Original article

Efficacy of Parenteral Cefotaxime Versus Combination of Piperacillin & Tazobactam as Empiric First Line Therapy in the Treatment of Spontaneous Bacterial Peritonitis

Ajit Khanal[1], Anil Kumar Mishra[2]

Abstract

Introduction: Cefotaxime is the empiric antibiotic of choice for spontaneous bacterial peritonitis (SBP). However, rising gram-positive pathogen rates have prompted consideration of piperacillin-tazobactam as an alternative. This study compares their efficacy in treating SBP among cirrhotic patients.

Methods: Thirty hospitalized cirrhotic patients diagnosed with SBP (ascitic fluid neutrophils > 250/mm^3) were randomized into two groups: 15 received cefotaxime (2g IV twice daily), and 15 received Piperacilin-Tazobactam (4.5 g IV every eight hours), both for five days. More than 25% reduction in neutrophil count after 48 hours defined treatment response.

Results: The response rate was 60% (9/15) in the cefotaxime group vs. 93.3% (14/15) in the piperacillin-tazobactam group (p=0.084). Among patients with prior SBP on quinolone prophylaxis, 75% receiving cefotaxime failed to respond, while 80% receiving Piperacillin-Tazobactam responded.

Conclusion: Piperacillin/Tazobactam is as effective as Cefotaxime and may be superior in patients with prior SBP episodes on prophylaxis. These common clinical scenarios suggest Piperacillin-Tazobactam could be a more suitable empiric first line therapy for SBP in cirrhotic patients.

Keywords: Ascitic fluid analysis; Cefotaxime; Cirrhosis; Neutrophil count; Piperacillin-Tazobactam; Spontaneous bacterial peritonitis(SBP).

Author affiliations:

[1] Department of Gastroenterology, Bir Hospital, Kathmandu, Nepal.

[2] Department of Hepatology, Bir Hospital, Kathmandu, Nepal.

Correspondence:

Dr. Ajit Khanal,
Department of Gastroenterology,
Bir Hospital, Kathmandu, Nepal.

Email: ajit.khanal@gmail.com

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Introduction

Spontaneous bacterial peritonitis(SBP) in cirrhotic patients with ascites is treated with third- generation cephalosporins, intravenous cefotaxime (4-8g/day for 5-7 days), achieving resolution in approximately 90% and 30-day survival in ≥ 80%.[1] However, recent trends suggest rising resistance and increased Gram-positive bacterial prevalence, particularly in nosocomial infections.[2-5] The success rate of cefotaxime and amoxicillin-clavulanic acid in hospital-acquired SBP may be as low as 44%, prompting reconsideration of empirical therapy.[6-8] The International Ascites Club (2000) recommends initiating empirical antibiotics when ascitic fluid Neutrophil count exceeds 250cells/mm³, with repeat paracentesis after 48 hours to monitor response.[1] These guidelines, however, may require reevaluation due to the evolving microbial profiles and resistance patterns. This study aims to compare the efficacy of Cefotaxime versus Piperacillin-Tazobactam as initial empirical therapy in cirrhotic patients with SBP, and also to assess the real-world applicability of current international guidelines.

Methods

This hospital based, prospective interventional study was conducted among 30 consecutive cirrhotic patients diagnosed with spontaneous bacterial peritonitis (SBP), defined by an ascitic fluid Neutrophil count > 250/mm³. Patients were randomized to the Cefotaxime group (4g/day) and Piperacillin-Tazobactam group (4.5g every 8 hours), both administered with renal-adjusted dosing. Inclusion criteria encompassed all cirrhotic patients over 16 years with SBP, regardless of renal status. Exclusion criteria included secondary bacterial ascites, malignancies, hepatocellular carcinoma, peritoneal tuberculosis, peritoneal carcinomatosis, and pancreatitis.

After IRB approval and informed consent, each patient underwent thorough clinical evaluation and diagnostics including CBC, LFT, renal profile, abdominal ultrasound, chest X-ray, ascitic fluid analysis, and other investigations as indicated. A positive response was defined as a ≥ 25% reduction in ascitic fluid Neutrophil count at 48 hours. Negative response patients were switched to alternative intravenous antibiotics. Data analysis was performed using SPSS 21. Quantitative comparisons employed independent t-test; categorical outcomes were assessed using chi-square tests, with statistical significance at $p<0.05$.

Table 1. Age distribution of patients

Age Group(years)	Cefotaxime (%)	Piperacillin(%)
40-44	13.3	6.7
45-49	33.3	33.3
50-54	26.7	20.0
55-59	20.0	33.3
≥60	6.7	6.7

Results

Thirty patients with SBP were studied, evenly divided between the cefotaxime group (n=15) and the piperacillin-tazobactam group (n=15). All patients had ascitic fluid LDH<225U/L and glucose >50mg/dl. Based on demographics, the mean age was 50.93±5.19 years (Cefotaxime) vs. 52.53±4.73 years (Piperacillin-Tazobactam). The age distribution was comparable, with most patients in the 45 to 59 year range across both groups. The cefotaxime group had comparably more patients in the 40 to 44 age group (13.3%) (**Table 1**). The mean ages in the two groups were comparable at a p-value of 0.385 which is statistically insignificant (**Table 3**).

Table 2. Sex distribution of patients

Antibiotic	Males		Females		P value
	N	%	N	%	
Cefotaxime	11	73.3	4	26.7	0.70
Piperacillin	10	66.7	5	33.3	

Male patients made up 73.3% of the cefotaxime group and 66.7% of the Piperacillin/Tazobactam group, showing a notable male predominance in both. Female representation was significantly lower (26.7% in the Cefotaxime group

Table 3. Baseline Characteristics of Patients

Clinical parameters	Cefotaxime (Mean± SD)	Piperacillin/ Tazobactam (Mean± SD)	P value
Mean age (years)	50.93 ±5.19	52.23 ±4.73	0.385
Total WBC	7833.33 ±4556.89	6880.00 ±4118.81	0.553
Neutrophils	70.80 ±7.19	71.67 ±5.23	0.709
Lymphocytes	26.13 ±6.10	24.53 ±5.71	0.464
Platelets	63433.33 ±34598.14	76133.33 ±37069.18	0.340
Total Bilirubin	2.57 ±2.04	2.68 ±1.56	0.873
AST	50.33 ±14.57	52.67 ±13.48	0.652
ALT	33.67 ±8.12	34.67 ±7.43	0.728
PT	23.20 ±5.28	22.13 ±4.50	0.556
Urea	45.47 ±17.80	44.13 ±12.61	0.815
Creatinine	1.01 ±0.22	0.95 ±0.23	0.417
Sodium	134.20 ±4.41	133.53 ±4.17	0.674
Potassium	3.64 ±0.38	3.61 ±0.36	0.805
Hb%	9.67 ±1.54	9.39 ±1.41	0.608
Ascitis Fluid Total Cell Count at admission	600.00 ±313.32	592.67 ±246.85	0.944
Ascitic Neutrophil at admission	444.53 ±212.58	452.27 ±182.72	0.916
Ascitic Fluid Protein at admission	1.32 ±0.33	1.29 ±0.28	0.407
Ascitic Fluid LDH	160 ±26.72	148 ±25.89	0.222
Ascitic Fluid Glucose	69.73 ±8.44	67.6 ±7.45	0.469

Table 4. Ascitic parameters after 48 hours

Clinical parameters	Cefotaxime Mean ± SD	Piperacillin/ Tazobactam Mean ± SD	P value
Ascitic fluid total cells after 48 hrs.	356.67 ±241.33	319.00 ±157.73	0.617
Ascitic Neutrophil after 48 hrs	262.33 ±177.84	228.67 ±129.35	0.558

Table 5. The comparison of responses between first SBP and subsequent SBP presenters

SBP 1st Episode	Response		Total	P value
	Yes	No		
Yes	18(85.7%)	3(14.3%)	21(70%)	0.187
No	5(55.6%)	4(44.4%)	9(30%)	
Total	**23(76.7%)**	**7(23.3%)**	**30**	

and 33.3% in the Piperacillin/Tazobactam group) (**Table 2**). Across all measured clinical parameters- demographic, hematological, biochemical and ascitic fluid analysis- there were no statistically significant differences between the cefotaxime and Piperacillin/Tazobactam groups (**Table 3**).

Both antibiotics showed similar effectiveness in reducing ascitic fluid markers by 48 hours. No statistically significant difference was observed (**Table 4**).

Seventy percent patients experienced the first SBP episode. Out of 30% of those who comprised the subsequent SBP presenters, 88.9% received prophylaxis (55.6% Pip/Tazo, 33.3% cefotaxime). In overall 76.7% showed clinical response where Pip/Tazo group (93.3%) was higher vs. Cefotaxime (60%). Piperacillin/tazobactam demonstrated stronger clinical response and wider prophylactic use, though differences weren't statistically significant. Similarly, the first-time SBP presenter had higher response rates, especially with Piperacillin/Tazobactam (100%). Subsequent presenters responded less consistently across both treatments. Across groups, Pip/Tazo outperformed Cefotaxime, but differences lacked statistical significance (p>0.084) (**Table 6**).

Table 6. Distribution of Patients in the two groups as per SBP episodes

Parameters	Cefotaxime	Piperacillin/ Tazobactam	Total	P value
SBP First Episode				
Yes	11 (73.3%)	10 (66.7%)	21 (70.0%)	1.0
No	4 (26.7%)	5 (33.3%)	9 (30.0%)	
On SBP prophylaxis				
Yes	3 (37.5%)	5 (62.5%)	8 (88.9%)	
No	1 (100%)	0	1 (11.1%)	
Responders				
Yes	9 (60.0%)	14 (93.3%)	23 (76.7%)	0.084
No	6 (40.0%)	1 (6.7%)	7 (23.3%)	
Responses by presentation history				
First-time SBP presenters(responders)				
Yes	8 (72.7%)	10 (100.0%)	11 (52.3%)	0.214
No	3 (27.3%)	0	10 (0.47%)	
Subsequent SBP presenters (responders)				
Yes	1 (25.0%)	4 (80.0%)	4 (44.4%)	0.206
No	3 (75.0%)	1 (20.0%)	5 (55.5)	

Discussion

Stefania Angeloni, Cinzia Leboffe et al[9] in their study in 38 SBP episodes, report treatment success with Cefotaxime in 59% cases, which is almost exact to what we have observed in our study. 41% of Cefotaxime nonresponsive patients required modification of the initial antibiotic therapy to which 87% responded. They also conclude that the initial treatment with Cefotaxime failed more frequently than expected.

Bhat et al[10] in their study tried to see if Cephalosporin is still valid as first line empirical therapy. They also used the ascitic fluid polymorph count at admission as in our study to define SBP, however in contrast, in their study, they used the ascitic fluid polymorph count at 72 hours unlike in our study to define response to treatment. They analyzed records of 600 patients with suspected infection. They found an overall response rate to 3rd generation cephalosporin(ceftriaxone) at 62.8%, which is similar to the result of our study; and 70% for Piperacillin/Tazobactam, which is slightly lower than our result of 93.3%. They observed a response rate of 93.3% for cefoperazone-Sulbactam combination, which is exactly the same as our experience with Piperacillin/Tazobactam.

Felisart et al[11] and Rimola et al[12] reported SBP resolution rates with Cefotaxime at 75% and 71.8% respectively. These values though comparable to our observation are slightly higher.

In our study, we observed response rate to Cefotaxime at 60%, and that to Piperacillin/Tazobactam at 93.3%. We also observed that out of 21 patients with first episode of SBP, 18(85.7%) responded to either of the treatment and 3(14.3%) didn't respond. And out of 9 patients, who had already had previous episode of SBP, 5(55.6%) responded to either of the treatment and 4(44.4%) didn't respond. When we analyzed patients with previous SBP episodes closely, we found that 4 patients in the Cefotaxime group

had previous episodes, out of whom 3 were on prophylaxis with a Quinolone. Out of these patients, 3(75%) didn't respond to treatment while 1(25%) responded. In the Piperacillin/Tazobactam group, out of the 5 patients with previous SBP episodes, all were on quinolone prophylaxis. 4(80%) of them responded to treatment while 1(20%) didn't respond. Although p value was insignificant, it was obvious that more patients on the Cefotaxime group who were on prophylactic antibiotic didn't respond to treatment. The overall better result with Piperacillin/Tazobactam maybe because infection with Gram Positive bacteria in SBP maybe as high as 50% as mentioned by Fernandez et al[2] and as mentioned by them in patients who have had previous episodes of SBP and on antibiotic prophylaxis with a Quinolone, Gram Positive infection is more common and this explains the better performance of Pip/Tazo over Cefotaxime in the subsequent SBP presenters in our study.

Conclusion

Piperaciilin/Tazobactam showed superior clinical response in treating community-acquired SBP, both new and recurrent cases. Although the difference was not statistically significant, the observed trend favors its broader efficacy. The findings suggest the need for larger-scale studies to validate its advantage and potential empiric therapy choices in future.

References

1. Rimola A, Garcia-Tsao G, Navasa M, Piddock LJ, Planas R, Bernard B, Inadomi JM. Diagnosis, treatment and prophylaxis of spontaneous bacterial peritonitis: a consensus document.International Ascites Club. J Hepatol. 2000; 32: 142-153.
2. Fernandez J, Navasa M, Gomez J, Colmenero J, Vila J, Arroyo V, Rodes J. Bacterial infections in cirrhosis: epidemiological changes wi th invas ive procedures and norfloxacin prophylaxis. Hepatology. 2002; 35: 140-148.
3. Singh N, Wagener MM, Gayowski T. Changing epidemiology and predictors of mortality in patients with spontaneous bacterial peritonitis at a liver transplant unit. Clin Microbiol Infect. 2003; 9: 531-537.
4. Cholongitas E, Papatheodoridis GV, Lahanas A, Xanthaki A, Kontou-Kastellanou C, Archimandritis AJ. Increasing frequency of Gram-positive bacteria in spontaneous bacterial peritonitis. Liver Int. 2005; 25: 57-61.
5. Campillo B, Dupeyron C, Richardet JP, Mangeney N, Leluan G. Epidemiology of severe hospital-acquired infections inpatients with liver cirrhosis: effect of long-term administration of norfloxacin. Clin Infect Dis. 1998; 26: 1066-1070.
6. Park YH, Lee HC, Song HG, Jung S, Ryu SH, Shin JW, Chung YH, Lee YS, Suh DJ. Recent increase in antibiotic-resistant microorganisms in patients with spontaneous bacterial peritonitis adversely affects the clinical outcome in Korea. J Gastroenterol Hepatol. 2003; 18: 927-933.
7. Acevedo J, Fernandez J, Castro M et al. Current efficacy of recommended empirical antibiotic therapy in patients with cirrhosis and bacterial infection. J. Hepatol. 2009; 50 (Suppl. 1): S5 (abstract).
8. Umgelter A, Reindl W, Miedaner M et al. Failure of current antibiotic first line regimens and mortality in hospitalized patients with spontaneous bacterial peritonitis. Infection. 2009; 37: 2-8.
9. Stefania Angeloni, Cinzia Leboffe, Parente A et al. Efficacy of current guidelines for the treatment of spontaneous bacterial peritonitis in the clinical practice. World J Gastroenterol. 2008 May 7; 14(17):2757-2762.
10. Bhat G, Vandana KE, Bhatia S, Suvarna D, Pai CG. Spontaneous ascitic fluid infection in liver cirrhosis: bacteriological profile and response to antibiotic therapy. Indian J Gastroenterol. 2013 Sep;32(5):297-301.
11. Felisart J, Rimola A, Arroyo V, PerezAyuso R, Quintero E, Gines P, et al. Cefotaxime is more effective than is ampicillintobramycin in cirrhotics with severe infections. Hepatology. 1985;5:457-62.
12. Rimola A, Salmeron J, Clemente G, Rodrigo L, Obrador A, Miranda M, et al. Two different dosages of cefotaxime in the treatment of spontaneous bacterial peritonitis in cirrhosis: results of a prospective, randomized, multicenter study. Hepatology. 1995;21:674-9.