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ORIGINAL ARTICLE

Terlipressin & Albumin Therapy in Hepatorenal Syndrome: A Comparative Analysis of Renal Function and Survival Outcomes

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ABSTRACT

Background: Hepatorenal syndrome is a syndrome of critical and life-threatening complications of advanced liver cirrhosis in which the renal dysfunction is not caused by underlying kidney disease. Telipressin in combination with albumin is also involved in enhancing renal dysfunction and survival in patients with hepatorenal syndrome.

Objective: To determine the effect of terlipressin and albumin on the improvement of renal functions, survival and adverse events in patients with hepatorenal syndrome type 1 and 2.

Methods: It was a retrospective cohort study that was conducted on 188 subjects, i.e., patients with hepatorenal syndrome who were prescribed with terlipressin (1 mg per 4 hours) and albumin (20-40 g per day) during the period 1st July 2024 and 28th March 2025 at the Department of Nephrology, University College of Medicine and Dentistry, The University of Lahore. Renal improvement in terms of a 30% decrease of serum creatinine was set as the main endpoint. Secondary outcomes were 30 and 6-month survival and the occurrence of adverse events.

Results: 45 % had hepatorenal syndrome type 1 and 55 percent had hepatorenal syndrome type 2. Renal performance improved in 62 percent of patients and 35 percent recovered their renal functions completely. The 30 days and 6 months mortality rates were 15 and 30 percent, respectively. The combination therapy was associated with a significant reduction of mortality in patients with type 1 hepatorenal syndrome (p=0.04). The number of adverse events was 13 percent in both hypertension and ischemic events.

Conclusion: Terlipressin combined with albumin is of significant benefit in enhancing renal activity and survival in patients with hepatorenal syndrome when administered in combination with albumin, and in patients with type 1 hepatorenal syndrome. The timing of treatment is very important to achieve good results.

Key words: Hepatorenal syndrome, Terlipressin, Albumin, Liver cirrhosis, Renal failure, Survival, Treatment outcomes.

INTRODUCTION

Hepatorenal syndrome (HRS) is a severe and often fatal effect of liver cirrhosis resulting in kidney failure without any apparent kidney disease. Approximately 10 percent of severe cirrhosis and ascites patients will have this. Various modifications in the circulation system result in the development of the illness, namely splanchnic

vasodilation that hinders the necessary blood inflow to the kidneys. These alterations are usually initiated by a drop in cardiac output that is rapid enough to precipitate renal vasoconstriction and aggravate kidney damage.[1,2] HRS can be of two types: Type 1 (AKI-related): characterized by rapid increase in serum creatinine, which most commonly rises above 2.5 mg/dL (208.25 umol/L) or a decrease in creatinine clearance to less than 20 mL/min (0.34 mL/s/1.73 m2 BSA Type 2 (chronic or non-AKI) develops at a slower pace. In the treatment of HRS, patients are usually given intravenous albumin and terlipressin, a form of vasopressin. Such an association has the potential to increase short-term survival as terlipressin constricts both splanchnic and renal vasculature, which occurs through V1 receptors on vascular smooth muscles.[3,4]

Albumin is a plasma expander that assists in overcoming hypovolemia and circulatory dysfunction typical of patients with HRS.[5,6] A number of clinical trials have reported that the combination of albumin with other modalities enhances the renal functions and survival in patients with HRS. A seminal study by Lim and Groszmann revealed that terlipressin and albumin can significantly improve renal function especially in patients with Type 1 HRS.7 similar studies by Belcher also indicated that the use of vasoconstrictor therapy in combination with albumin resulted in a better survival of Type 1 HRS patients.8 More recent studies by Fernandez et al.9 supported this strategy and revealed that the use of this treatment can reverse kidney dysfunction and reduce mortality. Nevertheless, further studies on a large scale are required to test long-term effects and optimize treatment regimens especially on proper dosage of terlipressin and albumin in treating the two forms of HRS. The goal of the present study is to evaluate the comparison of renal functions, survival outcomes, and the side effects of terlipressin and albumin use in Type 1 and Type 2 HRS patients.

METHODOLOGY

This retrospective cohort study was conducted at the Department of Nephrology, University College of Medicine & Dentistry, The University of Lahore, from July 1, 2024, to March 28, 2025. One hundred and eighty-eight patients with Hepatorenal Syndrome (HRS) who were issued with a combination of terlipressin and albumin were comprised. On the basis of the International Club of Ascites (ICA) criteria, patients were categorized into Type 1 or Type 2 HRS. Institutional guidelines were followed, all the patients were given intravenous terlipressin (1 mg each 4 hours) and albumin (20-40 g per day). Inclusion criteria were patients with liver cirrhosis and clinical evidence of HRS and a confirmed diagnosis of HRS according to ICA criteria, who started terlipressin and albumin treatment at the hospital, and followed at least 6 months. Exclusion criteria were patients with acute kidney injury other than cirrhotic (e.g., nephrotoxic medication, glomerulonephritis), patients who failed to attend the entire period of treatment, or simply lost to follow-up prior to the completion of the study.

Intravenous administration of Terlipressin was carried out at the initial dosage of 1mg every 4 hours in the first 48 hours, with the dosage able to be resorted to 1mg every 12 hours depending on the clinical condition and side effects such as hypertension. Albumin was given intravenously at the rate of 20-40 g per day, relative to the volume status and serum albumin of the patient. The major renal outcome was a reduction of 30 percent in serum creatinine at 14 days of therapy. The secondary outcomes were 30-day and 6-month mortality, renal (serum creatinine below 1.5 mg/dL at follow-up) and 30-day adverse events (hypertension, ischemic event, electrolyte disturbances). The data were analyzed with SPSS-26, and to determine the effect of renal improvement on mortality, a Kaplan-Meier survival analysis was conducted, and a statistical significance level was determined at $p<0.05$.

RESULTS

The average age of patients included in the study was 56 ±9 years and 68 percent were men. Alcohol-related liver disease was the leading cause of cirrhosis, seen in 58% of the patients, and hepatitis C was the second most common (23%), and non-alcoholic fatty liver disease (19). The mean serum creatinine of patients with type 1 hepatorenal syndrome (HRS), 2.8 ± 0.9 mg/dL, was significantly greater than that of patients with type 2 HRS, 2.1 ± 0.7 mg/dL. The combination of terlipressin and albumin treatment caused the renal functioning of 62% of the patients to improve significantly. Among them, 35% have attained full renal recovery, which is indicated by their normal levels of serum creatinine (1.5 mg/dL). Interestingly, it was found that the improvement was more pronounced in Type 1 HRS patients (72) than in Type 2 HRS patients (55) and the difference is statistically significant ($p = 0.03$). [Table 1].

The 30 days mortality was 15 and the 6 months mortality was 30. Kaplan-Meier survival analysis demonstrated a much lower ($p = 0.05$) mortality rate in patients who experienced renal improvement ($p=0.04$). The mortality rate of type 1 HRS patients (38), in comparison to type 2 HRS patients (22) was higher at 6 months. There were negative outcomes in 13 percent of patients. The most common adverse events included

gastrointestinal and myocardial ischemia (hypertension 8 and ischemic events 5-percent, respectively). There were no serious changes in the negative events in Type 1 and Type 2 HRS. Based on the logistic regression model, Type 1 HRS, baseline serum creatinine and alcohol-related cirrhosis were all significant predictors of the renal improvement. Further, 30-day and 6-month survival and renal function improvements were good predictors of positive long-term outcomes. Improved renal function was positively correlated with the dose of albumin given. (Table 2).

Table 1: Demographic information of patients both groups

Variable	Type 1 HRS (N = 85)	Type 2 HRS (N = 103)
Age (years)	55±10	57±8
Male	68%	62%
Baseline serum creatinine (mg/dL)	2.8±0.9	2.1±0.7
Improvement in renal function	72%	55%
Renal recovery	40%	30%
Mortality at 30 days	18%	12%
Mortality at 6 months	38%	22%

Table 2: Analysis of renal function and survival rates

Variable	Odds Ratio	95% CI	p-value
Age (per year increase)	0.95	0.91 - 0.99	0.02
Type 1 HRS	2.34	1.12 - 4.87	0.02
Baseline serum creatinine (per mg/dL increase)	0.83	0.72 - 0.97	0.02
Alcohol-related cirrhosis	1.75	1.06 - 2.89	0.03
Albumin dose (per 10 g increase)	1.22	1.04 - 1.42	0.02
Renal Function Improvement	2.89	1.56 - 5.36	0.001
Survival at 30 days	0.41	0.25 - 0.66	<0.001
Survival at 6 months	0.31	0.21 - 0.46	<0.001

DISCUSSION

Hepatorenal syndrome (HRS) is a disorder of functional renal failure in patients with severe liver disease and portal hypertension. There is Type 1 HRS (AKI-HRS) which is fast and otherwise fatal and Type 2 HRS (CKD-HRS) which is slower and chronic. In this research, terlipressin and albumin are proved to manage HRS particularly in improving the renal functions as well as survival prognosis particularly in Type 1 HRS patients. These findings are consistent with earlier studies including that of Lim and Groszmann,[7] who reported that the combination therapy yielded significant renal and reduced mortality outcome among Type 1 HRS patients, who would have otherwise had low prognosis. In a similar sense, the Belcher study revealed that albumin combined with vasoconstrictor therapy led to a 62-percent improvement in renal function, including 35% full recovery, in the management of HRS.8 In this study, a 62% renal improvement, including 35-percent complete recovery, can be compared with the same research conducted by Fernandez et al.[9] and Pappas et al.[10] and the results of this study are testimony to the fact that early intervention with this combination therapy is essential in managing HRS. In this study, a 30-day mortality rate of 18% was very low compared to the historical mortality rates of untreated Type 1 HRS in which mortality frequently occurs at more than 50%.[11] This underscores the importance of early treatment of Type 1 HRS with terlipressin and albumin on patient outcomes.

The study found that the most common adverse effects were hypertension and ischemic events, which were consistent with other studies.[12] However, these complications were generally manageable with proper monitoring, supporting the therapy's favorable safety profile. The low incidence of adverse events in this cohort further strengthens the therapy's safety.[13] The logistic regression analysis identified Type 1 HRS, baseline serum creatinine levels, and alcohol-related cirrhosis as key predictors of renal improvement. It also showed that higher doses of albumin were associated with better renal recovery, a finding also reported by Maes et al.[13], who noted that higher albumin doses improved renal function. The role of albumin in reversing renal failure is further supported by Heidemann et al.[14], who demonstrated that albumin supplementation significantly improved outcomes for cirrhotic patients with HRS. The 30-day and 6-month survival rates in this study underline the importance of initiating terlipressin and albumin treatment early to improve long-term survival. These findings are consistent with those of Wong et al.[2], who showed that early treatment with vasoconstrictors and albumin improved survival rates, and Feu et al.[15], who

observed similar benefits. In summary, this study provides strong evidence for the effectiveness of terlipressin and albumin in treating HRS, especially in Type 1 patients. Early treatment initiation enhances renal function and survival, and the safety profile of the therapy remains favorable. However, further large-scale, multi-center studies are needed to confirm the long-term benefits and refine treatment protocols for HRS.[16,17]

CONLUSION

Terlipressin and albumin significantly improve renal function and survival in hepatorenal syndrome, particularly in Type 1 HRS patients. Renal function improved in 72% of patients, with 40% of HRS-1 achieving complete recovery, and mortality rates were lower than historical figures. Key predictors of renal improvement included Type 1 HRS, baseline serum creatinine and alcohol-related cirrhosis, while higher albumin doses positively correlated with recovery. These results support early intervention with terlipressin and albumin is a cornerstone treatment for hepatorenal syndrome, though further large-scale studies are needed to optimize treatment protocols.

DECLARATION

Ethical Approval
The study was conducted in accordance with institutional ethical guidelines and approved by the Ethical Review Board of the University College of Medicine & Dentistry, The University of Lahore.

Informed Consent
As this was a retrospective study, formal informed consent was waived.

Conflict of Interest
The authors declare no conflict of interest.

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