Original Article

Effect of Terlipressin in Cirrhotic Pts with Different Courses

Frequency of Rebleeding Between Short Course Terlipressin (24 Hours) and Usual Course (72 Hours) Terlipressin in Adult Cirrhotic Patients Presenting with Acute Variceal Rebleeding

Mehreen Zaman[1], Asif Raza Zaidi[2], Ali Hyder[3], Mahesh Kumar[4], Joher Amin[2] and Kashif Malik[2]

ABSTRACT

Objective: To compare frequency of rebleeding between short course terlipressin (24 hours) and usual course (72 hours) terlipressin given as an adjunct to conventional EVBL in adult cirrhotic patients presenting with acute variceal rebleeding.

Study Design:A randomized control trial

Place and Duration of study: This study was conducted at the Department of Gastroenterology, Shaikh Zaid Hospital Lahorefor One Year from July 2016 to June 2017.

Materials and Methods:100 cases were included through Non probability consecutive sampling. Patients were randomized to group A or B using lottery method. Written informed-consent was taken from all included patients. Rebleeding was assessed during 5 days of hospitalization (as per operational definition). All data was entered and analyzed using SPSS version 13.0. Chi-square test was used to compare the significant difference in rebleeding in both groups. A p-value of ≤0.05 was considered significant.

Results: The mean age of the patients was 55.16±5.56 years having 58 (58%) male and 42 (42%) female. Before start of treatment, hematemesis was observed in 45 (90%) randomized to short course which was remained in 5 (10%) patients after treatment. Patients randomized to usual course, hematemesis was observed in 36 (72%) cases which was remained in 4 (8%) patients after treatment. Before start of treatment, melena was observed in 42 (84%) randomized to short course which was remained in 5 (10%) patients after treatment. Patients randomized to usual course, melena was observed in 42 (84%) cases which was remained in 4 (8%) patients after treatment which is highly insignificant. After treatment, rebleeding was observed in 5 (10%) randomized to short course while with usual course, rebleeding was observed in 4 (8%) cases. The difference between both groups was highly insignificant (p>0.05).

Conclusion: It was concluded through results of this study that short course terlipressin is equally effective as usual course. Now we can recommend short course for management of variceal bleed to prevent rebleed instead of usual course.

Key Words: Variceal Bleeding, Rebleed, Endoscopic Band Ligation, Terlipressin, Cirrhosis, Hematemesis, Melena, Hypovolemic Shoc

Citation of articles: Zaman M, Zaidi AR, Hyder A, Kumar M, Amin J, Malik K. Frequency of Rebleeding Between Short Course Terlipressin (24 Hours) and Usual Course (72 Hours) Terlipressin in Adult Cirrhotic Patients Presenting with Acute Variceal Rebleeding. Med Forum 2019;30(2):130-133.

INTRODUCTION

Esophageal variceal bleeding (EVB) is a frequent and severe complication of patients with cirrhosis and is characterized by a high mortality and rebleeding rate[1]. It occurs in 10–20% of cirrhotic patients per year, occurring in 30% of patients with compensated cirrhosis and 60% with decompensated cirrhosis[2]. The guidelines recommended the use of certain vasoactive drugs, such as terlipressin, octreotide, vapreotide or somatostatin, given as an adjunct to the main therapy and continued for 3-5 days (72-120 hours)[3].

Adjuvant pharmacological treatment is the standard of care along with EVL for the control of esophageal variceal bleeding Terlipressin and octreotide are two common agents used as an adjuvant agent in the management of variceal bleeding[4].The risk of re-bleed

[1.] Jinnah Hospital, Lahore.
[2.] Department of Gastroenterology, Shaikh Zyed Hospital, Lahore.
[3.] Department of Gastroenterology, SMBBMU, Larkana
[4.] Department of Gastroenterology, CMCH, Larkana

Correspondence: Mehreen Zaman, Assistant Registrar, Jinnah Hospital, Lahore.
Contact No: 0301-8200133
Email: drmehrynniazl@gmail.com

Received: August, 2018
Accepted: November, 2018
Printed: February, 2019

is highest in the first 5 days which is perhaps the reason for recommendation of the vasoactive agents for the same duration of time[5]. Randomized control trial was conducted comparing frequency of rebleeding in patients of acute variceal bleeding receiving usual course of terlipressin for 72 hours with patients receiving short course of terlipressin for 24 hours.[6]
Multiple single arm studies are available regarding rebleeding frequency in the usual and short course group. A study shows that the rate of rebleeding was 20% in patients of acute variceal bleed receiving terlipressin for 24 hours[7]. The aim of to compare frequency of rebleeding between short course terlipressin (24 hours) and usual course (72 hours) terlipressin given as an adjunct to conventional EVBL in adult cirrhotic patients presenting with acute variceal rebleeding.

MATERIALS AND METHODS

A Randomized control trial was carried out in the inpatient wards of Shaikh ZaidHospital Lahore. 100 patients presenting with acute variceal hemorrhage having both sex between age 30-60 years with hematemesis (frank blood or coffee ground emesis) and Malena (black tarry stools) were included. Patients were randomized to group A or B using lottery method of allocation using random number technique. Approval of the ethical committee was sought and all ethical considerations were strictly observed. Thorough history was taken and complete physical examination was performed. Routine lab investigations was done to take initial hemostasis and resuscitation. Both groups received the Terlipressin as a bolus of 2 mg followed by 1mg every 6 hours for the first 24 hours and endoscopic variceal band ligation was performed in all patients within 12 hours of admission.Group A: Short course terlipressin (SCT 24 hour group):After the initial 24 h of terlipressin, the patients received "terlipressin dummy" containing 5 % dextrose water administered every 6-h intervals for the following 48 h, in a 5 ml pre-filled syringe. Group B:Usual course terlipressin (UCT 72 hour group):The patients continued to receive "active terlipressin" at a dose of 1 mg every 6 h for the following 48 h in a 5 ml pre-filled syringe. All patients were monitor and follow up accordingly to continuous non-invasive cardiac and hemodynamic monitoring including cardiac rhythm, pulse rate, blood pressure, and oxygen saturation. All patients received IV omeprazole 40 mg and prophylactic IV ceftriaxone 2g daily for three days. Antibiotics was stopped if there is no other indication to continue. Statistics: All data was entered and analyzed using SPSS version 13.0. Quantitative data like age was presented by Mean and standard deviation. Qualitative data gender and rebleeding were presented by frequency and percentages. Chi-square test was used to compare the significant difference in rebleeding in both groups. A p-value of ≤0.05 was considered significant.

RESULTS

Total 100 patients were enrolled in this study with the mean age of 55.16±5.56 having 58 (58%) male and 42 (42%) female. The male-to-female ratio was 1.4:1. Out of 100, 81 (81%) patients who presented with hematemesis while 84 (84%) patients with melena. Before start of treatment, hematemesis was observed in 45 (90%) randomized to short course while 36 (72%) cases in usual course and the difference was significant. Melena was observed in 42 (84%) randomized to short course while 42 (84%) cases was observed to usual course, difference was highly insignificant (Table 1).

Table 1: Distribution of Hematemesis& Melena before treatment in accordance with study group.

Variables (N=100)		Study group		Total	p-values
		Short course	Usual course		
Hema-temesis	Yes	45 (90%)	36 (72%)	81 (81%)	0.022
	No	5 (10%)	14 (28%)	19 (19%)	
Melena	Yes	42 (84%)	42 (84%)	84 (84%)	1
	No	8 (16%)	8 (16%)	16 (16%)	

Table No.2: Distribution of Melena, Hypovolemic shock, Hematemesis & Rebleeding after treatment in accordance with studyv group

Variable (n=100)		**Study group (N=100)**		**Total**	**p-value**
		Short course	**Usual course**		
Melena	Yes	5 (10%)	4 (8%)	9 (9%)	0.727
	No	45 (90%)	46 (92%)	91 (91%)	
Hypovo-lemic shock	Yes	4 (8%)	3 (6%)	7 (7%)	0.695
	No	46 (92%)	47 (94%)	93 (93%)	
Hemate-mesis	Yes	5 (10%)	4 (8%)	9 (9%)	0.727
	No	45 (90%)	46 (92%)	91 (91%)	
Rebleeding	Yes	5 (10%)	4 (8%)	9 (9%)	0.727
	No	45 (90%)	46 (92%)	91 (91%)	

After treatment, melena was observed in 5 (10%) randomized to short course while 4 (8%) cases in usual course while hypovolemic shock was observed in 4 (8%) randomized to short course and 3 (6%) cases in usual course. Moreover, hematemesis was observed in 5 (10%) randomized to short course while4 (8%) cases

in usual course. Rebleeding was observed in 5 (10%) randomized to short course while4 (8%) cases in usual course, but all the difference were highly non-significant (Table 2)

DISCUSSION

The management of VB remains a clinical challenge with a high mortality. Standardization in supportive and new therapeutic treatments seems to have improved survival within the last 25 years. Terlipressin and somatostatin and analogues are the two types of medicine, which has been evaluated. In meta-analysis, only Terlipressin have demonstrated effects on control of bleeding and on mortality.[8]

It has been concluded in recent placebo controlled trials that terlipressin is as safe as other commonly used treatments for acute VB. It significantly reduces the mortality of VBcompared to placebo, and this beneficial effect persists even when the analysis is limited to high quality studies. When used as an adjuvant to endoscopic sclerotherapy, terlipressin improves hemostasis, and has an effect on reducing mortality that approaches statistical significance. Therefore, these data support the use of terlipressin as initial treatment of acute VB, with or without adjuvant endoscopic treatment[9].

Before start of treatment, hematemesis was observed in 45 (90%) randomized to short course which was remained in 5 (10%) patients after treatment. Patients randomized to usual course, hematemesis was observed in 36 (72%) cases which was remained in 4 (8%) patients after treatment. Melena was observed in 42 (84%) randomized to short course which was remained in 5 (10%) patients after treatment. Patients randomized to usual course, melena was observed in 42 (84%) cases which was remained in 4 (8%) patients after treatment. Hypovolemic shock was observed in 4 (8%) randomized to short course while in 3 (6%) cases randomized to usual course. The difference between both groups was highly insignificant ($p>0.05$). This showed no difference between both groups.

After treatment, rebleeding was observed in 5 (10%) randomized to short course while in 4 (8%) cases randomized to usual course. The difference between both groups was highly insignificant ($p=0.727$). This showed that both treatment regimens are equally effective in preventing rebleeding.One randomized trial compared short and usual course of terlipressin. A total of 130 eligible patients were randomized to receive terlipressin for 24 hours short course or 72 hours usual course. There was one failure to control VB (1.5%) in usual course and none in short course terlipressin ($p = 0.50$). The 30-day re-bleeding rate was 1.5% and 3.1% in usual course, and short course terlipressin, respectively ($p = 0.50$). The 30-day failure to control bleeding was observed in 14 patients; seven in each group ($p = 0.494$). It was concluded that in patients with VB, a 24-h course of terlipressin is as effective as a 72-h course when used as an adjunctive therapy to successful EVBL[10]. This was the only reported study of this nature which compared short course with usual course. No more randomized trials are available which compared short and usual course. This also concluded that both methods are equally effective as we found in our study.

CONCLUSION

It was concluded through results of this study that short course terlipressin is equally effective as usual course. Now we can recommend short course for management of variceal bleed to prevent rebleed instead of usual course.

Author's Contribution:

Concept & Design of Study:	Mehreen Zaman
Drafting:	Asif Raza Zaidi, Ali Hyder
Data Analysis:	Mahesh Kumar, Joher Amin, Kashif Malik
Revisiting Critically:	Mehreen Zaman, Asif Raza Zaidi
Final Approval of version:	Mehreen Zaman

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Wang MT, Liu T, Ma XQ, He J. Prognostic factors associated with rebleeding in cirrhotic inpatients complicated with esophageal variceal bleeding. Chinese Med J Beijing 2011;124(10):1493.
2. Amitrano L, Guardascione MA, Manguso F, Bennato R, Bove A, DeNucci C, et al. The effectiveness of current acute variceal bleed treatments in unselected cirrhotic patients: refining short-term prognosis and risk factors. The Am J Gastroenterol 2012; 107(12):1872-8.
3. Angulo P, Kleiner DE, Dam-Larsen S, Adams LA, Bjornsson ES, Charatcharoenwitthaya P, et al. Liver fibrosis, but no other histologic features, is associated with long-term outcomes of patients with nonalcoholic fatty liver disease. Gastroenterol 2015;149(2):389-97.
4. Seo YS, Park SY, Kim MY, Kim JH, Park JY, Yim HJ, et al. Lack of difference among terlipressin, somatostatin, and octreotide in the control of acute gastroesophageal variceal hemorrhage. Hepatol 2014;60(3):954-63.
5. Wang MT, Tao L, Jian HE. Prognostic factors associated with rebleeding in cirrhotic inpatients complicated with esophageal variceal bleeding. Chinese Med J 2011;124(10):1493-7.
6. Salim A, Malik K, Haq IU, Butt AK, Alam A. Comparison of 12-hour with 72-hour terlipressin

therapy for bleeding esophageal varices. J Coll Phys Surg Pak 2017;27:334-7.
7. Wang C, Han J, Xiao L, Jin CE, Li DJ, Yang Z. Efficacy of vasopressin/terlipressin and somatostatin/ octreotide for the prevention of early variceal rebleeding after the initial control of bleeding: a systematic review and meta-analysis. Hepatol Int 2015; 9(1):120-9.
8. Hung TH, Tsai CC, Tseng KC, Hsieh YH, Tseng CW. No mortality difference following treatment with terlipressin or somatostatin in cirrhotic patients with gastric variceal hemorrhage. Saudi journal of gastroenterology: official journal of the Saudi Gastroenterol Association 2016;22(3):220.
9. Rockey DC, Elliott A, Lyles T. Prediction of esophageal varices and variceal hemorrhage in patients with acute upper gastrointestinal bleeding. J Investigative Med 2016; 64(3):745-51.
10. Azam Z, Hamid S, Jafri W, Salih M, Abbas Z, Abid S, et al. Short course adjuvant terlipressin in acute variceal bleeding: A randomized double blind dummy controlled trial. J Hepatol 2012; 56(4):819-24.