COMPARISON OF THE EFFICACY OF OCTREOTIDE VERSUS TERLIPRESSIN IN THE PREVENTION OF EARLY VARICEAL REBLEED AFTER ENDOSCOPIC BANDING AND LIGATION

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ABSTRACT

Objective: To compare the efficacy of terlipressin versus octreotide after endoscopic variceal band ligation (EVL) in prevention of early variceal rebleed.

Study Design: Randomized controlled trial.

Place and Duration of Study: Department of Gastroenterology, Military Hospital, Rawalpindi, from Jan 2011 to Jun 2011.

Material and Method: All patients fulfilling the inclusion criteria were selected through consecutive sampling. Both male and female patients between ages of 30 and 60 years were included in study. All patients received same intravenous antibiotics, intravenous vitamin K, syrup lactulose and underwent upper GI endoscopy with band ligation was done by gastroenterologist. After the procedure, all patients were placed randomly in two groups based on lottery method. Group-A received octreotide and group-B received terlipressin. The group-A received intravenous octreotide at the rate of 50ugm/hour and group-B received terlipressin 1 mg/4 hourly for 5 days after band ligation. Both groups were observed daily for evidence of early rebleed i.e. hematemesis, melena or both. For efficacy to be labelled, both must be absent. End point of the study was the prevention of early rebleed efficiently. Symptoms of hematemesis, melena or both were also recorded in proforma by close monitoring of patient.

Results: Efficacy of terlipressin versus octreotide after EVL in prevention of early variceal rebleed was recorded as 87.69% (n=57) in group-A and 96.92% (n=63) in group-B while remaining 12.31% (n=8) in group-A and 3.08% (n=2) in group-B were not effectively treated, *p*-value was calculated as 0.04 which shows a significant difference in both groups.

Conclusion: Terlipressin was significantly more effective than octreotide once combined with EVL in preventing early variceal rebleed in our study.

Keywords: Esophageal variceal band ligation, Early variceal rebleed, Octreotide, Terlipressin,

INTRODUCTION

Cirrhosis is a chronic disease of the liver resulting into dis organization of hepatic lobule and vascular architecture leading to ascities, spontaneous bacterial peritonitis, hepatic encephalopathy[1]. Major causes of cirrhosis worldwide are attributed to alcohol, hepatitis B infection and hepatitis C infection[2]. Prevalence of cirrhosis is 4-10% and incidence 240 patients per million of inhabitants[3].

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Gastroesophageal varices develop as a result of gradually increasing blood flow which enters the dilated splanchnic bed and the portal vein where blood flow encounters intrahepatic resistance. Porto-systemic collateral veins develop to bypass the cirrhotic liver. The pressure is very high in these collaterals, resulting in the venous walls to expand and form esophageal varices, which eventually may rupture and bleed[4]. Gastroesophageal varices develop in about 30% of patients with compensated cirrhosis and in 60% of patients with decompensated cirrhosis. 10-20% of cirrhotic patients per year present with

Esophageal variceal bleed (EVB)[5]. The presence of gastroesophageal varices is related to the severity of liver disease, 40% of child A patients have varices whereas they are present in 85% of child C patients. Rate of variceal hemorrhage 5% to 15% per year. Moreover, patients with an Hepatic venous pressure gradient (HVPG) >20 mmHg (measured within 24 hours of variceal bleed) are at a higher risk for early rebleeding or failure to control bleeding (83% vs 29%) and a higher mortality in 1st year (64% vs 20%) compared to those patients who have lower pressure. Six hundred and thirty percent of patients with initial bleeding episodes have fatal outcome and approximately 70% of those who survive have recurrent episodes of bleeding. Mortality rate is about 30% within first two weeks after acute bleeding episode[7].

The vasoactive drugs currently used in the management of acute variceal bleeding are terlipressin, somatostatin and octreotide. Data favour the use of terlipressin, as mortality is reduced, and it may have an added role in maintaining renal function. Starting vasoactive therapy before diagnostic endoscopy is supported by trials and prolonged therapy up to 5 days has been used, as this is the period of greatest risk of early rebleeding[8]. Management of patients with bleeding oesophageal varices includes treatment of acute variceal bleeding and prevention of re-bleeding after an initial bleeding episode[9]. A recent study showed early rebleeding rates of 9% in patients treated with octreotide and band ligation[12]. We planned this study with the view to compare the efficacy of terlipressin and octreotide with band ligation in prevention of early variceal rebleeding in local population, so that an effective approach to avoid this dreadful complication could be adopted safely.

MATERIAL AND METHODS

This randomized controlled trial study was carried out at Military Hospital Rawalpindi from Jan 2011 to Jun 2011, which is a tertiary care centre. A total of 130 patients with upper GI bleed presenting to medical emergency fulfilling the inclusion criteria (patients between 30 to 50 years of age, both male and female, having upper GI bleed) were selected through non probability consecutive sampling. Permission was obtained from "Hospital Ethical Committee". Written informed consent was obtained from the patients or their attendants. Name, age, and hospital ID number were entered in the porforma. Both male and female patients between ages of 30 and 60 years were included in study. All patients received same intravenous antibiotics, intravenous vitamin K, syrup lactulose and underwent endoscopy and band ligation was done by gastroenterologist. After the procedure, all patients were placed randomly in two groups based on lottery method. Group-A received octreotide and group-B received terlipressin.

The group-A received intravenous octreotide at the rate of 50ugm/hour and group-B received terlipressin 1 mg/4 hourly for 5 days after band ligation. Both groups were observed daily for evidence of early rebleed i.e. hematemesis, melena or both. For efficacy to be labelled, both must be absent. End point of the study was the prevention of early rebleed efficiently. Symptoms of hematemesis, melena or both were also recorded in proforma by close monitoring of patient. Control of bias and confounding factors was done by strictly following the exclusion criteria. All the data had been analysed through statistical package for social sciences (version 14.0). Mean and standard deviation was calculated for quantitative variables like age of the patient. Frequencies and percentages were calculated for qualitative variables like gender and efficacy. Chi square test was used to compare the efficacy in two groups, age and gender wise distribution among the groups. A *p*-value less than 0.05 was considered significant.

RESULTS

A total of 130 patients fulfilling the inclusion/exclusion criteria were enrolled to compare the efficacy of terlipressin versus octreotide after EVL in prevention of early variceal rebleed. Age distribution of the patients

was done which showed that 36.92% in group-A and 44.62% in group-B were between 30-45 years and 63.08% in group-A and 55.38% in group-B were between 46-60 years of age, mean ± SD was calculated as 46.74 ± 7.58 and 46.37 ± 7.95 respectively, A *p*-value is 0.4. (table-I). Gender distribution revealed 56.92% (n=37) in group-A and 63.08% (n=41) in group-B were male and 43.08%(n=28) in group-A and 36.92%(n=24) in group-B were females (table-II). Comparison of efficacy of terlipressin versus octreotide after EVL in prevention of early varicealrebleed was recorded as 87.69% (n=57) in group-A and 96.92% (n=63) in group-B while remaining 12.31% (n=8) in group-A and 3.08% (n=2) in group-B were not effectively treated, A *p*-value was calculated as 0.04 which shows a significant difference in both groups (table-III).

Table-I: Age distribution among the two study groups (n=130).

Age (in years)	Group-A Octreoitide (n=65)		Group-B Terlipressin (n=65)	
	No. of patients	Percentage (%)	No. of patients	Percentage (%)
30-45	24	36.92	29	44.62
46-60	41	63.08	36	55.38
Total	65	100	65	100
Mean+SD	46.74 ± 7.58		46.37 ± 7.95	

A p-value=0.4

Table-II: Gender distribution among the two study groups (n=130).

Gender	Group-A Octreoitide (n=65)		Group-B Terlipressin (n=65)	
	No. of patients	Percentage (%)	No. of patients	Percentage (%)
Male	37	56.92	41	63.08
Female	28	43.08	24	36.92
Total	65	100	65	100

A p-value=0.47

Table-III: Comparison of efficacy of terlipressin v/s octreotide after endoscopic band ligation in prevention of early varicealrebleed (n=130).

Efficacy	Group-A Octreoitide (n=65)		Group-B Terlipressin (n=65)	
	No. of patients	Percentage (%)	No. of patients	Percentage (%)
Yes	57	87.69	63	96.92
No	8	12.31	2	3.08
Total	65	100	65	100

A *p*-value=0.04

DISCUSSION

Approximately 30% of patients with compensated cirrhosis and 60% of patients with decompensated cirrhosis have gastro esophageal varices[10,14]. Annually 10-20% of cirrhotic patients present with EV Band it is more frequent in those who have large varices[10,11]. Mortality of esophageal variceal bleeding is very high despite appropriate management. In nearly 70-80% of episodes of variceal bleeding endoscopic intervention combined with pharmacologic treatment achieves control of bleeding[13]. In order to control acute esophageal variceal bleeding, EVL has been the recommended preferred procedure although endoscopic injection sclero-therapy (EIS) can also be used in this setting if EVL proves technically difficult[15,16]. Adjuvant pharmacological treatment is recommended along with EVL for the control of esophageal variceal bleeding. Terlipressin and octreotide are two most common agents used as an adjuvant agent along with EVL in the management of variceal bleeding. Both agents have equivalent results to endoscopic therapy in randomized studies[13]. We planned this study with the view to compare the efficacy of terlipressin and octreotide with band ligation in prevention of

early varicealrebleeding in local population, so that an effective approach to avoid this dreadful complication could be adopted safely. In this randomized controlled results reveled that terlipressin (96.92%) is more effective than octreotide (87.69%) in combination with EVL for the prevention of early varicealrebleed. The findings are consistent with a study showing early rebleeding rates of 9% in patients treated with octreotide and band ligation[12]. In our study we found alternate hypothesis that "there is a difference in the efficacy of terlipressin and octreotide in combination with endoscopic band ligation in prevention of early varicealrebleed" is justified and its efficacy to control variceal bleed when used as adjuvant agent in combination with endoscopic band ligation in patients with EVB. Another study of 30 patients showed that terlipressin was more potents to octreotide when pharmacotherapy was used alone in acute EVB[13]. However, another study had shown that both octreotide and terlipressin agents were equally efficacious in the control of EVB[12]. This study has also revealed another important factor that the use terlipressin was associated with shorter hospital stay. This could be due to the fact that higher number of patients in terlipressin had significantly low rate of active bleeding compared to patients in octreotide group at base line when seen at initial endoscopic intervention.

CONCLUSION

Terlipressin was significantly more effective than octreotide in combination with EBL for the prevention of early variceal rebleed.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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