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COMPARISON BETWEEN ORAL OFLOXACIN AND INTRAVENOUS CEFOTAXIME FOR UNCOMPLICATED SPONTANEOUS BACTERIAL PERITONITIS: A COMPARATIVE COHORT STUDY FROM PAKISTAN

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ABSTRACT

Background: Objective: To compare the efficacy and safety of oral ofloxacin versus intravenous cefotaxime in patients with uncomplicated spontaneous bacterial peritonitis (SBP) in a real-world clinical setting.

Materials and Methods: It was a comparative cohort study done at a Teaching Hospital which included sixty cirrhotic patients complaining uncomplicated SBP. Diagnosis was based on ascitic fluid PMN count >250/mm³. Patients were assigned to two treatment groups based on clinical discretion and patient financial circumstances. One group (n=30 patients) received par-oral Ofloxacin 400 mg BD for 7 days, while other group (n=30 patients) received IV Cefotaxime 2 g BD for 7 Days. The primary outcome was resolution of infection (acitic fluid PMN count <250/mm³) and Secondary outcomes included fever resolution, abdominal pain relief, and six-month mortality.

Results: Initial features were same among both groups. After seven days, PMN count normalized in 28 of 30 cefotaxime patients (93%) and 26 of 30 ofloxacin patients (87%) (p=0.38). Fever resolved in 93% of both groups. Abdominal pain resolved in all 22 cefotaxime patients who had pain at baseline (100%) and in 24 of 26 ofloxacin patients with baseline pain (92%, p=0.49). mortality rate after six-months was 7% (n=2) and 10% (n=3) in cefotaxime and ofloxacin group (p=0.64) respectively. No patient discontinued treatment due to adverse effects. The most common bacterial isolate was Escherichia coli (54% of positive cultures), followed by Staphylococcus aureus (25%).

Conclusion: Both oral ofloxacin and intravenous cefotaxime are effective for uncomplicated SBP, with no statistically significant difference in outcomes. Oral ofloxacin is a reasonable and cost-effective alternative where hospital admission or intravenous access poses challenges.

Keywords: Spontaneous bacterial peritonitis, ofloxacin, cefotaxime, cirrhosis, comparative cohort study, Pakistan.

INTRODUCTION

Among other complications of liver cirrhosis, SBP is fatal in approximately 20% of hospitalized patients with ascites mainly due to severe inflammation resulting by the bacterial entry in to peritoneal cavity from the gut.[1] Without prompt antibiotic treatment, mortality approaches 100%; even with appropriate therapy, it remains between 20% and 40%.[2]

The standard of care for SBP is prompt empirical intravenous antibiotics, typically a third-generation cephalosporin such as cefotaxime or ceftriaxone.[3,4] These drugs have excellent activity against the gram-negative enteric organisms – primarily Escherichia coli and Klebsiella species – that cause the majority of SBP cases. Multiple randomized trials have confirmed response rates of 80-90% with cefotaxime.[5,6]

However, intravenous therapy has significant practical disadvantages in resource-limited settings like Pakistan. It requires hospital admission, intravenous access, nursing supervision, and sterile supplies – all of which add substantially to the cost of care. A week of intravenous antibiotics with hospitalization can cost PKR 35,000-50,000, a sum that is unaffordable for many patients.[7] Furthermore, patients from rural areas may travel long distances to reach a hospital capable of providing intravenous therapy, and many cannot afford to stay for the full treatment course.

Oral antibiotics offer potential solutions to these problems. They are cheaper, do not require hospital admission, and can be administered at home or in basic health units. Ofloxacin, a fluoroquinolone antibiotic, has properties that make it particularly attractive for SBP treatment. It is well absorbed from the gastrointestinal tract, achieves excellent penetration into ascitic fluid, and reaches levels that exceed the minimum inhibitory concentration for most SBP pathogens within hours of the first dose.[8] The landmark trial by Navasa and colleagues in 1996 first demonstrated that oral ofloxacin was as effective as intravenous cefotaxime for patients with uncomplicated SBP.[9] However, that study was conducted in Spain, where antibiotic resistance patterns and healthcare systems differ from those in South Asia. More recent data from Pakistan on this comparison are lacking.

This comparative cohort study was planned to find out the effectiveness and safety of oral ofloxacin versus IV cefotaxime in patients with uncomplicated SBP reporting to tertiary care hospital, Pakistan. Our goal was to determine whether oral ofloxacin could serve as a practical, cost-effective alternative to intravenous therapy in this resource-limited setting.

MATERIALS AND METHODS

This was a comparative cohort study conducted at the Medicine Department of Gujranwala Teaching Hospital/ GMC Gujranwala, Pakistan, from Sept.2025 to March 2026. Approval from the Institutional Review Board of FMDC (Ref No. IRB/2025/53) was obtained. A written informed consent from all participants was taken and the study conducted in accordance with the Declaration of Helsinki. We enrolled 60 adult patients (age ≥18 years) with cirrhosis diagnosed based on a combination of clinical features, laboratory findings and abdominal ultrasound findings.

Uncomplicated SBP was diagnosed by paracentesis showing ascitic fluid polymorphonuclear (PMN) count greater than 250/mm³ in the absence of clinical, radiological, or laboratory evidence of secondary peritonitis.[3]

Uncomplicated SBP was defined as the absence of the following exclusion criteria: septic shock (systolic blood pressure <90 mmHg despite fluid resuscitation), hepatic encephalopathy (any grade), active gastrointestinal bleeding, and serum creatinine >3 mg/dL. Patients who had received antibiotic therapy for SBP within the 48 hours before presentation were also excluded.

Patients were assigned to treatment groups based on clinical discretion and patient financial circumstances, not by randomization. This was a pragmatic comparative effectiveness study reflecting real-world treatment decisions. Thirty patients (n=30) received oral ofloxacin 400 mg (two 200 mg tablets) every 12 hours for seven days and 30 received intravenous cefotaxime 2g dissolved in 100 ml of normal saline, infused over 30 minutes every 12 hours for seven days. All patients received concurrent supportive care according to standard hospital protocols, including diuretics for ascites management when appropriate, vitamin K for coagulopathy, and nutritional support.

The primary outcome was microbiological response as normalization of ascitic fluid PMN count < 250/mm³ after seven days of antibiotic therapy. And secondary outcomes included; Resolution of fever (temperature <37.5°C sustained for 48 hours), Resolution of abdominal pain (patient-reported absence of pain), Resolution of abdominal tenderness on physical examination, In-hospital mortality, Six-month mortality (assessed by outpatient follow-up or telephone contact) and Adverse effects requiring treatment discontinuation.

Treatment failure was defined as persistent ascitic fluid PMN count ≥250/mm³ after seven days, death attributed to infection before resolution, or need for antibiotic change due to clinical deterioration.

In the first hour of admission, diagnostic paracentesis was carried out using a 22-gauge needle , about 60ml ascetic fluid was drawn from the left lower quadrant under aseptic conditions. A portion was sent for cell count and cell cultures and antibiotic susceptibility found following Clinical and Laboratory Standards Institute (CLSI) guidelines.[10, 11]

Statistical Analysis. Data were analyzed using SPSS version 26 (IBM Corp., Armonk, NY, USA). Continuous variables (age, baseline PMN count) were expressed as mean ± standard deviation or median with interquartile range and compared using the independent t-test or Mann-Whitney U test as appropriate. Categorical variables (sex, fever resolution, mortality) were expressed as frequencies and percentages and compared using the chi-square test or Fisher's exact test. A two-sided $p \leq 0.05$ was considered statistically significant. All analyses were conducted on an intention-to-treat basis –

patients were analyzed according to the group to which they were assigned, regardless of whether they completed the full treatment course.

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RESULTS

A total of 60 patients were included, 30 in each treatment group. The mean age of the cohort was 54.3 years. Males comprised 62% of patients. Table 1 summarizes their baseline demographic and clinical characteristics. The two groups were well balanced, with no statistically significant differences.

Table 1: Baseline characteristics of study patients (N=60)

Characteristic	Cefotaxime (n=30)	Ofloxacin (n=30)	P-value
Age (years, mean ± SD)	53.8 ± 11.2	54.8 ± 10.4	0.71
Male sex, n (%)	19 (63)	18 (60)	0.79
Cause of cirrhosis, n (%)			
Hepatitis C	19 (63)	16 (53)	0.43
Hepatitis B	8 (27)	9 (30)	0.78
Cryptogenic	3 (10)	5 (17)	0.71
Presenting features, n (%)			
Fever	29 (97)	30 (100)	0.99
Abdominal pain	22 (73)	26 (87)	0.19
Abdominal tenderness	23 (77)	26 (87)	0.32
Jaundice	17 (57)	18 (60)	0.80
Baseline PMN count (/mm³, median, range)	403 (251-1000)	412 (250-1000)	0.82

Table 2 shows the distribution of organisms among positive cultures. There was no significant difference in organism distribution between the two treatment groups.

Table 2: Organisms isolated from Ascitic fluid (n=28 positive cultures)

Organism	Cefotaxime group (n=12)	Ofloxacin group (n=16)	Total (%)
Escherichia coli	6	9	15 (54)
Staphylococcus aureus	3	4	7 (25)
Klebsiella species	2	3	5 (18)
Pseudomonas aeruginosa	1	0	1 (4)

Primary outcome – infection resolution. After seven days of treatment, ascitic fluid PMN count normalized < 250/mm³ in patients of both groups is shown in Table 3. The difference of 6.6 percentage points was not statistically significant (p=0.38; 95% confidence interval for the difference: -8.2% to 21.4%).

Table 3: Primary and Secondary outcomes after seven days of treatment

Outcome	Cefotaxime (n=30)	Ofloxacin (n=30)	P-value
Primary			
PMN count <250/mm³ at day 7, n (%)	28 (93)	26 (87)	0.38
Secondary			
Fever resolution, n (%)	27/29 (93)	28/30 (93)	0.97
Abdominal pain resolution, n (%)	22/22 (100)	24/26 (92)	0.49
Abdominal tenderness resolution, n (%)	22/23 (96)	23/26 (88)	0.61
In-hospital mortality, n (%)	1 (3.3)	1 (3.3)	1.00
Six-month mortality, n (%)	2 (6.7)	3 (10.0)	0.64

Secondary Outcomes – clinical improvement. Are mentioned in table 3.

Mortality. One patient in each group died during the initial hospitalization (3.3% in-hospital mortality). Both deaths were attributed to progressive liver failure rather than uncontrolled infection. At six months of follow-up, ofloxacin group had three (10%) and cefotaxime group had two (6.7%) additional deaths (p=0.64), statistically not significant. All late deaths were due to complications of end-stage liver disease unrelated to SBP.

Treatment failures. Six patients (10%) showed treatment failure. Table 4 provides details of these six patients. All six had baseline PMN counts above 600/mm³, and five of the six had Child-Pugh class C cirrhosis. The two patients with *Staphylococcus aureus* infection both failed initial therapy but eventually recovered after adding vancomycin. One patient in the ofloxacin group died from progressive liver failure on day 10.

Table 4: Detailed characteristics of the six patients who failed treatment

Patient	Age/Sex	Child-Pugh class	Baseline PMN	Organism	Treatment	Day 7 PMN	Final outcome
1	58/M	C	890	E. coli	Cefotaxime	320	Switched to meropenem, recovered
2	62/F	C	720	Klebsiella	Cefotaxime	410	Continued same drug, recovered slowly
3	55/M	B	980	E. coli	Ofloxacin	450	Switched to cefotaxime, recovered
4	48/F	C	850	S. aureus	Ofloxacin	380	Added vancomycin, recovered
5	65/M	C	620	Negative	Ofloxacin	310	Died from liver failure on day 10
6	52/M	C	910	Negative	Ofloxacin	520	Continued ofloxacin, recovered slowly

Safety and tolerability. No patient in either group discontinued antibiotic therapy due to adverse effects. Mild gastrointestinal symptoms (nausea, loose stools) were reported by three patients (10%) in the ofloxacin group and one patient (3%) in the cefotaxime group, but none required treatment interruption. No hypersensitivity reactions, nephrotoxicity, or neurotoxicity were observed.

Antibiotic susceptibility. During Susceptibility testing, all tested *E. coli*, *Klebsiella*, and *Pseudomonas* isolates were fully susceptible to both cefotaxime and ofloxacin. Among the five *S. aureus* isolates tested, four (80%) were susceptible to both drugs, and one showed intermediate susceptibility. No isolate showed complete resistance to either antibiotic.

DISCUSSION

Our comparative cohort study evaluated the effectiveness of oral ofloxacin and the IV cefotaxime for treating uncomplicated SBP tertiary care hospital. Both medicines demonstrated high efficacy, with response rates of 93% for cefotaxime and 87% for ofloxacin. The difference was not statistically significant, indicating that oral ofloxacin is a reasonable alternative for carefully selected patients.

Our findings align closely with the landmark Navasa trial from 1996, which reported response rates of 85% for cefotaxime and 84% for ofloxacin in a randomized controlled setting.[9] A more recent Indian randomized trial by Sharma and colleagues (2018) found similar results (91% vs 88%).[12] A 2021 Cochrane systematic review that pooled data from six trials concluded that oral fluoro-quinolones are non-inferior to intravenous cephalosporins for uncomplicated SBP.[13] Our study extends these findings to the Pakistani population, confirming that the results are generalizable to South Asian settings with different patterns of cirrhosis etiology (predominantly viral hepatitis rather than alcohol).

The advantages of oral ofloxacin in countries like Pakistan are substantial. The cost difference is dramatic.[7] Beyond direct drug costs, oral therapy avoids the need for hospital admission altogether. This is particularly valuable for patients who live far from tertiary care centers, who cannot afford to miss work for a week of hospitalization, or who have family responsibilities that prevent prolonged absence from home. Oral ofloxacin can be administered in basic health units or even at home with appropriate follow-up.

However, careful patient selection is essential. Oral ofloxacin should only be used in patients with uncomplicated SBP (hemodynamically stable, without encephalopathy, renal failure, and gastrointestinal bleeding). Patients with complicated SBP require intravenous antibiotics and hospital-level care.[4] In our study, we excluded such patients, and this likely contributed to the high response rates observed in both groups.

In microbiological profile in our cohort, *Escherichia coli* was the dominant pathogen (54% of positive cultures), consistent with global SBP literature.[14] However, the proportion of *Staphylococcus aureus* (25% of positive cultures) is substantially higher than the 10-15% typically reported from Western centers.[15,16] Similar findings have been reported from other South Asian studies, suggesting that healthcare-associated infections may play a larger role in our setting.[17,18]

The clinical implication is important. Standard empirical therapy with cefotaxime or ofloxacin provides excellent coverage for *E. coli* and other gram-negative enteric organisms but only moderate coverage for *S. aureus*.[19] In patients with risk factors for staphylococcal infection – recent hospitalization, indwelling catheters, prior invasive procedures – clinicians should consider adding vancomycin or another anti-gram-positive agent empirically, especially if the patient does not show clinical improvement within 48-72 hours.[3]

Six patients (10%) failed treatment in our study. Common features of very high initial PMN counts (all above 600/mm³) and advanced cirrhosis (five of six were Child-Pugh class C), suggest that the outcome depends more on the underlying liver

disease severity than the specific antibiotic. For such high-risk patients, clinicians should consider closer monitoring, longer courses of antibiotics (10-14 days instead of 7), and a lower threshold for adding a second antibiotic or transferring to intensive care.[3,4]

Both drugs were well tolerated. The absence of treatment discontinuations due to adverse effects is reassuring, especially for ofloxacin, which was given orally. Mild gastrointestinal symptoms occurred more frequently in the ofloxacin group (10% vs 3%), but none were severe enough to require stopping the medication. No nephrotoxicity, neurotoxicity, or hypersensitivity reactions were observed.

Limitations. Our study has several limitations that should be acknowledged. First, the non-randomized design introduces the possibility of selection bias, though initial features were similar between groups. Second, modest sample size (60 patients) and single centered study. Third, we did not perform a formal cost-effectiveness analysis, which would strengthen the economic argument for oral therapy. Fourth, the culture positivity rate (47%) – while improved by bedside inoculation – is suboptimal compared to high-income country standards, and susceptibility testing was not performed on all isolates due to resource constraints. Fifth, we did not measure drug levels in ascitic fluid or blood, so we cannot confirm adequate absorption in all ofloxacin-treated patients.

Strengths. Despite these limitations, our study has notable strengths. It reflects real-world clinical practice in a resource-limited public hospital, making the findings directly applicable to similar settings. The use of bedside inoculation into blood culture bottles improved culture yield beyond what is typically achieved in Pakistan. Follow-up was complete (no patients lost to follow-up), and the six-month mortality data provide important long-term outcome information.

CONCLUSION

The response of both medications was above 85%. Oral Ofloxacin is an effective and safe alternative to intravenous Cefotaxime for patients with uncomplicated SBP in resource-limited settings. IV Cefotaxime showed better response rate (93% vs 87%) but not statistically significant. Given the substantial cost savings, convenience of oral administration and potential for outpatient or home-based treatment, oral Ofloxacin represents a valuable treatment option where hospital admission or intravenous access poses barriers to care. However, careful patient selection is essential – oral therapy should be reserved for hemodynamically stable patients without encephalopathy, renal failure, or gastrointestinal bleeding. Patients with very high baseline PMN counts or Child-Pugh class C cirrhosis warrant closer monitoring regardless of which antibiotic is chosen.

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