 82% resolution rate for spontaneous bacterial peritonitis in the ceftriaxone group and a 91% resolution rate in the intravenous ciprofloxacin group [8]. Decompensated cirrhosis of the liver patients accounts for 13% of all cases of spontaneous bacterial peritonitis, which is defined as an infection of ascitic fluid [9]. In the case of spontaneous bacterial peritonitis, germs in the intestinal lumen invade the lymph nodes, leading to bacteremia and contamination of the ascitic fluid. Streptococcal pneumonia and Escherichia coli are the most prevalent bacteria and

viruses. The diagnosis is confirmed when the PMN count in the ascetic fluid is equal to or more than 250/mL. To detect early infections, diagnostic paracentesis is commonly performed on hospitalized cirrhotic patients with ascites. Many patients have fever, nausea, vomiting, mental abnormalities, and ileus as symptoms of infection; however, some individuals may not experience any symptoms at all [9]. Therapeutic options for Spontaneous Bacterial Peritonitis include several medications. It has been usual practice to utilize quinolones and third-generation cephalosporins. Two trials found that 78.3 to 78.4% of patients treated with Ciprofloxacin ended up with spontaneous bacterial peritonitis resolution, compared to 67% with Ceftriaxone [10]. This study aims to contrast the efficacy of Ceftriaxone with intravenous Ciprofloxacin in treating spontaneous bacterial peritonitis in a single setting and to determine comparative efficacy.

METHODS

This prospective interventional study was conducted at the Department of Medicine GHURKI Trust and Teaching Hospital, Lahore after getting approval with reference # 3335/HR/GTH. Non-probability sampling technique was used. A sample size of 356 patients (178 in each group) is calculated with a 5% level of significance, 95% power of the test and by taking an expected percentage of efficacy IV Ciprofloxacin as 93% and for Ceftriaxone as 81.4% for Spontaneous bacterial peritonitis patients with 95% CL [11, 12]. The following formula was used for the sample size n; $n=(Z\alpha/2+Z\beta)2 * (p1(1-p1) + p2(1-p2)) / (p1-p2)2$, where $Z\alpha/2$ is the critical value of the Normal distribution at $\alpha/2$ (e.g. for a confidence level of 95%, α is 0.05 and the critical value is 1.96), $Z\beta$ is the critical value of the Normal distribution at β (e.g. for a power of 80%, β is 0.2 and the critical value is 0.84) and p1 and p2 are the expected sample proportions of the two groups. Cirrhosis patients with SBP were included if they were 35–70 years old. Exclusion criteria were patients with a history of hemorrhagic ascites or systolic blood pressure (SBP) caused by trauma (RBC >50000/mm3) on ascites fluid testing. All patients with liver cirrhosis who met the inclusion criteria were chosen after the study received permission from the Institutional Review Board. Ultrasound of the abdomen revealed cirrhosis of the liver. Demographic data such as age, sex, residence, and socioeconomic status, were obtained after informed written consent. A sterile diagnostic ascitic fluid aspiration was conducted using a 20 cc syringe to confirm the diagnosis of SBP, which was based on the patient's medical history and physical examination. The 178 patients in group I were given 200 mg of ciprofloxacin intravenously every 12 hours, whereas the 178 patients in group II were given 1 g of ceftriaxone intravenously every 12 hours for six days. After six days of treatment, the effectiveness of the treatment was assessed by analyzing clinical symptoms. These symptoms included a normalization of the patient's temperature (from 98.6°F to 98.2°F) and the absence of abdominal pain (from palpatory testing to clinical examinations of the abdomen). Additionally, the hospital laboratory tested 20 cc of ascitic fluid (obtained by sterile paracentesis) for the neutrophil count. A performance was used to record all of the data that was obtained. After data collection was complete, SPSS version 23.0 was used for analysis. The mean and standard deviation were used to show quantitative variables such as age, body mass index (BMI), and ascitic fluid polymorphonuclear neutrophil count. Frequency and percentage are the best ways to display qualitative characteristics such as effectiveness and sex. A Chi-Square test was used to compare the two groups' effectiveness. Any p-value less than 0.05 was deemed to be statistically significant.

RESULTS

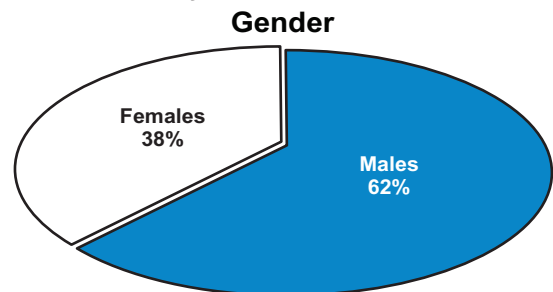There were a majority of 220 (61.8%) male and 136 (38.2%) female in all cases (Figure 1).

Figure 1: Distribution of Gender in All Cases

Patients in group I had a mean age of 53.21 ± 8.22 years with had body mass index of 24.6 ± 7.38 kg/m2 and in group II mean age was 53.15 ± 11.67 years and had a body mass index of 24.8 ± 6.20. There was the majority of cases from urban areas 208 (58.4%). 130 (36.5%) cases had poor socio-economic status, 178 (50%) cases were from the middle class and 48 (13.5%) cases had upper class. The most common symptom was abdomen pain, fever, hepatic encephalopathy and ileus (Table 1).

Table 1: Baseline Information of the SBP Patients

Characteristic	Group I (178)	Group II (178)	Total (356)
Mean Age (years)	53.21	53.15	106.36
Mean BMI (kg/m^2)	24.6	24.8	49.4
Area of Residence			
Urban	102 (28.7%)	106 (29.8%)	208 (58.4%)
Rural	76 (21.3%)	72 (20.2%)	148 (41.6%)
Socio-economic status			
Poor	60 (16.9%)	70 (19.7%)	130 (36.5%)
Middle	85 (23.9%)	93 (26.1%)	178 (50%)
Upper	33 (9.3%)	15 (4.2%)	48 (13.5%)
Clinical Symptoms			
Abdomen Pain	80 (22.5%)	50 (14.04%)	130 (36.5%)
Fever	60 (16.9%)	70 (19.7%)	130 (36.5%)
Hepatic Encephalopathy	20 (5.6%)	30 (8.4%)	50 (14.04%)
Ileus	18 (5.1%)	28 (7.9%)	46 (12.9%)

In group I efficacy was found in 142 (79.8%) and in group II effectiveness was found in 160 (89.9%) with p-value=0.007 (Table 2).

Table 2: Comparison of Effectiveness of Both Medicines

Variables	Group I (178)	Group II (178)	p-value
Efficacy			
Yes	142 (79.8%)	160 (89.9%)	0.007
No	36 (20.2%)	18 (10.1%)	

A reduction in ascetic fluid polymorph nuclear count in both groups was found after 6 days with p<0.003 (Table 3).

Table 3: Comparison of AFPN in Patients After 4 Days

Variables	Group I	Group II	p-value
At Start	7015 ± 158	7156 ± 237	0.000
After Treatment	967 ±147	1026 ± 465	>0.003

AFPN=Alpha-fetoprotein Negative

The frequency of complications in group II was higher found in 16 (8.9%) cases and in group I found in only 5 (2.8%) cases. 4 cases in group I and 2 cases in group II left against medical advice (AMA). The mortality rate was also non-significant among both groups (Table 4).

Table 4: Association of Adverse Events

Variables	Complications	Cases Left AMA	Mortality Rate
Group I	5 (2.8%)	4 (2.2%)	4 (2.2%)
Group II	16 (9.0%)	2 (1.1%)	5 (2.8%)
p-value	<0.0133	0.009	0.010

AMA=Against Medical Advice

Among 21 cases of complications, renal failure was found in 12 cases, followed by gastrointestinal hemorrhage in 6 cases and hepatic encephalopathy in 3 cases. (Table 5).

Table 5: Post-treatment Complications in Both Groups

Variables	Group I (178)	Group II (178)
Complications		
Renal Failure	3 (1.7%)	9 (5.1%)
Gastrointestinal Hemorrhage	1 (0.6%)	5 (2.8%)
Hepatic Encephalopathy	1 (0.6%)	2 (1.1%)
Total	5 (2.8%)	16 (9.0%)

DISCUSSION

Cirrhosis with ascites is a potentially deadly consequence. Even with conventional therapy, the infection-related death rate linked with SBP can reach 27%. Patients with chronic liver illness may first experience a symptomatic SBP as a kind of ascites. Patient lives can be saved by detecting infections early and administering antibiotics promptly. These antibiotic alternatives include ceftriaxone, cefotaxime, ampicillin, ciprofloxacin, ofloxacin, and metronidazole. Norfloxacin and ciprofloxacin are examples of fluoroquinolones; these antibiotics are efficient against most enterobacteria and aerobic gram-negative bacilli, thus they look like a good choice for prophylaxis. A previous case-control study found that 120 patients with cirrhosis with upper gastrointestinal bleeding who were given 500 mg of ciprofloxacin twice a day for seven days following endoscopy had a lower rate of confirmed bacterial infection (10% vs. 45%), but no mortality [13]. The empirical therapy of choice for cirrhotic individuals suffering spontaneous bacterial peritonitis was cefotaxime or ceftriaxone. Patients with cirrhosis who develop spontaneous bacterial peritonitis may benefit from using ciprofloxacin instead of cefotaxime or ceftriaxone. The percentage of spontaneous bacterial peritonitis cases resolved in the groups treated with intravenous ciprofloxacin (80%) and ceftriaxone (83%). Based on these findings, intravenous ciprofloxacin is a cost-efficient and almost equally effective alternative to cefotaxime and ceftriaxone for treating spontaneous bacterial peritonitis in cirrhotic patients [14, 15]. The frequency of SBP in cirrhotic patients and its reaction to various treatment regimens has been the subject of several local and international investigations. Famous antibiotics Ciprofloxacin (Fluoroquinolone) and ceftriaxone (3rd Generation Cephalosporin) were the subjects of this comparative investigation. Due to the rise of multiple drug resistance, there has been a noticeable drop in the effectiveness of both treatments recently; hence, it was important to determine if they are equivalent or not. With a p-value of 0.002, this research indicated that both Ciprofloxacin and ceftriaxone were very successful in treating SBP, with 79.8% and 89.1% of patients, respectively, benefiting from treatment. According to additional research, oral ciprofloxacin had a somewhat higher efficacy than ceftriaxone (80% vs. 76%). According to the previous study, the infection clearance rate with ciprofloxacin was 78.4% and with ceftriaxone, it was 80% [16]. Current findings are quite consistent with those of these investigations. Ceftriaxone was shown to be effective in curing 91% of SBP patients in a comparable past trial [17]. The results showed that there is no substantial difference in the effectiveness of the two drugs, cefotaxime and ciprofloxacin when it comes to treating SBP. In the current study majority, 220 (61.8%) were male and 136 (38.2%) were female in all cases. Included patients who had a mean age of 53.15 ± 11.67 years and had a body mass index of 24.8 ± 6.20 kg/m2. There were the majority of cases from urban areas 208 (58.4%). 130 (36.5%) cases had poor socio-economic status, 178 (50%) cases were from the middle class and 48 (13.5%) cases had high status. These results were comparable to the previous study conducted by MacIntosh [18]. Current analysis revealed a reduction in ascetic fluid polymorph nuclear count in both groups after 4 days with p<0.003, similar to the findings of previous studies [17]. The Frequency of

complications in group II was higher found in 16 (8.9%) cases and in group I found in only 5 (2.8%) cases. 4 cases in group I and 2 cases in group II left against medical advice. The mortality rate was also non-significant among both groups. These were in line with the previous findings [19, 20]. Ciprofloxacin and ceftriaxone both have the potential to save lives and improve the prognosis of SBP, but they require more clinical trials in this context due to limited access to healthcare. Its main drawback is that it is a single-center research with a small sample size. To validate and generalize these findings, a large-scale randomized multicenter clinical investigation is necessary.

CONCLUSIONS

It was concluded that the effectiveness of ciprofloxacin and ceftriaxone in resolving infections caused by spontaneous bacterial peritonitis is comparable and does not differ significantly.

Authors Contribution

Conceptualization: MUY
Methodology: MIS, FS, MAR
Formal analysis: MUY, FS, AM, MAR
Writing review and editing: MIS, AM, MAR

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

REFERENCES

[1] Bahar SA, Amjad A, Jan A, Wakil A, Manan S. A Comparison of Oral and Intravenous Treatments in Managing Spontaneous Bacterial Peritonitis. Pakistan Journal of Advances in Medicine and Medical Research. 2023; 2(01): 108-14. doi: 10.69837/pjammr.v2i01.30.

[2] Khan S, Inam T, Raja K, Ali R, Siddique FM, Fatima K. Compare the Efficacy of Oral Versus Intravenous Medicine in Treatment of Spontaneous Bacterial Peritonitis. Pakistan Journal of Medical & Health Sciences. 2022 Sep; 16(07): 814-. doi: 10.53350/pjmhs22167814.

[3] Khan AM, Haq M, Shah R, Khalil SK, Bakhtiar N, Masud F *et al*. Comparative Analysis of Intravenous Ceftriaxone and Ciprofloxacin for Treating Bacterial Peritonitis in Liver Cirrhosis. Pakistan Journal of Medical and Health Sciences. 2022 Oct; 16(08): 556-. doi: 10.53350/pjmhs22168556.

[4] Marciano S, Diaz JM, Dirchwolf M, Gadano A. Spontaneous Bacterial Peritonitis in Patients with Cirrhosis: Incidence, Outcomes, and Treatment Strategies. Hepatic Medicine: Evidence and Research. 2019 Jan; 11: 13-22. doi: 10.2147/HMER.S164250.

[5] Sanglodkar U, Jain M, Venkataraman J. Predictors of Immediate and Short-Term Mortality in Spontaneous Bacterial Peritonitis. Indian Journal of Gastroenterology. 2020 Aug; 39: 331-7. doi: 10.1007/s12664-020-01040-z.

[6] Wong F, Pappas SC, Curry MP, Reddy KR, Rubin RA, Porayko MK *et al.* Terlipressin Plus Albumin for the Treatment of Type 1 Hepatorenal Syndrome. New England Journal of Medicine. 2021 Mar; 384(9): 81828. doi: 10.1056/NEJMoa2008290.

[7] Mattos AA, Wiltgen D, Jotz RF, Dornelles CM, Fernandes MV, Mattos ÂZ. Spontaneous Bacterial Peritonitis and Extraperitoneal Infections in Patients with Cirrhosis. Annals of Hepatology. 2020 Sep; 19(5): 451-7. doi: 10.1016/j.aohep.2020.04.010.

[8] Yim HJ, Kim TH, Suh SJ, Yim SY, Jung YK, Seo YS *et al*. Response-Guided Therapy with Cefotaxime, Ceftriaxone, Or Ciprofloxacin for Spontaneous Bacterial Peritonitis: A Randomized Trial: A Validation Study of 2021 AASLD Practice Guidance for SBP. Official Journal of the American College of Gastroenterology. 2023 Apr; 118(4): 654-63. doi:10.14309/ajg.0000000000002126.

[9] Zaidi SA, Iqbal W, Kumar A, Jan I, Faryal S, Ahmed R. Comparative Analysis of Intravenous Ceftriaxone and Ciprofloxacin for the Treatment of Bacterial Peritonitis in Liver Cirrhosis. Pakistan Journal of Medical & Health Sciences. 2023 Mar; 17(01): 853-. doi: 10.53350/pjmhs2023171853.

[10] Prat LI, Wilson P, Freeman SC, Sutton AJ, Cooper NJ, Roccarina D *et al*. Antibiotic Treatment for Spontaneous Bacterial Peritonitis in People with Decompensated Liver Cirrhosis: A Network Meta-Analysis. Cochrane Database of Systematic Reviews. 2019 Sep. doi: 10.1002/14651858.CD013120.pub2.

[11] Haroon M, Tariq S, Khan MS. Comparing the efficacy of intravenous ciprofloxacin and ceftazidime for Treating Spontaneous Bacterial Peritonitis in Liver Cirrhosis Patients. Biological and Clinical Sciences Research Journal. 2022: 170. doi:10.54112/bcsrj.v2022i1.170.

[12] Sandhu GA, Ahmad Z, Tahir GA, Mumtaz J. Comparison of Efficacy of Intravenous Ciprofloxacin and Ceftriaxone in the Management of Spontaneous Bacterial Peritonitis in patient of Liver Cirrhosis. Annals of Punjab Medical College. 2016 Oct; 10(4): 213-6.

[13] Fatima I and Kulkarni AV. Evidence-based Commentary: Antibiotics for Prophylaxis of

Spontaneous Bacterial Peritonitis. Journal of Gastrointestinal Infections.2022 Jan; 12(01): 051-6.doi: 10.1055/s-0042-1757543.

[14] Gurusamy KS and Tsochatzis E. Treatment for Ascites in People with Decompensated Liver Cirrhosis: A Network Meta-Analysis. The Cochrane Database of Systematic Reviews. 2018; 2018(9). doi: 10.1002/14651858.CD013123

[15] Khan Z, Rashid A, Haider I, Suleman S, Badshah A, Khan I *et al.* The Efficacy of Ciprofloxacin and Cefotaxime in Patients with Cirrhosis Liver Presenting with Spontaneous Bacterial Peritonitis to a Tertiary Care Hospital. Journal of Medical Sciences. 2021 Jul; 29(02). doi: 10.52764/jms.21.29.2.2.

[16] Lee TH, Huang CT, Lin CC, Chung CS, Lin CK, Tsai KC. Similar Rebleeding Rate in 3-Day and 7-Day Intravenous Ceftriaxone Prophylaxis for Patients with Acute Variceal Bleeding. Journal of the Formosan Medical Association.2016 Jul; 115(7): 54752. doi: 10.1016/j.jfma.2016.01.006.

[17] Zafar MH, Asghar A, Ather U. Role of Oral Verses Intravenous Antibiotic in Patients with Spontaneous Bacterial Peritonitis. In Medical Forum Monthly.2018; 29(7).

[18] MacIntosh T.Emergency Management of Spontaneous Bacterial Peritonitis–A Clinical Review. Cureus. 2018 Mar; 10(3). doi: 10.7759/cureus.2253.

[19] Ameer MA, Foris LA, Mandiga P, Haseeb M. Spontaneous Bacterial Peritonitis.Stat Pearls Publishing. 2017 Aug.

[20] Bolia R, Srivastava A, Marak R, Yachha SK, Poddar U. Prevalence and Impact of Bacterial Infections in Children with Liver Disease—A Prospective Study. Journal of Clinical and Experimental Hepatology. 2018 Mar; 8(1): 35-41. doi: 10.1016/j.jceh.2017.08.007.