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Original Article

Comparison of Carvedilol and Endoscopic Band Ligation for the Prevention of Variceal Bleed in Patients of Cirrhosis

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Abstract

Objective: To compare carvedilol & endoscopic band ligation (EBL) for the prevention of variceal bleed in patients of cirrhosis.

Methods: This was a randomized control trial done at North Medical Unit, Mayo Hospital, Lahore from 1st December 2016 to 30th May 2017. After ethical approval of study, 250 patients of cirrhosis were taken through non-probability purposive sampling technique. Informed consent was taken from each patient. After taking demographic details patients were randomly divided into two groups by using simple lottery method. In group A, patients received carvedilol 12.5mg daily orally and in group B, EBL was done using a multibander device. Then patients were followed for 6 months afterwards for variceal bleed. The frequency of variceal bleed in two groups was compared by using Chi square test. P-value < 0.05 was considered significant.

Results: The mean age was 53.06±14.50 years. There were 41.2% females & 58.8% males. Variceal bleed (VB) was observed in 22 patients in which 6 patients were of carvedilol group and 16 were of EBL group. There was significant difference between two groups in response to therapy of VB i.e. p-value=0.026 was significant.

Conclusion: Carvedilol was more effective for VB prevention as compared to EBL in cirrhotic patients.

Keywords: Variceal Bleed, Comparison, Carvedilol, Endoscopic Band Ligation, Cirrhosis.

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Introduction

Variceal bleed is a serious complication of cirrhosis. It is the major reason of morbidity and mortality in patients of chronic liver disease (CLD) as a result of portal hypertension (PH). CLD affects 3.6 people out every 1000 adults and results in 32,000 deaths every year.[1] Due to the advancements in the field of Gastro-enterology in the past few decades, the mortality has decreased to greater extent, but still it's the major killer in patients of CLD.[2] It occurs when portal pressure exceeds in the elastic recoil of esophageal vessels.[3]

There are several pharmacological agents as well as therapeutic measures to prevent variceal bleed in CLD. These are beta-blocker, nitrates and endoscopic band ligation (EBL).[4] Non-selective beta-blocker such as carvedilol is used as a first-line therapy for primary prevention of variceal bleed. However, it has many side effects and has no mortality benefit. EBL has lower chances of bleed & many researches on EBL and beta-blockers have reached equivocal results.[5]

In literature controversial studies have also been found on various agents about prevention of variceal bleed that show EBL is better than beta-blockers. Similarly some trials have also shown that there is no mortality benefit with both the modalities. Current literature doesn't support any agent to be recommended as first line agent.[6]

In a study it was found that after six months of treatment the frequency of VB was very less with carvedilol than EBL (p=0.04).This showed significance difference between two treatment modalities.[4] In another trial, no significant difference was observed between two agents after 6 months of treatment (p=0.51).[7]

The mortality rate is higher among cirrhotic patients presenting with VB. So best treatment modality should be found out. On one side carvedilol is non-invasive and cheaper agent as compared to EBL. So we wanted to conduct this study to have local evidence in our population. So the aim of this study is to compare carvedilol and EBL for the prevention of variceal bleed in patients of cirrhosis.

Methods

This randomized controlled trial was done at North Medical unit, Mayo Hospital, Lahore from 1st December 2016 to 30th May 2017. After ethical approval of study, 250 patients of age 30 – 80 years of either gender with decompensated cirrhosis having grade I & II esophageal varices on endoscopy were included through non-probability, purposive sampling. Sample size was taken with 80% power of test, 5% level of significance and taking expected percentage of variceal bleed as 3% for carvedilol and 11% for EBL. All Patients with prior variceal bleeding, severe systemic illness like hypertension, diabetes mellitus, ischemic heart disease, psychiatric disease, obstructive airway disease, malignancy, portal vein thrombosis , pregnant or lactating females & already on beta-blockers or nitrates or allergic to carvedilol were excluded. Informed consent was taken from all patients. Demographic details were taken from all patients in study. Then by Simple lottery method patients were randomly divided into group A and B. In group A, patients received carvedilol 12.5mg daily orally and in group B, EBL was done using a multiband device. Then all patients were followed for any variceal bleed for 6 months. All the data was recorded on a predesigned proforma. Then it was analyzed using SPSS version 20. Quantitative variables e.g age were calculated as mean+standard deviation. Qualitative variables like gender and variceal bleed were calculated as percentages and frequencies. Chi square test was applied on both groups. P-value < 0.05 was considered as significant. Data was stratified for age, gender and grade of EV and Chi-square test was used taking p-value ≤0.05 as significant.

Results

The mean age was 53.06±14.5 years. Out of 250 patients, 147 (58.8%) were males and 103 (41.2%) females. The mean age in carvedilol group was 52.06±14.71 years with minimum and maximum ages of 30 & 80 years respectively. While the mean age in EBL group was 54.07±14.27 years with minimum age as 31 and maximum age as 80 years. Out of 147 males, 77 (52.4%) were from carvedilol group while 70 (47.6%) were from EBL group. Similarly 48 (46.6%) females were in carvedilol group while 55 (53.4%) were in EBL group.

In our study the 22(8.8%) patients had variceal bleed (VB) and variceal bleed (VB) was not observed in 228(91.2%) patients. Out of 22 patients with variceal bleed 6 patients had bleeding in Carvedilol group and 16 in EBL group. Similarly 119 patients in Carvedilol group and 109 in EBL group had no evidence of bleed on follow up. Statistically a significant difference was observed between the two groups i.e. p-value=0.026.

Total 8 male patients had Variceal bleed (VB), 3 in Carvedilol group and 5 in EBL group. Similarly no VB was seen in 139 patients consisting of 74 Carvedilol group and 65 EBL group patients. Statistically no significant difference was noted between the VB and study groups of the male patients i.e. p-value=0.139. On the other hand, 14 female cases had VB consisting of 3 from Carvedilol group and 11 from EBL group. 89 patients had no evidence of VB with 45 from Carvedilol group and 44 from EBL group. There was no significant statistical difference between the VB and study groups of the females i.e. p-value=0.049.

Table 1: *Descriptive Statistics of Age in Years*

		Study group		Total
		Carvedilol	EBL	
Age (Years)	n	125	125	250
	Mean	52.06	54.07	53.06
	SD	14.71	14.27	14.50
	Minimum	30.00	31.00	30.00
	Maximum	80.00	80.00	80.00

Table 2: *Comparison of Variceal Bleeds (VB) in both Study Groups*

		Study Group		Total
		Carvedilol	EBL	
Variceal bleed	Yes	6	16	**22**
	No	119	109	**228**
Total		**125**	**125**	**250**

p-value=0.026 (Significant)*

Table 3: *Comparison of Variceal Bleeds in both Study Groups with Respect to Gender of Patients (n=250)*

			Study Groups		p-value
			Carvedilol	EBL	
Male	VB	Yes	3	5	**0.47**
		No	74	65	
Female	VB	Yes	3	11	**0.049**
		No	45	44	

Discussion

In this study variceal bleed was noted in 22(8.8%) patients in whom 6 patients were from Carvedilol group

and 16 were from EBL group. According to our study significant difference was noted between VB and study groups i.e. p-value=0.026

Many researchers have studied EBL with carvediolol for the primary and secondary prevention of VB in CLD patients.[8] So this study was planned to see response of our local population. In this study the mean age was 53.06±14.50 years. Shah HA et al noted a mean age of 48 ± 12.2 years and concluded that carvedilol is not superior to EBL in preventing first variceal bleed in cirrhotic patients.[9] In Hayes and colleagues study, it was 54 years. Variceal bleed was noted in 8 patients (10%) of carvedilol group and 17 patients (23%) of EBL group on follow up.[10] Reiberger et al also studied the effect of carvedilol and EBL in 67 propranolol non-responders patients. 38 patients received carvedilol and 29 patients had EBL. They concluded better results with carvedilol (64%).[11] Tripathi et al studied both carvedilol and EBL. They concluded that there was lower bleeding with carvedilol but no mortality benefit.[12] Low oxygen delivery was also noted in EVL patients.[13] The relative hazard was 0.41; and 95% confidence interval was 0.19-0.96 [P 0.04]).[14]

In another study ,VB was lower (3%) with carvedilol as compared to EBL (11%) after 6 months follow up with significant difference between both groups (p= 0.04).[4] But another study concluded VB was 3.6% with carvedilol and 5.8% with EBL with insignificant results (p=0.51).[7]

In another study at Agha Khan University Pakistan it was concluded that carvedilol aand EBL had comparable variceal bleeding (8.5% vs. 6.9%) and related mortality (4.6% vs. 4.9%) and overall mortality (12.8% vs. 19.5%).[15]

A meta-analysis of four trials compared VBL with beta blocker and concluded EBL as better choice, but bleed and mortality were similar in both group.[16] Our study was single centered with relatively small sample size. A larger study can be done to validate these results.

Conclusion

It was concluded that Carvedilol was more effective as compared to EBL for VB prevention in cirrhotic patients.

Conflict of Interest: None

Funding Source: None

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