ORIGINAL ARTICLE

Effectiveness of Terlipressin and Albumin for the Treatment of Hepatorenal Syndrome

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ABSTRACT

Objective: To determine the effectiveness of terlipressinand albumin in the treatment of hepatorenal syndrome. **Study Design:**Randomized control trial.

Place and Duration of Study: Study was conducted at Medical department of Lady Reading Hospital MTI Peshawar for duration of one year from 1stNovember, 2019 to 30thOctober 2020.

Methodology: Ninety six patients of both genders were enrolled in this study. Patient's detailed demographics including age, sex, body mass index were recorded. They were divided into two equal groups; Group I patients received terlipression with albumin while in Group II patients received only albumin. Effectiveness of both medications was examined. Patients were followed for 14-days.

Results:There were 27 (56.25%) females and 21 (43.75%) males in group I with mean age of the patients were40.46 \pm 5.64 years while in group II females were 25 (52.08%) and males were 23(47.92%) with mean age 42.55 \pm 5.15 years. Mean BMI of the patients in group I was 24.22 \pm 6.18kg/m² but in group II mean BMI was 23.61 \pm 6.42 kg/m².Effectiveness in group I was 39 (81.25%) while in group II was 24 (50%).No significant difference was observed regarding 3-months mortality rate with p value <0.05.

Conclusion:We concluded in this study that the terlipression with albumin had higher effectiveness as compared to albumin alone.

Keywords: Hepatorenal Syndrome, Terlipression, Albumin, Effectiveness

INTRODUCTION

HRS is a fatal complication of advanced cirrhosis of ascites and hepatic insufficiency with about 50% of patients dying in 2 weeks after the onset[1]. Hepatorean syndrome is a functional reindeer failure in the production of chronic hepatitis and acute liver failure in patients with advanced liver and renal portal high blood pressure. The estimated annual HRS incidence in the United States is approximately 9 000-14 000 patients[2]. HRS is stated to occur with 7%-15% of patients suffering from advanced cirrhosis and ascites. The HRS-1 projection has been low, with over 80% death in 3 months and just 2-4 weeks median survival, if not treated[3]. Terlipressine was thoroughly researched as an HRS-1 splanchnic vasoconstrictor. Substantial evidence of improved renal function, the main purpose in HRS-1 patients, from clinical studies and publicized meta-analyzes has been shown[4,5]. In 2016 Terlipresin plus albumin was further studied in patients with cirrhosis and HRS-1 in order to increase renal function compared to the albumin alone. The HRS reversal rates were close to those of albumin for patients with terlipressine. [6]

Hepatorenal disease is widespread in one study and represents a significant problem in liver transplantation. No successful medical treatment for hepatorenal syndrome occurs. Forty-six patients were allocated to either terlipressine (1-2 mg/4 hour intravenous), vasopressin analog, and albumin (1 g/kg followed by 20-40 g/day) (n = 23) or albumin alone (n = 23) for up to 15 days. In patients with cirrhosis and hepatorenal syndrome relative to albumin, terlipressin and albumin treatment. [7]Terliprissin has been studied with the analog of vasopressin and the

administration of Terlipressin and albumin substantially increase the blood pressure and serum creatinine reduction in 42 to 77 & of cases2. Terliprissin is currently taught The study's reasoning, the function of terlipression and albumin have a combining effect on liver disease. The purpose of this study was to compare the effectiveness of hepatorenal syndrome terlipression and albumin for treatment.

MATERIAL AND METHODS

This randomized control trial was conducted at Medical department of Lady Reading Hospital MTI Peshawar for duration of one year from 1stNovember, 2019 to 30thOctober 2020.A total of 96 patients of both genders with ages 18 to 65 were enrolled. Patient's detailed demographics including age, sex, body mass index (BMI) were recorded after taking informed written consent. Patients with ischemic heart disease, renal failure and those with no written consent were excluded from this study. The patients were divided intwo equal groups; Group I (terlipression with albumin) while Group II (only albumin) received. Terlipressine was initially treated in patients with 2-4mg/day injected into the group I intravenous albumin 20-40 mg / day in contrast to Group II, 20-40 mg albumin per day for 15 days alone. The value of creatine was >1.5mg.dl. Chi-square and t-tests were conducted to verify maximum data variables and parameters. The data was entered and analyzed through SPSS 24.

RESULTS

There were 27 (56.25%) females and 21 (43.75%) males in group I with mean age of the patients were 40.46±5.64 years while in group II females were 25 (52.08%) and

males were 23 (47.92%) with mean age 42.55±5.15 years. Mean BMI of the patients in group I was 24.22±6.18kg/m² but in group II mean BMI was 23.61±6.42 kg/m². [Table 1).

Variable	Group I (n=48)	Group II(n=48)	
Gender			
Females	27 (56.25%)	25 (52.08%)	
Males	21 (43.75%)	23 (47.92%)	
Mean age(years)	40.46±5.64	42.55±5.15	
Mean BMI (kg/m²)	24.22±6.18	23.61±6.42	

Patients were treated with terlipressin initially 2-4mg per day along with intravenous albumin 20-40mg/day in group I as compared to this group II received 20-40mg albumin alone per a day for duration of 14-days. Regular follow up provided 39 (81.25%) effectiveness in the group I which received terlipression with albumin and as compared to this group II which received albumin only showed 24 (50%) effectiveness. There were no any significant difference was observed regarding 3-months mortality rate with p value<0.05 (Table 2).

Table 2: Comparison of effectiveness between both groups

Effectiveness	Group I		Group II	
	No.	%	No.	%
Yes	39	81.25	24	50
No	9	18.75	24	50
D volue < 0.05				

P-value<0.05

DISCUSSION

Hepatorenal syndrome is one of the terrible terminal conditions in progressive cirrhosis patients. Invariably fatal failure to treat HRS, especially type 1. [8] Hepatorenal syndrome is a major management issue in critical patients with proven organ failure. [9] The results of many recent studies using terlipression alone, or terlipressine and albumin together are consistent with our findings.

In this randomized trial 96 patients of both genders were presented. Majority patients 54.17% were females in this study. Patients were divided into 2-groups. There were 27 (56.25%) females and 21 (43.75%) males in group I with mean age of the patients were 40.46±5.64 years while in group II females were 25 (52.08%) and males were 23 (47.92%) with mean age 42.55±5.15 years. Mean BMI of the patients in group I was 24.22±6.18 kg/m² but in group II mean BMI was 23.61±6.42 kg/m². These findings were comparable to the some previous studies. [10-12]

In a study of 39 patients Nazar A et al. showed a 46 percent reply, with creatinine falling below 1.5 mg/dl. [13] Contrary to a small Licata A report, terlipressin and albumin were shown to be dysfunctionally disadvantaged, with a 9.1% response rate in 33 people. [14] The randomized studies recorded the rates of cumulative answer ranging from 40 percent to 60 percent in multiple meta-analysis. [15,16], in English.In our study patients were treated with terlipressin initially 2-4mg per day along with intravenous albumin 20-40mg/day in group I as compared to this group II received 20-40mg albumin alone per a day for duration of 14-days. Regular follow up provided 39 (81.25%) effectiveness in the group I which received terlipression with albumin and as compared to this group II which received albumin only showed 24 (50%) effectiveness. In a study by Heidemann J et al, 119 patients showed a greater degree of survival than those without a response to terlipressine and albumin. [17]. These aggregate findings indicate a longer durability than albumin alone in response to terlipressin.

In previous research, it has been shown that combined care with albumin/terlipressine in patients with acute hepatorenal syndrome associated with sepsis appears safe and successful and is still supportive in early administration of this medication in the USA and Canada[18]. The overall therapeutic response of 65.7 percent in our patient range was estimated to be about 55 percent, down to or below 1.5 mg/dL, consistent with previous research, which suggested that 40-60 percent of HRS patients receives terlipressinetherapy[19]. The 58.3% response rate in patients was observed in Wang, H study14. The reaction rate was 55% 15 in 119 HRS patients by Heidemann J et al.

Identifying these causes would make it possible to restrict this expensive care to the most likely patients to respond, thereby reducing treatment costs. Literature from our area contains very few reports of HRS therapy. With more and more centers in our country developing liver transplantation programs, studies like ours would make it possible to select a better alternative for treating HRS patients with liver transplantation.

CONCLUSION

In examining hepatorenalsyndrome terlipressine was more effective than albumin only. Patients with lower baseline serum creatinine most likely would follow this therapy.

REFERENCE

- Rajekar H, Chawla Y. Terlipressin in hepatorenal syndrome: 1 Evidence for present indications. Journal of gastroenterology and hepatology. 2011;26:109-14.
- 2 Colle I, Durand F, Pessione F, Rassiat E, Bernuau J, Barrière E, et al. Clinical course, predictive factors and prognosis in patients with cirrhosis and type 1 hepatorenal syndrome treated with Terlipressin: a retrospective analysis. Journal of gastroenterology and hepatology. 2002;17(8):882-8.
- Fabrizi F, Aghemo A, Messa P. Hepatorenal syndrome and 3. novel advances in its management. Kidney and Blood Pressure Research. 2013;37(6):588-601.
- Gluud LL, Christensen K, Christensen E, Krag A. Systematic review of randomized trials on vasoconstrictor drugs for hepatorenal syndrome. Hepatology. 2010;51(2):576-84.
- Schneider AG, Schelleman A, Goodwin MD, Bailey M, 5 Eastwood GM, Bellomo R. Contrast-enhanced ultrasound evaluation of the renal microcirculation response to terlipressin in hepato-renal syndrome: a preliminary report. Renal failure. 2015;37(1):175-9.
- Boyer TD, Sanyal AJ, Wong F, Frederick RT, Lake JR, O'Leary JG, et al. Terlipressin plus albumin is more effective than albumin alone in improving renal function in patients with cirrhosis and hepatorenal syndrome type 1. Gastroenterology. 2016;150(7):1579-89. e2.
- Martín-Llahí M, Pépin MN, Guevara M, Díaz F, Torre A, 7 Monescillo A, et al. Terlipressin and albumin vs albumin in patients with cirrhosis and hepatorenal syndrome: a randomized study. Gastroenterology. 2008;134(5):1352-9.
- 8 European Association for the study of the liver (EASL) EASL clinical practice guidelines on the management of ascites,

spontaneous bacterial peritonitis, and hepatorenal syndrome in cirrhosis. J Hepatol. 2010;53:397–417.

- 9. Hamilton M. Hepatorenal syndrome treatment with terlipressin and albumin. Critical Care. 2000;2(1):6039.
- Nguyen-Tat M, Jäger J, Rey JW, et al. Terlipressin and albumin combination treatment in patients with hepatorenal syndrome type 2. United European Gastroenterol J. 2019;7(4):529-537. doi:10.1177/2050640619825719
- Sarwar S, Khan AA. Hepatorenalsyndrome:Response to terlipressin and albumin and its determinants. Pak J Med Sci. 2016;32(2):274-278. doi:10.12669/pjms.322.9315
- BILAL RAFIQUE MALIK , HAMID KHALIL , MEHWISH EJAZ. Efficacy of Terlipressin and Albumin for treatment of Hepatorenal Syndrome of a tertiary care hospitals. P J M H S Vol. 14, NO. 2, APR – JUN 2020
- 13. Nazar A, Pereira GH, Guevara M, Martin-Llahi M, Pepin MN, Marinelli M, et al. predictors of response to therapy with terlipressin and albumin in patients with cirrhosis and type I hepatorenal syndrome. Hepatology. 2010;51:219–226.
- 14. Licata A, Maida M, Bonaccorso A, Macaluso FS, Cappello M, Craxi A. Clinical course and prognostic factors of

hepatorenal syndrome: a retrospective single center cohort study. World J Hepatol. 2013;5(12):685–691.

- 15. Arroyo V, Fernandez J. Management of hepatorenal syndrome in patients with cirrhosis. Nat Rev Nephrol. 2011;7(9):517–526.
- Cavallin M, Fasolato S, Marenco S, Piano S, Tonon M, Angeli P. The treatment of hepatorenal syndrome. Did Dis. 2015;33(4):548–554.
- Heidmann J, Bartels C, Berssenbrugge C, Schmidt H, Meister T. Hepatorenal syndrome: outcome of response to therapy and predictors of survival. Gastroenterol Res Pract. 2015;2015:457613.
- Runyon BA. Introduction to the revised American Association for the Study of Liver Diseases Practice Guideline management of adult patients with ascites due to cirrhosis 2012. Hepatology. 2013;57(4):1651-3.
- 19. Lata J. Hepatorenal syndrome. World Journal of Gastroenterology: WJG. 2012;18(36):4978.