ORIGINAL ARTICLE

Comparison of Carvedilol and Esophageal Variceal Band Ligation for Prevention of Variceal Bleed among Cirrhotic Patients

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ABSTRACT

Background: Variceal bleeding (VB) is one of the major causes of mortality in cases with cirrhosis. Present treatment methods for preventing VB includes β-blockers and esophageal variceal band ligation (EVBL). Carvedilol can reduce portal pressure more as compared to EVBL, but, there is no clinical evidence assessed the effectiveness of carvedilol as primary prophylaxis in cirrhotic patients.

Objective: To compare the frequency of variceal bleed with carvedilol versus esophageal variceal band ligation among cirrhotic patients.

Study design: Randomized control trial.

Setting: Department of Medicine, Mayo Hospital, Lahore.

Duration: 6months.

Methodology: 200 cases were randomized in 2group. In group A, carvedilol 12.5mg daily was given and in group B, EVBL was performed. EVBL in all patients was done by same consultant gastroenterologist. Then patients were shifted to the ward after surgery by researcher himself and were followed-up for 6 months. Patients were assessed during 6 months for variceal bleed.

Results: Mean age of patients was 53.06±14.50 years. There were 58.8% males and 41.2% females. VB was observed in 4.8% cases with Carvedilol and 12.8% with EVBL. The difference was statistically significant (P<0.05).

Conclusion: Our study results concluded that Carvedilol is more beneficial in preventing VB as compared to EVBL in cirrhotic patients.

Keywords: Variceal Bleed, Carvedilol, Esophageal Variceal Band Ligation, Cirrhosis

INTRODUCTION

Cirrhosis affects 3.6/1000 adults and is blamable for 32,000 deaths every year. Variceal bleeding is one of the major cause of cirrhosis-related morbidity and mortality[1]. Mortality rates associated with VB in cirrhotic patients is decreasing within past 4 decades, but the mortality rate is still high in cases of VB[2]. VB occurs when variceal tension overdoes the elastic limit of vessel[3]. Recent mode of treatment for preventing the first episode of VB comprises of beta-blocker and EVBL. EVBL has less chances of bleeding, without risking the life of patient, but β-blockers can be restricted due to adverse effects. Carvedilol is a non-cardio-selective vasodilating β-blocker. It is more beneficial in reducing portal hypertension which may lead to VB[4].

Carvedilol can be used as a prophylaxis for prevention of VBs in patients with cirrhosis. However, the mortality rate due to carvedilol is disputed. Trials on EVBL versus β-blockers for cirrhotic patients have results in equivocal consequences.[5] In literature controversial evidence has been observed i.e. EVBL is superior to β-blockers in preventing VB. In some trial, no mortality occurred either with EVBL and β-blocker. So, the available literature is deficient to recommend EVBL over β-blocker as first-line therapy[6].

Literature has reported that the frequency of VB is less with carvedilol as compared to EVBL but controversial results are also present. Lot of work has been done on prophylaxis management for prevention of VB as mortality rate is higher with VB among cirrhotic patients but still physicians and gastroenterologist focus on EVBL due to controversial results. However, carvedilol may be more beneficial as it is non-invasive and cheap method of preventing VB as compared to EVBL. So we conducted this study to confirm whether carvedilol is beneficial.

The objective of the study was to compare the frequency of variceal bleed with carvedilol versus esophageal variceal band ligation among cirrhotic patients.

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MATERIAL & METHODS

This randomized controlled trial was conducted in the Department of Medicine, Mayo Hospital, Lahore during a period of six months. Sample size was 250 cases (125 cases in each group) with power of test=80%, level of significance=5% and taking expected percentage of VB i.e., 3% in carvedilol and 11% in EVBL among cases of cirrhosis. Sampling technique was consecutive sampling techniques

Sample Selection: Cirrhotic cases aged 30–80 years of either gender having Cirrhosis (i.e. presence of all of the following: increased bilirubin (at least 30 mmol/L), enlarged or shrunken liver on USG, ascites and edema) with esophageal varices on endoscopy (grade I &II). Patients who already develop variceal bleed, pregnant or lactating females, allergic to carvedilol; already taking **β-blocker**, cancer patient and presence of severe systemic illness like cardiac problem (abnormal ECG), BP>140/90mmHg, DM (SBR>200mg/dl), h/o psychiatric disease, COPD or asthma, MAP <55mmHg or HR <50 bpm and portal vein thrombosis (on clinical examination) were not included.

Data collection procedure*:* Informed consent and demographics were obtained. Then patients were randomized in 2groups. In group A, carvedilol 12.5mg daily was given and in group B, EVBL was performed using a multibander device. All EVBL was done by a single consultant gastroenterologist. Then patients were shifted to the ward after EVBL by researcher himself and were followed-up for 6 months. Patients were assessed during 6 months for VB which was measured as hematemesis or melena with endoscopic evidence of VB during 6months of start of treatment. SPSS version 21.0 was used to analyses the data. κ^2 test was applied to compare VB in both groups. P-value≤0.05 was taken as significant.

RESULTS

The mean age of patients was 52.06±14.71 years in carvedilol group and 54.07±14.27 years in EVBL group. There were 147(58.8%) males, out of which 77(52.4%) belonged to carvedilol group while 70 (47.6%) belonged to EVBL group. There were 103 (41.2%) females, out of which 48(46.6%) belonged to carvedilol group while 55(53.4%) belonged to EVBL group. VB was present in 6 cases were taking Carvedilol and 16 underwent EVBL. A significant difference was observed between both groups for occurrence of VB (p-value=0.026) (Table 1).

VB among age > 50 years was observed in 3cases taking Carvedilol and 9 underwent EVBL. The difference was insignificant in patients >50 years old (p-value=0.184). VB among age ≤ 50 years was observed in 3 taking Carvedilol and 7 underwent EVBL. The difference was insignificant in patients ≤50 years old (p-value=0.139). VB among males was observed in 3 cases taking Carvedilol and 5 underwent EVBL. The difference was insignificant in males (p-value=0.139). VB among females was observed in 3 cases taking Carvedilol and 11 underwent EVBL. The difference was insignificant in females (p-value=0.049) (Table 2).

Table 1: characteristics of patients

	Study group	
	Carvedilol	**EVBL**
n	125	125
Age (Years)	52.06±14.71	54.07±14.27
Gender (m/f)	77/48	77/55
Variceal bleed	6 (4.8%)	16 (12.8%)*

*P<0.05

Table 2: Comparison of Variceal bleeds in both study groups

		Study Group		p-value
		Carvedilol	**EVBL**	
<50 years	Yes	3	9	0.184
	No	58	61	
≥50 years	Yes	3	7	0.139
	No	61	48	
Male	Yes	3	5	0.47
	No	74	65	
Female	Yes	3	11	0.049
	No	45	44	

DISCUSSION

In recent decade, several researchers compared EVBL with pharmacological treatment for prophylaxis of VB in cirrhotic patients[7]. So this study was conducted in local set-up. In our study, the mean age of patients was 53.06±14.50 years and 58.80% were males and 41.20% patients were females with male to female ration of 1.4:1. Shah HA et al showed the mean age of the patients 48±12.2 years; 122(72.7%) were males[8]. In Hayes and colleagues study, the mean age of patients was 54years[9]. In our study results VB was observed in 22(8.8%) patients (6 with Carvedilol and 16 with EVBL). According to our study, the difference was significant between both groups (p-value=0.026).

Reiberger et al assessed the response of varicella pressure with carvedilol in patients with failed treatment of propranolol. Among them, 56% maintained their hemodynamics with carvedilol, but 29 cases were managed with EVBL. Significant difference was observed with carvedilol i.e. lower bleeding rate, hepatic decompensation and mortality rate as compared to EVBL[10]. Tripathi et al have recently shown that the rates of VB were lower in cases treated with Carvedilol as compared to EVBL with no significant difference in mortality[11]. This study

along with other reports suggesting a significant decrease in Oxygen delivery in patients undergoing EVBL[12].

One study reported that the frequency of VB was 3% with carvedilol and 11% with EVBL after 6 months of initial treatment. There was significant difference between both groups (p=0.04)[4]. But another study reported that after 6 months the rate of VB was 3.6% with carvedilol and 5.8% with EVBL. The difference was insignificant (p=0.51)[13]. Tripathi et al., found in their study that carvedilol lowers the bleeding rates as compared to EVBL and survival rates were almost same (P>0.05). Carvedilol showed more efficacy in preventing first episode of VB (hazard=0.41; 95%CI; 0.19-0.96 [P 0.04]). Researchers concluded that carvedilol is more effective in preventing VB. It is a better option and can be given as for primary prophylaxis in cirrhotic patients at high-risk of VB[14].

A research conducted in Agha Khan University Pakistan recommended that carvedilol may not be better than EVBL in preventing first episode of VB in cirrhotic patients. Both EVBL and carvedilol had similar frequency of VB (8.5% vs. 6.9%), mortality due to VB (4.6% vs. 4.9%) and overall mortality (12.8% vs. 19.5%)[15]. The findings of Shah et al., also found that carvedilol is not more beneficial than EVBL in preventing VB in cirrhotic patients[8]. Hayes et al., compare carvedilol and EVBL in a randomized trial for the prevention of VB. VB occurred in 10% cases with carvedilol and 23% cases with EVBL[9]. A meta-analysis evaluated 4 randomized trials of EVBL and β-blocker, the risk of VB was reduced by 48% with EVBL compared to β-blocker, but VB-related mortality and all-cause mortality were similar in both groups (P>0.05)[16]. In our trial, among males, VB was found in 3patients with Carvedilol and 5 with EVBL (P>0.05). But among females, VB was found in 3 cases with Carvedilol and 11 with EVBL (p<0.05).

CONCLUSION

Our study results concluded that Carvedilol is more beneficial in preventing VB as compared to EVBL in cirrhotic patients.

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