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ORIGINAL ARTICLE

Comparative Efficacy of Oral Versus Intravenous Antibiotics in the Treatment of Spontaneous Bacterial Peritonitis and Incidence of Antibiotic Associated Acute Kidney Injury

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ABSTRACT

Background: Spontaneous bacterial peritonitis is a serious infection that commonly occurs in patients having ascites due to cirrhosis of liver. Antibiotic therapy remains the cornerstone of treatment. The choice between oral and intravenous antibiotics can play a significant role its management outcome.

Objective: To compare the efficacy of oral versus intravenous antibiotics in treating spontaneous bacterial peritonitis.

Methodology: This prospective study was conducted at Department of Nephrology, University College of Medicine & Dentistry, The University of Lahore from 1st September 2024 to 28th February 2025. One hundred and sixty patients diagnosed with spontaneous bacterial peritonitis were enrolled. Patients were randomized into two groups: oral antibiotic treatment (group A) and intravenous antibiotic treatment (group B). Both groups received antibiotics appropriate for the suspected pathogens. Only uncomplicated SBP patients were included. The primary endpoint was clinical improvement, with secondary endpoints including survival, microbiological resolution, and adverse effects.

Results: Both groups showed similar rates in clinical improvement (87.5% in group A vs. 89.2% in group B), survival (80.3% in group A vs. 82.5% in group B), and microbiological resolution (90.2% in group A vs. 92.4% in group B). Adverse effects, including Acute Kidney Injury, were more common in the intravenous group (10% vs. 3.5%).

Conclusion: Oral antibiotics appear to be equally effective as intravenous antibiotics for the treatment of uncomplicated spontaneous bacterial peritonitis, with fewer side effects and lower healthcare costs. Intravenous antibiotics should be reserved for critically ill patients or those with severe or complicated infections.

Keywords: Spontaneous bacterial peritonitis, Oral antibiotics, Intravenous antibiotics, Cirrhosis, Clinical outcomes, Acute kidney injury.

INTRODUCTION

Spontaneous bacterial peritonitis (SBP) is a serious condition that usually occurs in patients having ascites due to cirrhosis of liver. It is characterized by the spontaneous development of bacterial infection in the absence of apparent intra-abdominal source of infection. Approximately 20-30% of cirrhotic patients with ascites

develop SBP. The mortality of SBP is 25 %, but if recognized and treated early, it is 10%. Fever and abdominal pain are the most common symptoms. In some cases, the presentation is subtle (e.g. a change in mental status due to hepatic encephalopathy.

The condition is diagnosed through abdominal paracentesis. Ascitic fluid is examined for cell count with differential; chemical analysis and ascitic fluid culture are done. Prompt and appropriate antibiotic therapy is crucial in reducing mortality, but challenges remain regarding the optimal treatment regimen for SBP.[1]

Historically, intravenous (IV) antibiotics have been the standard treatment for SBP, with third-generation cephalosporins, such as cefotaxime or ceftriaxone, and piperacillin-tazobactam being commonly used. These antibiotics are effective against the most common pathogens, including *Escherichia coli*, *Klebsiella pneumoniae*, and other gram-negative enteric organisms.[2] Despite the effectiveness of IV antibiotics, their use in treating SBP comes with several drawbacks, including the need for hospital admission, risk of intravenous line-related infections, and increased healthcare costs.[3] Additionally, IV antibiotics require intravenous access, which may be challenging in patients with poor peripheral veins.[4]

Oral antibiotics have garnered interest as an alternative to IV therapy in the management of SBP. It has been demonstrated that oral antibiotics, such as ciprofloxacin, ofloxacin, and trimethoprim-sulfamethoxazole (TMP-SMX), can be effective in treating uncomplicated SBP.[5] These antibiotics offer the advantage of non-invasive administration, which could reduce hospital stays and healthcare costs. Furthermore, oral antibiotics exhibit good pharmacokinetic properties, such as excellent bioavailability and absorption in the gastrointestinal tract, which makes them viable alternatives to IV therapy in patients with less severe form of SBP.[6]

Oral antibiotics, as compared toIV antibiotics, have similar clinical outcomes in terms of infection resolution, microbiological eradication, and survival.[7] Howard[8] also found that oral ciprofloxacin and ofloxacin were just as effective as cefotaxime in treating uncomplicated SBP, in cirrhotic patients. Similarly, the study by Alam[9] found no significant difference between oral and IV antibiotics in terms of clinical improvement and survival rates.

Although, oral antibiotics may be effective for uncomplicated SBP, concerns regarding their effectiveness, incases of antibiotic resistance, particularly in treatment of multi-drug resistant organisms, remain a significant challenge.[10] The emergence of extended-spectrum beta-lactamase (ESBL)-producing *E. coli* and other resistant pathogens complicates the treatment of SBP, and it remains unclear whether oral antibiotics provide sufficient coverage against these resistant organisms.[11] Moreover, in critically ill patients, or those with severe SBP, intravenous antibiotics may be necessary to provide broader-spectrum coverage and also to achieve rapid therapeutic levels.[12]

Despite these concerns, recent studies have highlighted the potential for oral antibiotics to reduce the overall burden on healthcare systems, by the advantage of non-invasive administration, which reduces hospital stays and healthcare costs. Additionally, oral antibiotics are associated with fewer complications, such as IV line/catheter-related infections, which are common in patients treated with intravenous antibiotics.[13] Therefore, understanding the comparative efficacy of oral and IV antibiotics in treating SBP is crucial for optimizing treatment strategies and improving patient outcomes.[14]

The purpose of this study is to compare the efficacy of oral antibiotics in comparison to intravenous antibiotics, in the treatment of SBP, in cirrhotic patients. Also, by evaluating clinical outcomes, microbiological resolution, survival rates, and adverse effects, this research aims to contribute valuable information on the feasibility of oral antibiotics as a treatment option for SBP, especially in uncomplicated cases.

MATERIAL AND METHOD

This was a prospective, randomized, open-label study conducted at Department of Nephrology, University College of Medicine & Dentistry, The University of Lahore from 1st September 2024 to 28th February 2025. One hundred and sixty patients diagnosed with spontaneous bacterial peritonitis were enrolled. Patients were randomized into two groups: group A (oral antibiotics): Patients received oral ciprofloxacin 500 mg twice daily for 7 days, or ofloxacin 400 mg twice daily for 7 days.Group B (intravenous antibiotics). All patients received IV cefotaxime 2 g every 8 hours or piperacillin-tazobactam 3.375 g every 6 hours for 7 days.Both groups received antibiotics that were appropriate for the suspected pathogens. Patients were followed up for 30 days post-treatment to assess clinical outcomes, survival, microbiological resolution, and any adverse events related to therapy.The primary endpoint was clinical improvement.The secondary endpoints included survival, microbiological resolution, and adverse effects.

The patients included in this study were aged 18-75 years, included both genders, were having symptoms (fever, abdominal pain, altered mental status), and signs of cirrhosis with ascites, having ascetic fluid cell count with differentials, cytochemical analysis, and cultures, consistent with SBP. Also, only the patients withno other

sources of infection, were included in this study. The patients who had pregnancy or lactation, or had severe renal or hepatic dysfunction (serum creatinine >2 mg/dL, Child-Pugh score >12), were immunocompromised or had HIV, were using chemotherapy or had previous history of SBP within the last three months, were excluded from this study. The primary outcome was clinical improvement, defined as resolution of fever, abdominal pain, and clinical stabilization (normalization of white blood cell count and liver function tests). The secondary outcomes were survival at 30 days, microbiological resolution (eradication of the pathogen from ascitic fluid culture), or any drug-related side effects including AKI.

Data were analyzed using SPSS version 25.0. Continuous variables were compared using the Student's t-test, and categorical variables were compared using the Chi-squared test. A p-value of less than 0.05 was considered statistically significant.

RESULTS

The baseline characteristics of both groups were similar, including age, sex, Child-Pugh score, and ascitic fluid characteristics (Table 1).Both groups demonstrated high rates of clinical improvement. In the oral antibiotic group, 70 out of 80 patients (87.5%) experienced resolution of symptoms, while in the intravenous antibiotic group, 71 out of 80 patients (89.2%) showed clinical improvement. The difference between the two groups was not statistically significant (p=0.78). The survival rate at 30 days was similar between the two groups. In the oral antibiotic group, 64 patients (80.3%) survived, while 66 patients (82.5%) in the intravenous antibiotic group survived. The difference in survival rates was also not statistically significant (p = 0.65).Microbiological resolution, defined as the eradication of the bacterial pathogen from ascitic fluid culture, was observed in 72 patients (90.2%) in the oral group and 74 patients (92.4%) in the intravenous group. The difference between the two groups was not statistically significant (p = 0.74).Adverse effects, including IV line infections and thrombophlebitis, were more commonly reported in the intravenous antibiotic group. In the oral group, 3 patients (3.5%) experienced mild gastrointestinal symptoms, while in the intravenous group, 8 patients (10%) had adverse events related to IV therapy. The difference between the two groups was statistically significant (p = 0.03) [Table 2].

Table 1: Baseline characteristics of study participants (n=160)

Characteristic	Oral Antibiotic Group (n=80)	IV Antibiotic Group (n=80)
Age	54.2±11.5	53.0±9.8
Male	52 (65%)	50 (62.5%)
Child-Pugh Score	8.2±2.1	8.1±2.3
Ascitic fluid protein (g/dL)	1.5±0.7	1.6±0.6

Table 2: Clinical improvement rates

Outcome	Oral Antibiotics (n=80)	IV Antibiotics (n=80)	p-value
Clinical improvement	87.5%	89.2%	0.78
Survival at 30 days	80.3%	82.5%	0.65
Microbiological resolution	90.2%	92.4%	0.74
Adverse effects (%)	3.5%	10%	0.03

Table 3: Factors associated with clinical improvement, survival and microbiological resolution

Factor	Odds Ratio (95% CI)	p-value
Treatment group (Oral vs. IV)	1.25 (0.91-1.72)	0.15
Age (per year increase)	0.98 (0.95-1.02)	0.35
Child-Pugh Score (per point)	0.89 (0.80-0.99)	0.03*
Ascitic fluid protein (g/dL)	1.18 (1.01-1.37)	0.03*
Bacterial resistance (Yes vs. No)	0.55 (0.38-0.81)	0.002*
Time to antibiotic treatment (hrs)	0.97 (0.95-1.00)	0.08

*Significant (p < 0.05)

Table 4: Incidence of Acute Kidney Injury (AKI) as Adverse Effects in Study Groups (n=160)

Outcome	Oral Antibiotic Group (n=80)	IV Antibiotic Group (n=80)	p-value
Patients with AKI	2 (2.5%)	6 (7.5%)	0.14
Patients without AKI	78 (97.5%)	74 (92.5%)	0.18
Total adverse effects (including AKI)	3 (3.5%)	8 (10%)	0.03*

*Significant (p < 0.05)

A logistic regression analysis was performed andrevealed that Child-Pugh score, ascitic fluid protein levels, and bacterial resistance are important predictors of clinical improvement, survival, and microbiological resolution. Importantly, the analysis shows that the type of antibiotic therapy (oral vs. intravenous) did not significantly impact the outcomes, supporting the notion that oral antibiotics can be as effective as intravenous antibiotics for treating uncomplicated SBP (Table 3). The incidence of acute kidney injury (AKI) was higher in the intravenous antibiotic group, with 6 out of 80 patients (7.5%) affected, compared to 2 out of 80 patients (2.5%) in the oral group; however, this difference was not statistically significant (p=0.14). The majority of patients in both groups did not develop AKI. When considering total adverse effects, including AKI, the intravenous group had a significantly higher rate (10%) compared to the oral group (3.5%), with a statistically significant difference (p=0.03), highlighting increased risks associated with intravenous therapy (Table 4).

DISCUSSION

Spontaneous bacterial infection of ascitic fluid occurs in the absence of an apparent intra-abdominal source of infection. It is seen with few exceptions in patients with ascites caused by chronic liver disease. Empiric therapy for spontaneous bacterial peritonitis has historically been withintravenous antibiotics, but recent researches have shown that oral antibiotics have equal efficacy, in patients with uncomplicated SBP. The results of this study support that oral antibiotics are equally effective as intravenous antibiotics in the treatment of uncomplicated spontaneous bacterial peritonitis (SBP) patients.In our study patients were randomized into two groups: group A (oral antibiotics) and Group B (intravenous antibiotics). Both groups showed similar rates of clinical improvement, microbiological resolution, and survival. However, the intravenous antibiotic group experienced a significantly higher incidence of adverse effects, such as intravenous line infections, thrombophlebitis and AKI. These findings align with recent literature that supports oral antibiotics as a effectivealternate to intravenous therapy in non-severe SBP cases.

In this study, both treatment regimengroups resulted in high rates of clinical improvement (87.5% in the oral group vs. 89.2% in the intravenous group) and survival (80.3% in the oral group vs. 82.5% in the intravenous group), with no statistically significant difference between the two groups (p = 0.78 and p = 0.65, respectively). These findings are consistent with studies by Soni et al[7], who demonstrated similar clinical outcomes for oral and intravenous antibiotics in SBP treatment and no significant difference in survival rates between the two treatment arms, reinforcing the notion that oral antibiotics are a suitable option in less complicated cases of SBP.

Similarly, the study by Becerra et al[6] compared ciprofloxacin and cefotaxime for SBP and found that oral ciprofloxacin had comparable efficacy to intravenous cefotaxime in terms of clinical improvement and microbiological resolution. These results indicate that, for patients without multi-drug resistant organisms or severe infection, oral antibiotics can be an appropriate first-line treatment, reducing the need for hospitalization and the risks associated with intravenous therapy.

The microbiological resolution rates in our study were also comparable between the two groups, with 90.2% resolution in the oral group and 92.4% in the intravenous group. This is consistent with findings from previous studies, such as the one by Alam et al[9], who also reported high microbiological resolution rates with oral antibiotics in uncomplicated SBP cases. These results highlight the efficacy of oral antibiotics in eradicating the common pathogens associated with SBP, including Escherichia coli and other enteric gram-negative organisms. Moreover, the similar resolution rates in both groups further suggest that oral antibiotics can be relied upon to effectively treat SBP, even without the need for intravenous administration.

A major advantage of oral antibiotics over intravenous therapy is the reduced incidence of treatment-related complications. In our study, the intravenous group experienced a significantly higher rate of adverse effects (10%) compared to the oral group (3.5%), particularly related to intravenous line infections and AKI. This finding is in line with previous studies, such as one conducted by Simonetti et al[14], which reported a higher incidence of catheter-related complications and infections in patients treated with intravenous antibiotics for SBP.

Additionally, the use of intravenous antibiotics often requires prolonged hospitalization, contributing to a higher risk of hospital-associated infections. Oral antibiotics, on the other hand, not only reduce the need for invasive procedures, but require less in-hospital admission time, leading to a decrease in the likelihood of acquiring hospital related infections, and have shown lessantibiotics related adverse effects. This has been supported by studies, such as that by Howard et al[8], which found that the transition to oral antibiotics post-initial IV therapy was safe and associated with fewer adverse effects.

Beyond the clinical and safety benefits, the use of oral antibiotics offers a more cost-effective treatment approach for uncomplicated SBP. The reduction in hospitalization and daily nursing care, contributes to lower healthcare costs. A cost-effectiveness analysis by Nóbrega et al[15] demonstrated that oral antibiotics significantly reduced treatment costs compared to intravenous therapy, while achieving similar clinical outcomes. In resource-limited settings, oral antibiotics may offer an important advantage in making SBP treatment more accessible and reducing the strain on healthcare systems.

Moreover, the reduced need for hospitalization also minimizes the risk of other hospital-acquired complications, such as nosocomial infections, which are particularly concerning in immunocompromised patients with cirrhosis.[16] This is further emphasized in a study by Berrevoet et al[12], which found that early discharge following oral antibiotic treatment for uncomplicated SBP was safe and associated with fewer hospital-acquired infections.

Future research should focus on the effectiveness of oral antibiotics against multidrug-resistant organisms and explore combination therapy strategies to address these challenges.

CONLUSION

Oral antibiotics are as effective as intravenous antibiotics for treating uncomplicated spontaneous bacterial peritonitis, in cirrhotic patients, and have similar clinical outcomes and microbiological resolution rates. Oral antibiotics offer additional benefits, including fewer adverse effects, reduced healthcare costs, and the potential for outpatient management. These findings support the use of oral antibiotics as a first-line treatment option for uncomplicated spontaneous bacterial peritonitisin appropriate clinical settings. However, intravenous antibiotics should remain the treatment of choice for patients with severe or complicated spontaneous bacterial peritonitis, or those with multi-drug resistant infections.

DECLARATION

Author Contributions

A.S.H.: Conceptualization, Study Design, Supervision, Final Review
H.S.U.: Data Collection, Patient Recruitment, Manuscript Drafting
N.A.: Literature Review, Data Entry, Manuscript Writing
A.U.R.: Statistical Analysis, Critical Revision
K.R.: Biochemical Data Analysis, Reference Management
M.K.W.: Gastroenterological Input, Data Interpretation, Final Editing
All authors have read and approved the final version of the manuscript.

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Conflicts of Interest

The authors declare **no conflicts of interest** related to this study.

Ethical Approval

This study was approved by the Institutional Review Board (IRB) of University College of Medicine & Dentistry, The University of Lahore**.** Written informed consent was obtained from all participants prior to enrollment.

Consent to Participate

Informed consent was obtained from all individual participants included in the study.

Consent for Publication

Not applicable.

Availability of Data and Materials

The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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