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ORIGINAL ARTICLE

Comparison of Cefotaxime with Ofloxacin in Treatment of Spontaneous Bacterial Peritonitis in Liver Cirrhosis Patients

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ABSTRACT

Background: Ofloxacin (Quinolone) is effective antibiotic against Gram-negative bacteria and has high bioavailability with minimum duration of therapy.

Objective: The study aimed to compare the ofloxacin and cefotaxime efficacy in treatment of spontaneous bacterial peritonitis in Liver cirrhosis subjects.

Study design: It is a randomized controlled trail study conducted at Department of Medicine, Federal Govt Polyclinic Hospital Islamabad, from August 2021 January 2022.

Material and Methods: A total of one hundred and seventy six (n=176) adult subjects of both gender between age 18-65 years presented with ascitic fluid infection with PMN counts ≥ 250 cells/mm^3 were enrolled in the study. The 88 subjects were randomly assigned by lottery method into Group I (Ofloxacin) and group II (Cefotaxime). Outcome of interventions was assessed clinically and through lab investigations (PMN counts) at day 3 and day 5. Culture reports were available at 5th day. The collected data was analyzed statistically by the SPSS software.

Results: Mean age was 53.1 years ± 8.1 SD in group I while it was 53.2 years ± 8.4 SD in group II. Abdominal pain was the most frequent complaint (70.5% in group I and 67% in group II) followed by nausea and fever. On day 3, efficacy was 44.3% in group I and 39.8% in group II. On day 5, efficacy was observed to be 90.9% in group I and 80.7% in group II. All the subjects were sensitive to the antibiotics they were receiving. Therapy was not proved to be efficacious in 25 subjects in group I and 17 in group II. Resistant Escherichia coli was the most frequent organism in these cases. Therapy was modified as per sensitivity reports. No mortality was observed in both groups during hospital stay. Both the therapies were well tolerated and no significant side effects were observed in both groups.

Conclusions: The efficacy of Ofloxacin was significantly better on day 5 compared to Cefotaxime in subjects. Ofloxacin is a better option than Cefotaxime in treating spontaneous bacterial peritonitis. However, further studies with larger sample size required.

Keywords: Ofloxacin, Cefotaxime, bacterial peritonitis, antibiotics.

INTRODUCTION

The most frequent bacterial infection in people with liver cirrhosis is spontaneous bacterial peritonitis (SBP). The negative outcomes poor mortality risk is associated with it. Regardless of the etiology patients may acquire SBP. Depending on the geographic area, the profile of SBP-inducing bacteria can differ even between different hospitals within a single country. Eastern Europe and Asia are dominated by Enterobacteriaceae that produce ESBL[1-2].

The pathogenesis of SBP is still not fully understood, however, several predisposing factors have been identified. Most of the subjects with spontaneous bacterial peritonitis have advanced cirrhosis. The risk factors include, H/O previous episode of spontaneous bacterial peritonitis, Serum total bilirubin concentration >2.5 milligram/dL, ascitic fluid total protein concentration < 1 gram/dL, variceal hemorrhage, malnourished patients. Patients on proton pump inhibitors[3-4]. A typical small intestine motility resulted from cirrhosis eventually increases the risk of intestinal bacterial overgrowth and translocation. The risk of SBP rises with the progression of liver disease. The frequent use of proton pump inhibitors in this patient population have exacerbated the phenomena by reducing gastric acidity and increasing intestinal permeability, which encourages bacterial translocation and colonization of the mesenteric lymph nodes[5-6]. Quinolones are currently used as antibiotics alternative to cephalosporins for the treatment of spontaneous bacterial peritonitis. Ofloxacin (Quinolone) is effective against Gram-negative bacteria and has high bioavailability with minimum duration of therapy (five days). As Resistance to third generation cepahlosporins has also been reported in Pakistan therefore the highly recommended drug for the treatmen of SBP are third generation cephalosporins[7-8]. The physicians are using ceftriaxone for treatment of SBP in patients with cirrhosis.

Since there is emerging resistance to treatment of SBP, which challenge the physicians to modify the existing treatment strategies. Rationale of the study was to evaluate the efficacy of quinolones (ofloxacin) and third generation cephalopsorins (Cefotaxime)[9-10]. This study pave the way towards the better treatment decisions in future. This would help the physicians to choose better antibiotics for the subjects suffering from Spontaneous bacterial peritonitis (SBP)[11-12].

MATERIAL AND METHODS

It is a randomized controlled trail study conducted at the Department of medicine, Federal Govt Polyclinic Hospital Islamabad, for the duration of six months from August 2021 January 2022. A total of one hundred and seventy six (n=176) adult subjects of both gender between age 18-65 years presented with ascitic fluid infection with PMN counts ≥ 250 cells/mm^3 were enrolled in the study. The subjects suspected of having SBP underwent abdominal paracentesis before receiving any antibiotic. 20 mL volume syringes of ascitic fluid was used for the tests. A few milliliters of ascitic fluid was used for Gram staining. The elevated ascitic fluid absolute polymorphonuclear cell (PMN, also referred to as neutrophils) count (≥250 cells/mm^3) depicted the SBP. The absolute PMN count in the ascitic fluid is calculated by multiplying the total white blood cell count by differential.

Eighty eight (n=88) subjects were randomly assigned by lottery method into Group I (Ofloxacin) and group II (Cefotaxime). Outcome of interventions was assessed clinically and through lab investigations (PMN counts) at day 3 and day 5. Culture reports were available at 5th day. The collected data was analyzed statistically by the SPSS software. Clinical features like abdominal pain, fever or altered mental status of every participant was examined strictly. All data was processed and analyzed using SPSS version 21.0. For continuous variables like age, CBC,

prothrombin time, LFTs, mean ± S.D were calculated. For categorical variables like gender, symptoms, side effects frequency and percentages were calculated. Chi square test was used to compare the efficacy between the two groups at 3rd and 7th day of treatment.

RESULTS

Age distribution was similar in both groups with mean age of 53.1 years ± 8.1 SD in group while it was 53.2 years ± 8.4 SD in group II as shown in table 1. Males and females distribution was also similar in both groups with M:F of 0.69:1 in group I and 0.73:1 in group II as shown in table 2.

Table 1: Age distribution in both groups

Groups	Gender	Mean age (years)	STD. deviations
Ofloxacin	Males	52.6	8.4
	Females	53.4	7.9
	Total	53.1	8.1
Cefotaxime	Males	52.4	9.4
	Females	53.7	7.7
	Total	53.2	8.4

Outcome of interventions was assessed clinically and through lab investigations (PMN counts) at day 3 and day 5. Culture reports were available on 5th day.

Table 2: Gender distribution in both groups

Gender	Group		Total
	Ofloxacin	Cefotaxime	
Males	36	37	73
	40.9%	42.0%	41.5%
Females	52	51	103
	59.1%	58.0%	58.5%
Total	88	88	176
	100.0%	100.0%	100.0%
M:f	0.69:1	0.73:1	

On day 3, efficacy was observed in 44.3% (n=39/88) subjects in Ofloxacin group and it was 39.8% (n=35/88) in Cefotaxime group. Patients were improved clinically and PMN counts were <250 cells/mm^3. The difference, however, was not significant (P=0.324 table 4). Therapy was continued in these subjects till day 5 when efficacy was again estimated, culture/sensitivity reports were also available at that time.

Table 3: Baseline cell counts in both groups

Group		TLC (cells/mm^3)	PMN (cells/mm^3)	Platelets (cells/mm^3)
Ofloxacin	Mean	9140.2	463.5	117787.1
	SD	1987.1	190.4	17184.5
Cefotaxime	Mean	10159.3	485.9	116049.1
	SD	1879.8	171.4	18002.1

Same therapy was also continued in all those subjects whom efficacy was not observed as per our operational definition i.e PMN counts<250cells/mm^3, as those subjects were clinically improved and their PMN counts declined from baseline, though did not fall below 250 cells/mm^3 till day 5 when culture and sensitivity reports were available.

Table 4: Efficiency at day 3 in both groups

Efficacy	Group		Total	P-value chi-square
	Ofloxacin	Cefotaxime		
Present	39	35	74	0.324
	44.3%	39.8%	42.0%	
Absent	49	53	102	
	55.7%	60.2%	58.0%	
Total	88	88	176	
	100.0%	100.0%	100.0%	

On day 5, efficacy was observed in 90.9% (n=80/88) subjects in Ofloxacin group and it was 80.7% (n=71/88) in Cefotaxime group. Patients were improved clinically and PMN counts were <250 cells/mm^3. The difference was statistically significant (P=0.041 table 5). Drug sensitivity was confirmed on sensitivity reports and all these subjects were sensitive to the antibiotics they were receiving. Same therapy was continued in these subjects for two more days.

Table 5: Efficiency at day 5 in both groups

Efficacy	Group		Total	P-value chi-square
	Ofloxacin	Cefotaxime		
Present	80	71	151	0.041
	90.9%	80.7%	85.8%	
Absent	8	17	25	
	9.1%	19.3%	14.2%	
Total	88	88	176	
	100.0%	100.0%	100.0%	

There were twenty five (n=25, 8 in Ofloxacin group and 17 in cefotaxime group) subjects in whom therapy was not proved to be efficacious and PMN counts were still >250cells/mm^3. Resistant E.coli was the most frequent organism found followed by Staph. aureus and MRSA. Therapy was modified as per sensitivity reports and subjects were kept in the hospital till they were clinically improved and their PMN counts became <250 cells/mm^3. No mortality was observed in both groups during hospital stay. Both the therapies were well tolerated and no significant side effects were observed in both groups. Similar trends were noted when data was stratified for age and gender on day 5. Efficacy was better in Ofloxacin group as compared to Cefotaxime group.

DISCUSSIONS

The guidelines for antibiotic therapy for SBP were published in 2000 and since then not much changes developed in the antibiotic recommendations. Cefotaxime in a dose of 2 grams BD has been advocated in 1990s and since then it is still recommended as a regimen of first choice for the treatment of SBP. Our results are comparable with already published reports on the use of Ofloaxacin in SBP subjects[13-14]. Taskiran et al., in their comparative trial evaluated the effectiveness of Ofloxacin and Cefotaxime for the treatment of SBP. They evaluated combined oral and intravenous Ofloxacin with IV cefotaxime. 30 subjects with cirrhosis and SBP were assigned to receive either cefotaxime for 7 days ofloxacin for two days followed by oral ofloxacin for five days (n=13). Their results demonstrated similar outcomes in both groups (infection resolution on day 7: 82.4% in the cefotaxime and 92.3% in the ofloxacin group[15].

Hospital survival rates were also similar (82.4% and 100%, respectively). The results are quite similar to present study results where we achieved infection resolution in 90.9% (n=80/88) subjects in Ofloxacin group and 80.7% (n=71/88) in Cefotaxime group. In the other study, Navasa et al., evaluated and compared ofloxacin with cefotaxime for the treatment of SBP[16]. They randomized 103 subjects with uncomplicated SBP to ofloxacin (64 subjects) and cefotaxime (59 subjects). Their results demonstrated that infection was resolved in 84% of patients in the ofloxacin group and 85% in the cefotaxime group. The results are similar to the present study results, yet efficacy was better in the present study (90.9%) with oflaxacin. The difference may be attributed to the fact that we used intravenous ofloxacin as compared to oral oflaxacin, which was used by Navasa et al. Several authors evaluated quinolones other than ofloxacin for the treatment of SBP.

Chavez et al[17] in their systematic review analyzed different types of antibiotic therapies being reported for the treatment of SBP. They included 13 studies in their analysis and all of them were randomized controlled trials. They reported that there is no significant difference in efficacy between higher dosage or longer duration of therapy and lower dosage or shorter duration of therapy with 3rd generation cephalosporins and in patients with less severe disease (uncomplicated SBP), quinolones may be considered as

the first treatment option. Quinolones are better option than third Generation cephalosporins in treatment of SBP as efficacy and cost savings are concerned. Other advantages of Quinolones are its simple oral administration after two days of treatment, thereby decreasing the duration of average hospital stay and increased patient satisfaction in the form of oral treatment.

Angelini et al[18] assessed the effectiveness of quinolones (ciprofloxacin, from IV to oral step-down therapy), in comparison with ceftazidime in one hundred and sixteen subjects with spontaneous bacterial peritonitis. Initially ciprofloxacin was administered in a dose of 200 mg BD (intravenous) and subsequently was switched to oral dose of 500 mg BD when sign and symptoms of disease disappeared. Ceftazidime was given in a dosage of 2 grams BD[19-20]. In patients who had renal dysfunction, dose of both the antibiotics was accordingly adjusted. They reported that infection was resolved in 80% of subjects who received ciprofloxacin and in 84% who received Ceftazidime.

Although the current practice is in favor of third generation cephalosporins as a standard treatment for SBP, treatment with qunilones have shown promising results. The study has few limitations therefore there is need of further comparative trials with larger sample size to accurately determine the role the quinolone play in treatment of SBP[21-23].

CONCLUSION

The efficacy of Ofloxacin was significantly better on day 5 compared to Cefotaxime in subjects. ofloxacin is a better option than Cefotaxime in treating spontaneous bacterial peritonitis. However, further studies with larger sample size required.

REFERENCES

1. Rostkowska KA, Pasternak AS, SimonKA. Spontaneous bacterial peritonitis – therapeutic challenges in the era of increasing drug resistance of bacteria. Clin Exp Hepatol. 2018;4(4): 224–231.
2. Oliveira AM, Branco JC, Barosa R. Clinical and microbiological characteristics associated with mortality in spontaneous bacterial peritonitis: A multicenter cohort study. Eur J Gastroenterol Hepatol. 2016;28:1–7.
3. Jalan R, Fernandez J, Wiest R. Bacterial infections in cirrhosis: A position statement based on the EASL Special Conference 2013. J Hepatol. 2014;60:1310–24.
4. Ding X, Yu Y, Chen M, Wang C, Kang Y, Lou J at al. Causative agents and outcome of spontaneous bacterial peritonitis in cirrhotic patients: community-acquired versus nosocomial infections. BMC Infect Dis. 2019;19(1):463-66.
5. Li YT, Yu CB, Huang JR, Qin ZJ, Li LJ. Pathogen profile and drug resistance analysis of spontaneous peritonitis in cirrhotic patients. World J Gastroenterol. 2015;21(36):10409-17.
6. Bibi S, Ahmed W, Arif A, Khan F, Alam SE. Clinical, laboratory and bacterial profile of Spontaneous Bacterial Peritonitis in Chronic Liver Disease patients. J Coll Physicians Surg Pak. 2015;25(2):95-99.
7. Zaman A, Kareem R, Mahmood R, Hameed K, Khan EM. Frequency of microbial spectrum of spontaneous bacterial peritonitis in established cirrhosis liver. J Ayub Med Coll Abbottabad. 2011;23(4):15-17.
8. Obstein KL, Campbell MS, Reddy KR, Yang Y-X. Association between model for end-stage liver disease and spontaneous bacterial peritonitis. Am J Gastroenterol. 2007;102:2732–2736.
9. [1] Nousbaum JB. Spontaneous bacterial peritonitis in patients with cirrhosis. Presse Med. 2015;44(12 Pt 1):1235-42.
10. [1] Albillos A, Lario M, Mon AM. Cirrhosis-associated immune dysfunction: Distinctive features and clinical relevance. J Hepatol. 2014;61:1385–96.
11. Friedrich K, Nüssle S, Rehlen T, Stremmel W, Mischnik A, EisenbachC. Microbiology and resistance in first episodes of spontaneous bacterial peritonitis: implications for management and prognosis. J Gastroenterol Hepatol. 2016;31(6):1191-95.
12. Fernandez J, Bert F, Nicolas-Chanoine MH. The challenges of multidrug-resistance in hepatology. J Hepatol. 2016;65:1043–1054.
13. Oey RC, DeMan RA, Erler NS, Verbon A, Buuren HR. Microbiology and antibiotic susceptibility patterns in spontaneous bacterial peritonitis: a study of two Dutch cohorts at a 10 years interval. United European Gastroenterol J. 2017;6(4):614–21.
14. Sarwar S, Tarique S, Waris U, Khan AA. Cephalosporin resistance in community acquired spontaneous bacterial peritonitis. Pak J Med Sci. 2019;35(1): 4–9.
15. Taşkiran B, Colakoğlu O, Sözmen B, Unsal B, Aslan SL, Buyraç Z. Comparison of cefotaxime and ofloxacin in treatment of spontaneous bacterial peritonitis. Turk J Gastroenterol. 2004;15(1):34-38.Ariza X, Castellote J, Lora-Tamayo J. Risk factors for resistance to ceftriaxone and its impact on mortality in community, healthcare and nosocomial spontaneous bacterial peritonitis. J Hepatol. 2012;56:825–32.
16. Navasa M, Follo A, Llovet JM, Clemente G, Vargas V, Rimola A. Randomized, comparative study of oral ofloxacin versus intravenous cefotaxime in spontaneous bacterial peritonitis. Gastroenterology. 1996;111(4):1011-17.
17. Chavez-Tapia NC, Soares-Weiser K, Brezis M, Leibovici L. Antibiotics for spontaneous bacterial peritonitis in cirrhotic subjects. Cochrane Database Syst Rev. 2009:CD002232
18. Angeloni S, Leboffe C, Parente A. Efficacy of current guidelines for the treatment of spontaneous bacterial peritonitis in the clinical practice. World J Gastroenterol. 2008;14:2757–2762.
19. Ariza X, Castellote J, Lora-Tamayo J. Risk factors for resistance to ceftriaxone and its impact on mortality in community, healthcare and nosocomial spontaneous bacterial peritonitis. J Hepatol. 2012;56:825-59.
20. Chavez-Tapia NC, Soares-Weiser K, Brezis M, Leibovici L. Antibiotics for spontaneous bacterial peritonitis in cirrhotic subjects. Cochrane Database Syst Rev. 2009;(1):CD002232.
21. Tuncer I, Topcu N, Durmus A, Turkdogan MK. Oral ciprofloxacin versus intravenous cefotaxime and ceftriaxone in the treatment of spontaneous bacterial peritonitis. Hepatogastroenterology. 2003;50(53):1426-30.
22. Yim HJ, Suh SJ. Comparison of efficacy of cefotaxime, ceftriaxone, and ciprofloxacin for the treatment of spontaneous bacterial peritonitis in patients with liver cirrhosis: a randomized controlled trial. EASL Liver Tree™. 2017;167470;FRI-017
23. Han Paik Y, Seo YS. The Korean Association for the Study of the Liver (KASL). KASL clinical practice guidelines for liver cirrhosis: Ascites and related complications. Clin Mol Hepatol. 2018 Sep; 24(3): 230–77.