ORIGINAL ARTICLE

Comparison of Carvedilol and Propranolol in the Treatment of Portal Hypertension in Cirrhosis

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ABSTRACT

Cirrhosis of liver is a major international and national health hazard that causes very significant morbidity and mortality in our country. In Pakistan, the commonest cause of liver cirrhosis is chronic viral hepatitis. Portal hypertension is one of the major complications of liver cirrhosis.[4] Carvedilol is a nonselective β-blocker with α_1-adrenergic blocking activity. It has been shown to decrease portal pressure in cirrhotic patients. Additionally, carvedilol has a greater portal hypotensive effect than propranolol alone in patients with cirrhosis.[9]

Objective: To compare the efficacy of carvedilol and propranolol for the treatment of portal hypertension in patients of liver cirrhosis.

Study Design and Place of Study: It was a randomized clinical trial. This study was conducted in the Department of Medical Unit-II, Sir Ganga Ram Hospital, Lahore. It was six months study from 26th March to 26th September 2010.

Materials and Methods: One hundred patients of liver cirrhosis with portal hypertension were selected for this study. The patients were randomly divided into group A and B by using lottery method. Group A patients were given propranolol 40mg and group B patients were given carvedilol 25mg. Portal flow velocity was measured before and 90 minutes after the administration of the above mentioned drugs by a radiologist on Doppler ultrasonography and more than 20% decrease was considered as efficacy.

Results: The mean age of the patients in group A was 51.6±11.3 years and in group B was 54.6±9.4 years. In group A, there were 37 (74%) male and 13 (26%) female patients and in group B, there were 27 (54%) male and 23 (46%) female patients. In group A, there were 12 (24%) patients had efficacy of treatment and in group B, there were 26 (52%) patients had efficacy of treatment.

Conclusion: It is concluded from this study that carvedilol is more effective than propranolol for the treatment of portal hypertension in patients of liver cirrhosis. As in our study carvedilol is effective in 52% patients and propranolol in 24% patients.

Key Words: Liver cirrhosis, portal hypertension, carvedilol, propranolol.

INTRODUCTION

Cirrhosis of liver is a major international and national health hazard that causes very significant morbidity and mortality in our country. Liver cirrhosis is the consequence of hepatocellular injury that leads to both fibrosis and nodular regeneration in the liver. The clinical features result from hepatic cell dysfunction, portosystemic shunting and portal hypertension.[1]

In Pakistan, the commonest cause of liver cirrhosis is chronic viral hepatitis. It is estimated that about 5-8% and 7-10% people in our country are suffering from hepatitis B and C respectively.[2] International trials have shown that ten year survival for decompensated liver cirrhosis is 7%.[3]

Portal hypertension is one of the major complications of liver cirrhosis.[4] Variceal bleeding is one of the dreaded outcomes of portal hypertension.[5] Ruptured gastro-esophageal varices are the most severe and frequent causes of upper gastrointestinal bleeding in patients suffering from liver cirrhosis, accounting for 80% of all bleeding episodes, associated with 20% mortality at 6 weeks.[6]

Non-selective β-adrenergic blockers (propranolol, nadolol) or prophylactic band ligation decrease absolute risk of variceal bleeding by approximately 10% per year and reduce mortality by almost 5%.[7] Beta blockers remain as first line therapy in patients with cirrhosis and large esophageal varices.[8] Propranolol is known to decrease portal hypertension in cirrhotic patients with portal hypertension however a substantial number of patients do not respond to propranolol administration.[9] Carvedilol is a nonselective β-blocker with α_1-adrenergic blocking activity. It has been shown to decrease portal pressure in cirrhotic patients. Additionally, carvedilol has a

greater portal hypotensive effect than propranolol alone in patients with cirrhosis.[9] Carvedilol decreased HVPG greater than 20% of beseline values or to ≤12 mmHg in a greater proportion of patients (64% vs. 14%, P <0.5).[10] Despite all the therapeutic efforts, mortality from bleeding gastrointestinal varices due to portal hypertension is up to 20% so we still need to ascertain the most effective treatment, so the rationale for this study is to compare propranolol and carvedilol to find an effective treatment of portal hypertension.

MATERIALS AND METHODS

It was a randomized clinical trial. This study was conducted in the Department of Medical Unit-II, Sir Ganga Ram Hospital, Lahore. It was six months study from 26th March to 26th September 2010. One hundred patients of liver cirrhosis with portal hypertension were selected for this study. The patients were randomly divided into group A and B by using lottery method. Group A patients were given propranolol 40mg and group B patients were given carvedilol 25mg. Portal flow velocity was measured before and 90 minutes after the administration of the above mentioned drugs by a radiologist on Doppler ultrasonography and more than 20% decrease was considered as efficacy.

RESULTS

The mean age of the patients in group A was 51.6±11.3 years and in group B was 54.6±9.4 years. In group A, there were 12 (24%) patients in the age range of 30-40 years, 14 (28%) patients in the age range of 41-50 years, 15 (30%) patients in the age range of 51-60 years and 9 (18%) patients in the age range of 61-65 years. In group B, there were 2 (4%) patients in the age range of 30-40 years, 19 (38%) patients in the age range of 41-50 years, 17 (34%) patients in the age range of 51-60 years and 12 (24%) patients in the age range of 61-65 years (Table 1). In group A, there were 37 (74%) male and 13 (26%) female patients and in group B, there were 27 (54%) male and 23 (46%) female patients (Table 2).

In group A, there were 10 (20%) patients in Child Pugh class A, 24 (48%) patients were in Child Pugh class B and 16 (32%) patients were in Child Pugh class C. In group B, there were 10 (20%) patients in Child Pugh class A, 21 (42%) patients were in Child Pugh class B and 19 (38%) patients were in Child Pugh class C (Table 3).

In group A, the mean portal flow velocity at baseline was 18.2±1.9 and in group B was 19.3±1.6. In group A, there were 18 (36%) patients in portal flow velocity range of 15-17, 26 (52%) patients in the portal flow velocity range of 18-20 and 6 (12%) patients in the portal flow velocity range of 21-23. In group B, there were 7 (14%) patients in portal flow velocity range of 15-17, 30 (60%) patients in the portal flow velocity range of 18-20 and 13 (26%) patients in the portal flow velocity range of 21-23 (Table 4).

Table 1: Distribution of patients by age

Age (Years)	Group A (n=50)		Group B (n=50)	
	No.	Percentage	No.	Percentage
30-40	12	24.0	2	4.0
41-50	14	28.0	19	38.0
51-60	15	30.0	17	34.0
61-65	9	18.0	12	24.0
Mean±SD	51.6±11.3		54.6±9.4	

Table 2: Distribution of patients by sex

Sex	Group A (n=50)		Group B (n=50)	
	No.	Percentage	No.	Percentage
Male	37	74.0	27	54.0
Female	13	26.0	23	46.0
Total	50	100.0	50	100.0

Table 3: Distribution of patients by portal flow velocity at baseline

Portal flow velocity (cm/sec)	Group A (n=50)		Group B (n=50)	
	No.	Percentage	No.	Percentage
15-17	18	36.0	7	14.0
18-20	26	52.0	30	60.0
21-23	6	12.0	13	26.0
Mean±SD	18.2±1.9		19.3±1.6	

Table 4: Distribution of patients by portal flow velocity at 90 minutes

Portal flow velocity (cm/sec)	Group A (n=50)		Group B (n=50)	
	No.	Percentage	No.	Percentage
12-14	13	26.0	10	20.0
15-17	31	62.0	31	62.0
18-20	6	12.0	9	18.0
Mean±SD	15.7±1.7		15.9±1.5	

Table 5: Distribution of patients by efficacy

Efficacy	Group A (n=50)		Group B (n=50)	
	No.	Percentage	No.	Percentage
Yes	12	24.0	26	52.0
No	38	76.0	24	48.0
Total	50	100.0	50	100.0

Table 6: Comparison of Child Pugh classification with efficacy

Efficacy	Group A (n=50)			Group B (n=50)		
	Child A No. (%)	Child B No. (%)	Child C No. (%)	Child A No. (%)	Child B No. (%)	Child C No. (%)
Yes	3 (6.0)	6 (12.0)	3 (6.0)	8 (16.0)	9 (18.0)	9 (18.0)
No	7 (14.0)	18 (36.0)	13 (26.0)	4 (8.0)	12 (24.0)	8 (16.0)
Total	10 (20.0)	24 (48.0)	16 (32.0)	12 (24.0)	21 (42.0)	17 (34.0)

In group A, the mean portal flow velocity at 90 minutes was 15.7±1.7 and in group B was 15.9±1.5. In group A, there were 13 (26%) patients in portal flow velocity range of 12-14, 31 (62%) patients in the portal flow velocity range of 15-17 and 6 (12%) patients in the portal flow velocity range of 18-20. In group B, there were 10 (20%) patients in portal flow velocity range of 12-14, 31 (62%) patients in the portal flow velocity range of 15-17 and 9 (18%) patients in the portal flow velocity range of 18-20 (Table 5).

As far as efficacy of treatment, in group A, there were 12 (24%) patients had efficacy of treatment and 38 (76%) patients had non efficacious treatment. In group B, there were 26 (52%) patients had efficacy of treatment and 24 (48%) patients had non efficacious treatment (Table 6). In the comparison of Child Pugh classification with efficacy of treatment, in group A, out of 12 (24%) who had efficacy of treatment, there were 3 (6%) patients had Child Pugh class A, 6 (12%) patents had Child Pugh class B and 3

(6%) patients had Child Pugh class C. In group B, out of 26 (52%) who had efficacy of treatment, there were 8 (16%) patients had Child Pugh class A, 9 (18%) patents had Child Pugh class B and 9 (18%) patients had Child Pugh class C (Table 7).

DISCUSSION

Cirrhosis is a chronic disease of the liver in which diffuse destruction and regeneration of the hepatic parenchymal cells have occurred and in which a diffuse increase in connective tissue has resulted in disorganization of the lobular and vascular architecture.[11]

In Pakistan, the commonest cause of liver cirrhosis is chronic viral hepatitis. It is estimated that about 5-8% and 7-10% people in our country are suffering from hepatitis B and C respectively.[2] International trials have shown that ten year survival for decompensated liver cirrhosis is 7%.[3]

Portal hypertension is one of the major complications of liver cirrhosis.[4] Variceal bleeding is one of the dreaded outcomes of portal hypertension.[5] Ruptured gastro-esophageal varices are the most severe and frequent causes of upper gastrointestinal bleeding in patients suffering from liver cirrhosis, accounting for 80% of all bleeding episodes, associated with 20% mortality at 6 weeks.[6]

Non-selective β-adrenergic blockers (propranolol, nadolol) or prophylactic band ligation decrease absolute risk of variceal bleeding by approximately 10% per year and reduce mortality by almost 5%.[7]

Beta blockers remain as first line therapy in patients with cirrhosis and large esophageal varices.[8] Propranolol is known to decrease portal hypertension in cirrhotic patients with portal hypertension however a substantial number of patients do not respond to propranolol administration.[9]

Carvedilol is a nonselective β-blocker with α_1-adrenergic blocking activity. It has been shown to decrease portal pressure in cirrhotic patients. Additionally, carvedilol has a greater portal hypotensive effect than propranolol alone in patients with cirrhosis.[9] Carvedilol decreased HVPG greater than 20% of beseline values or to </=12 mmHg in a greater proportion of patients.[10]

In this study the mean age of the patients in group A was 51.6±11.3 years and in group B was 54.6±9.4 years, compared with the study of Snchez-del-Monte et al[12] the mean age of the patients was 53.3 years and is online with this study.

In this study in group A, there were 74% male and 26% female patients and in group B, there were 54% male and 46% female patients and does not go with the study of Snchez-del-Monte et al[12] there were 35% male and 65% female patients.

In this study the efficacy of treatment in group A was found in 24% patients and in group B was in 52% patients in the management of portal hypertension, compared with Banares et al[10] the efficacy of propranol was14% and carvedilol was 64% in the management of portal hypertension, which is slightly higher than this study.

In another study conducted by Bruha et al[13] the efficacy of carvedilol in the management of portal hypertension was found in 42% patients, while in our study the efficacy of carvedilol in the management of portal hypertension was found in 52% patients, which is comparable with above study.

In another study conducted by Castaro et al[14] the efficacy of propranolol in the treatment of portal hypertension in cirrhosis was found in 35% patients, while in our study the efficacy of propranolol was found in 24% patients, which does not go with this study.

Carvedilol is a promising agent, and seems to be more effective than propranolol. The efficacy in primary prevention of variceal bleeding suggests that carvedilol has a role in the management of portal hypertension.[15]

So comparing different studies it appears that carvedilol is more effective than propranolol in the treatment of portal hypertension in cirrhosis.

CONCLUSION

It is concluded from this study that carvedilol is more effective than propranolol for the treatment of portal hypertension in patients of liver cirrhosis. As in this study carvedilol is effective in 52% patients and propranolol in 24% patients.

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