ORIGINAL ARTICLE

Efficacy of Terlipressin and Albumin for treatment of Hepatorenal Syndrome of a tertiary care hospitals

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ABSTRACT

Background: Hepatorenal syndrome (HRS) is a fatal complication of advanced cirrhosis with ascites and liver failure, with nearly 50% of patients dying within 2 weeks after the onset. HRS reportedly occurs in 7%–15% of patients with advanced cirrhosis and ascites; the estimated annual incidence of HRS in the United States is approximately 9,000–14,000 patients
Aim: To compare the efficacy of Terlipression and albumin for treatment of hepatorenal syndrome
Setting: Department of Medicine, East Medical Ward , Mayo Hospital, Lahore.
Duration: .From January to December 2019.
Methods:: Randomized control trial. Patients were randomly allocated in 2 groups by using computer generated random numbers table,30, 30 patients included in Group A and Group B. Terlipression plus Albumin was given in group A and dopamine was given in group B. Independent sample t test was applied for continuous variables and chi square test was used for categorical parameters. P value < 0.05 was considered as statistically significant
Results: The mean age of Group A was 38.43±10.94years and the mean age of Group B was 40.56±12.44years. There were 13(43.3%) and 12(40%) females in group A while there were 17(56.7%) females and 18(60%) females in group B. Among groups, Efficacy was present in 21(70%) in group A patients out of which 30 cases. But among controls, Efficacy was present in 12(40%) in group B patients out of which 30 cases. There was statistically significant difference was observed between both groups (p<0.001)
Conclusions: Terlipressin with albumin an effective therapeutic intervention for hepatorenal syndrome as compare to dopamine
Key words: Terlipressin, Albumin, Hepatorenal syndrome,,

INTRODUCTION

Hepatorenal syndrome (HRS) is a fatal complication of advanced cirrhosis with ascites and liver failure, with nearly 50% of patients dying within 2 weeks after the onset[1]. Hepatoreanl syndrome is the development of functional renal failure in patients with advanced liver disease and renal portal hypertension, is the setting of chronic hepatitis and acute hepatic failure.

HRS reportedly occurs in 7%–15% of patients with advanced cirrhosis and ascites; the estimated annual incidence of HRS in the United States is approximately 9,000–14,000 patients[2] The prognosis for HRS-1 is poor, with more than 80% mortality within 3 months and a median survival time of only 2–4 weeks if left untreated[3].

Terlipressin has been studied extensively as a splanchnic vasoconstrictor for HRS-1 treatment. Substantial data from clinical investigations and published meta-analyses have provided evidence that terlipressin improves renal function, which is the primary goal of therapy in HRS-1 patients[4,5]. In another study was done in 2016, Terlipressin plus albumin was associated with greater improvement in renal function vs albumin alone in patients with cirrhosis and HRS-1. Patients had similar rates of HRS reversal with terlipressin as they did with albumin[6].

In one study, hepatorenal syndrome is common and is major issue in liver transplantation. There is no effective hepatorenal syndrome medical treatment. Forty-six patients with cirrhosis and hepatorenal syndrome, were randomly assigned to receive either terlipressin (1-2 mg/4 hour, intravenously), a vasopressin analogue, and albumin (1 g/kg followed by 20-40 g/day) (n = 23) or albumin alone (n=23) for a maximum of 15 days. Treatment with Terlipressin and albumin in patients with cirrhosis and hepatorenal syndrome as compared to albumin[7]. Terliprissin is currently studied vasopressin analogue, the administration of Terlipressin and albumin significantly improve glomerular filtration rate and increasing the arterial pressure and reduction in serum creatinine in 42 to 77& of cases[2].

The rationale of the study, role of the Terlipression and albumin combine effect on hepatorenal syndrome. The objective of the study was to compare the efficacy of Terlipression and albumin for treatment of hepatorenal syndrome

MATERIAL AND METHODS

This randomized control Trial was conducted in the Department of Medicine, Mayo Hospital, Lahore. Data was collected from Department of Medicine of the above mentioned hospitals to complete the sample size and strictly fulfilling selection criteria during a period of one year i.e. from: Janurary to December 2019 . Sample size of 60 patients is estimated using 95% confidence level, 5% margin of error and taking expected frequency of Renal

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syndrome as sample technique was simple random sampling.

Inclusion Criteria:

Patients aged between 20-70years, both genders

Only hepatorenal failure diagnosis patients included.

Cretanine level > 2.0mg.dl

Exclusion Criteria: Pregnant females. Allergic of any medicine, ESRD. Liver transplant, cardiac patients .

Data Collection Procedure: 60 patients of hepatorenal syndrome, who were admitted in East medical ward mayo hospital, fulfilling the inclusion criteria was included in the study. Informed consent was obtained. Demographic details of patients (name, age, sex, BMI) were obtained. Patients were randomly allocated in 2 groups by using computer generated random numbers table,30, 30 patients included in Group A and Group B. Terlipression plus Albumin was given in group A and dopamine was given in group B. After detailed clinical history and examination, complete blood count, liver function tests, renal function tests, serum electrolytes, urine complete examination and abdominal ultrasound were carried out in all patients. All patients were given intravenous albumin 1g/kg up to maximum of 100 gm. Ascitic fluid was examined for differential count, biochemistry and culture. All the data was recorded in proforma.

Data Analysis plan: SPSS version 21.0 was used to enter and analyzed the data. Quantitative variables were expressed as mean ± standard deviation (SD) while qualitative variables were given as percentage. Independent sample t test was applied for continuous variables and chi square test was used for categorical parameters. P value < 0.05 was considered as statistically significant.

RESULTS

In this study, we included 60 patients; 30 group 1 (Terlipressin) and 30 for group B (Albumin). The mean age of group A was 38.43±10.94years and the mean age of group B was 40.56±12.44years. There were 13(43.3%) and 12(40%) females in group A while there were 17(56.7%) females and 18(60%) females in Group B (Table 1).

Before treatment, the mean AST of Group A was 42.96±13.35/liter while mean AST of Group B was 56.10±12.74 / liter that was AST value increase the normal range. The mean ALT of Group A was 56.26±13.56 / liter while mean ALT of Group B was 55.70±13.21/liter. There was significantly high AST and ALT among Group A as compared to Group B (p<0.001). The mean creatinine of Group A was 2.85±1.47/liter while mean creatinine of Group B was 3.54±1.08/liter. There was significantly high in normal range of Group A as compare to Group B. Table 2

After treatment, the mean AST of group A was 31.33± 8.73/liter while mean AST of group B was 34.76±5.95/ liter that was AST value decrease the normal range. The mean ALT of group A was 32.80±12.51/ liter while mean ALT of group B was 36.13±7.43/liter. There was significantly high AST and ALT among group A as compared to group B (p<0.001). The mean creatinine of group A was 1.12±0.36/liter, While mean creatinine of group B was 1.38±0.59/liter. There was significantly low in normal rang group A as compare to group B (Table 2).

Among groups, Efficacy was present in 21(70%) in group A patients out of which 30 cases. But among controls, Efficacy was present in 12(40%) in group B patients out of which 30 cases. There was statistically significant difference was observed between both groups (p<0.001) (Table 3).

Table 1: Demographic characteristics of patients

	Group A	**Group B**
N	**30**	**30**
Age (years)	38.43±10.94	40.56±12.44
Gender		
Male	13(43.3%)	12(40%)
Female	17(56.7%)	18(60%)

Table 2: Comparison of Patients before and after treatment

Characteristics	**Group A**	**Group B**	**Signifi-cance**
AST/litre	42.96±13.35	56.10±12.74	0.45
ALT/litre	56.26±13.56	55.70±13.21	0.87
Creatinine mg/dl	2.85±1.47	3.54±1.08	0.43
After Treatment			
AST	31.33± 8.73	34.76±5.95	0.049
ALT	32.80±12.51	36.13±7.43	0.21
Creatinine	1.12±0.36	1.38±0.59	0.23

Table 3: Efficacy of Terlipression combine Albumin with Dopamine

Efficacy	**Group**		**Total**
	Group A	**Group B**	
Yes	21(70%)	12(40%)	33(55%)
No	9(30%)	18(60%)	27(45%)
Total	30(100%)	30(100%)	60(100%)

P value 0.20

DISCUSSION

Chronic liver disease is a common disease in Pakistan due to an extraordinary increase in the incidence of hepatitis B and C viruses. Hepatorenal syndrome is a main cirrhosis complication. Hepatorenal syndrome occurs in critically ill patients with established organ failure and represents a significant management problem.(8) Our results are in keeping with results of several recent trials using Terlipression alone or Terlipressin and albumin together.

Many treatment procedures can be used for hepatorenal syndrome, such as vasoconstrictors and albumin, transjugular intrahepatic stent shunt and extracorporeal albumin dialysis, but vasoconstrictors is the most commonly used therapy due to its therapeutic impact and comfort[9]. Vasoconstrictors also serve as a bridge waiting for liver transplantation at the same time. Terlipressin is the vasoconstrictor that is most successful and commonly used. It can not only reduce portal flow and thus decrease portal pressure, but also decrease the magnitude of systemic vasodilatation, resulting in an increase in systemic blood pressure, which in turn will enhance cardiac perfusion pressure[10] and kidney function.

A very recent study indicates that combined Albumin/Terlipressin treatment appears to be safe and effective in patients presenting with acute hepatorenal syndrome associated with sepsis, further supporting early administration of this treatment .1 this medicine is not available in the USA and Canada up to now[11].

Overall treatment response 70% in our patient series, as judged by dropping creatinine values to or below 1.5 mg/dL was approximately 55% overall, which is in well accordance with previous studies which have indicated terlipressin treatment response in 40–60% of HRS patients[12] In result, combine response of Terlipressin and albumin was seen in 70% of patients as compare to sarwar study response rate was 58.3%[13]. Wang, H et al, response rate of combination of terlipressin and albumin was 58.3%

Complete response to combination of terlipressin and albumin was seen in 70% of patient in our study. Wang, H study was seen in 58.3%response rate of the patients[14]. In a study of 119 patients with HRS by Heidemann J et al., response rate was 55%[15]. Nazar A et al. has shown 46% response with decline in creatinine below 1.5mg/dl in a study of 39 patients[16]. In a small study by Licata A has shown dismal outcome with terlipressin and albumin with response rate of 9.1% in a study of 33 patients[17].

CONCLUSION

Terlipressin with albumin an effective therapeutic intervention for hepatorenal syndrome as compare to dopamine. This treatment is more likely to react to patients with reduced baseline serum creatinine.

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