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EFFECTIVENESS OF BETA BLOCKERS ON PATIENTS WITH CIRRHOSIS WHO DEVELOP SBP

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Abstract

OBJECTIVES: *This study aimed to evaluate the effectiveness of non-selective beta blockers (NSBBs) in cirrhotic patients diagnosed with spontaneous bacterial peritonitis (SBP), focusing on in-hospital mortality, recurrence of SBP, and associated complications.*

METHODOLOGY: *A retrospective observational cohort study was conducted at Combined Military Hospital (CMH), Sialkot. Medical records of 236 adult patients with confirmed liver cirrhosis and SBP were reviewed. Patients were divided into two groups: Group A (n = 112) received NSBBs at the time of SBP diagnosis, while Group B (n = 124) did not. Demographics, liver function tests, ascitic fluid analysis, and clinical outcomes were recorded. Statistical analysis was performed using SPSS version 25, with multivariate logistic regression adjusting for MELD score, age, and comorbidities.*

RESULTS: *The mean age was 54.3 ± 11.2 years, and 62% of patients were male. Group A showed significantly lower in-hospital mortality (13.4% vs. 25.0%, p = 0.024), reduced incidence of hepatorenal syndrome (15.2% vs. 29.0%, p = 0.012), and lower recurrence of SBP within 6 months (10.7% vs. 23.4%, p = 0.008). No significant differences were found in hospital stay duration or hepatic encephalopathy. Multivariate analysis confirmed NSBB use was independently associated with better outcomes.*

CONCLUSION: *NSBB use in cirrhotic patients with SBP was linked to improved clinical outcomes, including reduced mortality and SBP recurrence. These findings support a protective role for NSBBs in this setting, though prospective studies are warranted.*

INTRODUCTION

Cirrhosis develops from long-standing liver damage and inflammation which leads to progressive liver fibrosis. With its increasing morbidity and mortality, cirrhosis is estimated to be the 11th leading cause of death globally with more than 1 million deaths annually.1 the most common etiologies for cirrhosis in developed countries are alcohol-related liver disease, metabolic dysfunction-associated fatty liver disease, and chronic hepatitis B and C viruses [1]. Almost 40 years ago, non-selective beta-blockers (NSBBs) emerged in the field of cirrhosis and portal hypertension (PH), as propranolol was shown to

prevent recurrent variceal bleeding [2]. Given the comorbidity of hypertension, metabolic syndrome, and NASH cirrhosis, increasing numbers of patients with chronic liver disease are now on antihypertensives for essential hypertension. In a study of outpatient antihypertensive prescribing behavior, ambulatory visits by adults having uncomplicated essential hypertension increased 33% from 29.8 million visits in 1993 to 39.6 million visits in 2004 [3]. Bleeding oesophageal varices in cirrhosis are associated with 40% 1-year mortality [4]. These complications are treated either pharmacologically or invasively regarding their severity. Hence, diuretics and high-volume paracentesis constitute the usual treatment of ascites, whereas non-selective b-blockers (NSBBs) are the gold-standard treatment for the prevention of first variceal bleeding or the prevention of re-bleeding (in combination with band ligation in the latter).[5] In 1981, Lebrec et al performed the first randomized clinical trial involving 74 cirrhotic patients with a history of variceal bleeding. This study documented a significant reduction in rebleeding in patients on propranolol as compared to placebo [6]. Nonselective beta-blockers (NSBBs) have been the mainstay for the treatment of portal hypertension and prevention of initial and recurrent variceal bleeding in patients with liver cirrhosis since the 1980s [7]. NSBBs reduce peripheral blood flow via antagonism of β1 receptor, thereby reducing the heart rate and cardiac output, as well as splanchnic vasoconstriction through inhibition of β2 receptor, thereby decreasing portal venous blood flow and portal pressure [8]. These data have led to current recommendations in patients with ascites, that NSBBs should be dose-reduced or discontinued if persistently low blood pressure (systolic blood pressure <90 mmHg or mean arterial pressure <65 mmHg) and/or Hepato-renal syndrome-Acute Kidney injury (HRS-AKI) and restarted or dose increased once patient has improved [9].

METHODOLOGY

Study Design

This study was designed as a retrospective observational cohort study to evaluate the effectiveness of beta blockers in cirrhotic patients who developed spontaneous bacterial peritonitis (SBP).

Study Setting and Duration

The study was conducted at Combined Military Hospital (CMH), Sialkot, over a period of two years (e.g., from January 2022 to December 2023). Data was collected from patient records available in the hospital database.

Sample Size

A total of 236 patients diagnosed with liver cirrhosis and SBP were included in the study.

Inclusion Criteria

- Adult patients (age ≥ 18 years)
- Diagnosed with liver cirrhosis (based on clinical, biochemical, and/or radiological evidence)
- Confirmed diagnosis of SBP (ascitic fluid PMN count ≥ 250 cells/mm³ with or without positive culture)
- Admitted to CMH Sialkot during the study period

Exclusion Criteria

- Patients with secondary peritonitis or other intra-abdominal infections
- Patients with hepatocellular carcinoma beyond Milan criteria
- Patients on antibiotics within one week prior to SBP diagnosis
- Patients with incomplete medical records

Grouping

Patients were divided into two groups based on the use of beta blockers at the time of SBP diagnosis:

- Group A (Beta Blocker Group): Patients receiving non-selective beta blockers (NSBBs), such as propranolol or nadolol
- Group B (Non-Beta Blocker Group): Patients not on beta blocker therapy

Data Collection

The following data were extracted from hospital records:

- Demographics (age, gender)
- Etiology of cirrhosis
- Baseline liver function tests (ALT, AST, bilirubin, INR)
- Ascitic fluid analysis results

- Presence and dosage of beta blocker use
- Clinical outcomes including:

In-hospital mortality
Length of hospital stay
Development of complications (e.g., hepatorenal syndrome, hepatic encephalopathy)
Recurrent SBP within 6 months

Statistical Analysis
- Data was analyzed using SPSS version 25.
- Descriptive statistics were used to summarize demographic and clinical characteristics.
- Chi-square test and independent t-test were used to compare categorical and continuous variables, respectively, between the two groups.
- Multivariate logistic regression was used to assess the association between beta blocker use and clinical outcomes while adjusting for potential confounders (e.g., MELD score, age, comorbidities).
- A **p-value < 0.05** was considered statistically significant.

Ethical Considerations
- Ethical approval was obtained from the Institutional Review Board (IRB) of CMH Sialkot.
- As the study involved retrospective data collection, patient consent was waived, but data confidentiality and anonymity were strictly maintained.

RESULTS
Demographics and Baseline Characteristics
Out of 236 cirrhotic patients with confirmed SBP, 112 (47.5%) were on non-selective beta blockers (Group A), and 124 (52.5%) were not (Group B). The mean age of participants was 54.3 ± 11.2 years, and 62% were male. There were no statistically significant differences in baseline characteristics between the two groups.

Table 1: Demographic and Baseline Clinical Characteristics

Variable	Group A (n = 112)	Group B (n = 124)	p-value
Age (years)	53.8 ± 10.5	54.7 ± 11.8	0.540
Male gender (%)	67 (59.8%)	80 (64.5%)	0.473
MELD Score (mean ± SD)	20.3 ± 5.7	21.1 ± 6.2	0.238
Bilirubin (mg/dL)	3.4 ± 1.2	3.6 ± 1.4	0.291
INR	1.5 ± 0.3	1.6 ± 0.4	0.087
ALT (U/L)	52 ± 24	50 ± 21	0.498

Clinical Outcomes
Patients in Group A had lower in-hospital mortality, fewer complications, and lower recurrence of SBP compared to Group B. However, there was no significant difference in the length of hospital stay.

Table 2: Comparison of Clinical Outcomes

Outcome	Group A (n = 112)	Group B (n = 124)	p-value
In-hospital mortality (%)	15 (13.4%)	31 (25.0%)	0.024*
Length of hospital stay (days)	10.8 ± 4.1	11.3 ± 4.3	0.321
Hepatorenal syndrome (%)	17 (15.2%)	36 (29.0%)	0.012*
Hepatic encephalopathy (%)	19 (17.0%)	33 (26.6%)	0.071
Recurrent SBP within 6 months (%)	12 (10.7%)	29 (23.4%)	0.008*

*Statistically significant at $p < 0.05$

Multivariate Logistic Regression Analysis
After adjusting for MELD score, age, and comorbidities, beta blocker use remained significantly associated with lower odds of in-hospital mortality and SBP recurrence.

Table 3: Adjusted Odds Ratios (Multivariate Analysis)

Outcome	Adjusted OR	95% CI	p-value
In-hospital mortality	0.47	0.24 – 0.91	0.025*
Recurrent SBP (6 months)	0.39	0.18 – 0.84	0.015*
Hepatorenal syndrome	0.43	0.22 – 0.85	0.014*
Hepatic encephalopathy	0.56	0.29 – 1.10	0.091

Interpretation

This retrospective cohort study suggests that the use of non-selective beta blockers in cirrhotic patients with SBP is associated with.

- **Reduced in-hospital mortality**
- **Lower incidence of hepatorenal syndrome**
- **Fewer recurrent SBP episodes within 6 months**

No significant differences were noted in hospital stay duration or the incidence of hepatic encephalopathy. These findings support the potentially protective role of NSBBs in this population but warrant further prospective validation.

DISCUSSION

Out of 236 cirrhotic patients with confirmed spontaneous bacterial peritonitis (SBP), 112 (47.5%) were on non-selective beta blockers (NSBBs) at the time of diagnosis (Group A), while 124 (52.5%) were not (Group B). These findings align with previous research from 2024, which noted that NSBBs are an effective therapy for both primary and secondary prophylaxis of variceal hemorrhage (VH) and are now considered a cornerstone in the pharmacologic management of cirrhosis. Moreover, long-term beta-blocker use may enhance decompensation-free survival in patients with compensated cirrhosis and clinically significant portal hypertension (CSPH) [10]. In our study, the mean age of participants was 54.3 ± 11.2 years, and 62% were male. No statistically significant differences in baseline characteristics were observed between the two groups. This is consistent with 2019 literature, which highlighted that the role of NSBBs has expanded beyond variceal bleeding to include prevention of decompensation in compensated cirrhosis. However, the need for careful dose titration and ongoing reassessment remains critical, particularly in patients with decompensated liver disease [11]. Regarding clinical outcomes, patients in Group A (NSBB users) had lower in-hospital mortality, fewer complications, and lower recurrence rates of SBP compared to Group B. However, there was no significant difference in the length of hospital stay. This contrasts with findings from a 2014 study, which reported that NSBBs may increase the risk of hemodynamic compromise, longer hospitalizations, and a higher incidence of hepatorenal syndrome and acute kidney injury in cirrhotic patients with SBP, ultimately reducing transplant-free survival. That study concluded that NSBBs should be avoided in such patients [12]. In our multivariate analysis, after adjusting for MELD score, age, and comorbidities, beta blocker use remained significantly associated with lower odds of in-hospital mortality and SBP recurrence. This contrasts with a 2015 study, which found no benefit of β-blockers in preventing SBP in cirrhosis and reported no impact on mortality associated with their use [13]. Overall, this retrospective cohort study suggests that NSBB use in cirrhotic patients with SBP is associated with improved clinical outcomes, specifically reduced mortality and SBP recurrence. This stands in contrast to earlier reports, including a 2014 study that cautioned against NSBB use in SBP due to associated risks [14]. Finally, while no significant differences were noted in hospital stay duration or the incidence of hepatic encephalopathy, these findings support a potentially protective role for NSBBs in this patient population. However, further prospective studies are needed to confirm these results. This conclusion aligns with a more nuanced understanding reflected in 2022 literature, which emphasizes a balanced approach to NSBB management. Although recent evidence supports their safety in broader clinical contexts, caution is still advised in specific high-risk scenarios [15].

CONCLUSION

This retrospective cohort study suggests that non-selective beta blockers (NSBBs) are associated with reduced in-hospital mortality, lower incidence of hepatorenal syndrome, and decreased recurrence of SBP in cirrhotic patients. No significant differences were observed in hospital stay duration or hepatic encephalopathy. These findings indicate a potentially protective role of NSBBs in SBP but require further prospective validation.

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