ORIGINAL ARTICLE

The Effectiveness of Carvedilol Versus Propranol in Preventing Recurrence of Bleeding in Cirrhotic Patients: A Comparative Study

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ABSTRACT

Aim: To determine the effectiveness of carvedilol versus propranol to prevent recurrence of bleeding in cirrhotic patients.
Study design: Controlled trial study
Place and duration of study: Department of Medicine, Pir Abdul Qadir Shah Jeelani Institute of Medical Sciences, Gambat from 1st April 2020 to 30th November 2020.
Methodology: One hundred and eighty patients of ages between 20-60 years were presented in this study. Patients detailed demographics age, sex, body mass index and Child-Turcotte-Pugh (CTP) class were recorded. Patients were equally (n=90) divided into two groups. Group I had 90 patients and received carvedilol while group II had 90 patients and received propranol for 8 months. Reoccurrence of bleeding in cirrhotic patients among both groups were observed at 4th and 8th months in which pulse rate, arterial pressure and portal vein flow were recorded.
Results: There were 120 (66.7%) male patients (60 in Group I and 60 in Group II) and 60 (33.3%) were females (30 in Group I and 30 in Group II). Mean age of the patients in group I was 42.18±9.77 years with mean BMI 27.15±7.18 kg/m^2 and in group II mean age was 42.84±4.96 years with mean BMI 27.61±2.81 kg/m^2. Child-Turcotte-Pugh class did not show any significantly difference among both groups. 24 (26.7%) reoccurrence of blooding observed in group I and 45 (50%) reoccurrence of bleeding was in group II. After 4 and 8 months, in carvedilol group I pulse rate, mean arterial pressure and portal vein flow was found lower as compared to propanol group II with p value < 0.05.
Conclusion: Carvedilol drug was more effective and safe to prevent reoccurrence of bleeding in cirrhotic patients as compared to propanol drug.
Keywords: Carvedilol, Propanol, Portal vein flow, Mean arterial pressure

INTRODUCTION

Esophageal varices veins can be observed at the time of first diagnosis in around 30% of cirrhosis patients.[1] Esophageal varices bleeding is a life-threatening portal hypertension complication, responsible for nearly 80% of all bleeding episodes in cirrhosis patients.[2] Depending on the existence of many risk factors.[3] the annual incidence for variice haemorrhage is 5-15%.[4,5] Moreover, varicose recovery takes place in 1-2 years at a rate of 63%.[6] Esophageal varices bleeding is still high in mortality, despite improvement in management procedures.[7]

Beta-adrenergic antagonists (β-blockers) in portal hypertension have, for more than 3 decades, been well known. Non-selective β-blockers are commonly used since the 1980s, when Lebrec et al[8] published the first article on their role in portal hypertension[8], the NSBB had a dual mode of portal pressure deduction, i.e. a reduction of heart production and splanchnic blood flow due to the receptor blockade β-1. It has been shown that NSBBs have decreased their frequency of esophageal varices through bleeding (primary prophylactic) and secondary prophylaxis.[9-12] The effects of portal hypertensive gastropathy and spontaneous bacterial peritonitis have also been shown to be preventative bleeding. In clinical hepatology, they have been referred to as "aspirin" because of their very diversified effects on patients with cirrhosis and widespread use.[13-15] In trials conducted to test his efficacy of heart failure[16], carvedilol proved to be 2-4 times more effective than propranolol as a beta-receptor blocker. It is a subject of constant discussion if the same effect applies to its potential in reducing portal venous pressure.

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MATERIAL AND METHODS

This study was conducted at Department of Medicine, Pir Abdul Qadir Shah Jeelani Institute of Medical Sciences, Gambat from 1st April 2020 to 30th November 2020 and comprised of 180 patients. After taking informed written consent, detailed demographics including age, sex, BMI and CTP class were recorded after taking informed consent. Those patients who did not agree, were excluded. Cirrhotic patients with age group 20-60years were enrolled in this study. Patients were equally (n=90) divided into two groups. Group I had 90 patients and received carvedilol

while group II had 90 patients and received propranol for 8 months. Reoccurrence of bleeding in cirrhotic patients among both groups were observed at 4th and 8th months in which pulse rate, arterial pressure and portal vein flow were recorded. Complete data was analyzed by SPSS 24.

RESULTS

One hundred and twenty (66.7%) patients were males (60 in Group I and 60 in Group II) and 60 (33.3%) were females (30 in Group I and 30 in Group II). Mean age of the patients in group I was 42.18±9.77 years with mean BMI 27.15±7.18 kg/m^2 and in group II mean age was 42.84±4.96 years with mean BMI 27.61±2.81 kg/m^2. Child Turcotte-Pugh class did not show any significantly difference among both groups (Table 1). Twenty four (26.7%) reoccurrence of blooding observed in group I and 45 (50%) reoccurrence of bleeding was in group II. After 4 and 8 months, in carvedilol group I pulse rate, mean arterial pressure and portal vein flow was found lower as compared to propanol group II with p value < 0.05 (Table 2).

Table 1: Baseline detailed characteristics of enrolled cases

Variable	Group I	Group II	Total
Gender			
Male	60 (66.7%)	60 (66.7%)	120 (66.7%)
Female	30 (33.3%)	30 (33.3%)	60 (33.3%)
Mean age (years)	42.18±9.77	42.84±4.96	
Mean BMI	27.15±7.18	27.61±2.81	
Child Turcotte Pugh			
Class A	6 (6.7%)	7 (7.8%)	13 (7.22%)
Class B	25 (27.8%)	26 (28.9%)	51 (28.3%)
Class C	59 (65.5%)	56 (62.22%)	115 (63.9%)

Table 2: Comparison of reoccurrence bleeding among both groups

Variable	Group I	Group II	P value
Recurrence of bleeding	24 (26.7%)	45 (50%)	0.05
At start	4 (4.44%)	5 (5.6)	0.75
4 months	12 (13.33%)	21 (23.33)	0.91
8 months	8 (8.9%)	19 (21.11)	0.09
Decrease in MAP (mmHg)			
At start	-8.21±0.91	-7.09±0.54	0.82
4 months	-11.32±0.89	-6.14±0.85	0.04
8 months	-13.08±4.13	-7.87±0.75	0.03
Heart rate (gm/dL)			
At start	84±21	83±45	0.88
4 months	72±14	78±23	0.04
8 months	66±91	73±63	0.05
Portal vein flow (ml/min)			
At start	911.15±118.87	905.45±129.87	0.98
4 months	741.32±95.87	801.32±101.45	0.06
8 months	599.32±66.87	687.18±123.78	0.02

DISCUSSION

We found carvedilol to have an advantageous effect on bleeding in cirrhosis patients. Portal hypertension is one of the most debilitating complications of liver disorders. The portal hypertension induces higher resistance to the flow of veins due to strong liver parenchyma.[17] Although both medications have been used for primary preventive intervention, carvedilol is used less frequently for secondary variceal bleeding prophylaxis than propranolol. Propranolol decreases portal pressure by decrease the portal blood flow by decreasing the cardiac flow and reduced azygous blood flow as a result of ß-1 blocks of receptors and vasoconstrictions, due to the non-opposed alpha vasoconstriction effect, which leads to arteriolar blockage (beta 2 blocking)[18]. The latest version is available.

There were 120 (66.7%) males greater than that of females 60 (33.3%). Mean age of the patients in group I was 42.18 ± 9.77 years with mean BMI 27.15±7.18 kg/m^2 and in group II mean age was 42.84±4.96 years with mean BMI 27.61±2.81 kg/m^2. Child Turcotte-Pugh class did not show any significantly difference among both groups. These were comparable to the previous some studies.[19,20] The use of carvedilol to avoid varicceal bleeding, hepatic decompensation, and mortality in 50 per cent propranolol non-respondents was found to achieve a hamodynamic response with an improved outcome of 26.7 per cent.[21] The reduction in sizeable portal pressure and intrahepatical resistance of carvedilol indicates a greater therapeutic capacity, albeit less widely used in secondary prophylaxis. Therefore, based on this advantage of carvedilol used in our analysis for secondary varicella prophylaxis, carvedilol has demonstrated an essentially comparable advantage, while propranolol is not the strongest. In our study, the findings of the study conducted by Gupta et al[18] are identical for carvedilol and propranolol HR and MAP decreased by 4 months and 8 months.

Rebled propranolol was more prevalent than carvedilol (21.11 vs 8.9 percent). The rebleeding rate of carvedilol is comparable to that of 61 percent (37 of 61) after 30 months in median follow-up by Lo et al.[22] An additional study by Faust et al[17] in which 25 (36 percent) out of 69 patients treated with propranolol had a 28-month follow-up duration of rebled at least once. The need to withhold medications temporarily for a few days between the two classes was comparable. A recent retrospective retrospective review has shown no variations in the incidence of SBP between users of NSBB and not patients in 607 patients suffering from cirrhosis by Mandorfer et al.[23] The SBP event rates between NSBB and non-NSBB patients were comparable. NSBB use was nevertheless associated with improved transplant-free survival and decreased hospitalisation in patients without SBP. In comparison, Mandorfer et al[23] demonstrated that hemodynamic compromising and lowering of the blood pressure, decreased transplant free survival, increased rates of admission and hepatorenal syndrome and acute renal injury were correlated with SBP in patients established. In another study, the use of NSBB (propranolol) was found to decrease survival for 1 year in patients who do not take this medication refractory ascites (median survival: 5 mo vs 20 mo respectively).[24]

Sinagra and co-authors[25] also reported long-term extreme hypotension, due to their ability to decrease MAPs which was also found in the present study. But none of the enrolled patients in this study reported a drop in blood pressure to avoid or minimise the dose.

CONCLUSION

Carvedilol drug was more effective and safe to prevent reoccurrence of bleeding in cirrhotic patients as compared to propanol drug.

REFERENCES

1. Meseeha M, Attia M. Esophageal varices. [Updated 2017 Oct 11]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2018.
2. D'Amico G, De Franchis R; Cooperative Study Group. Upper digestive bleeding in cirrhosis. Post-therapeutic outcome and prognostic indicators. Hepatology 2003;38:599-612.
3. North Italian Endoscopic Club for the Study and Treatment of Esophageal Varices. Prediction of the first variceal hemorrhage in patients with cirrhosis of the liver and esophageal varices: a prospective multicenter study. N Engl J Med 1988;319:983-9,
4. Haq I, Tripathi D. Recent advances in the management of variceal bleeding. Gastroenterol Rep (Oxf) 2017;5:113-26.
5. Al-Busafi SA, McNabb-Baltar J, Farag A, Hilzenrat N. Clinical manifestations of portal hypertension. Int J Hepatol 2012;2012:203794
6. D'Amico G, Pagliaro L, Bosch J. The treatment of portal hypertension: a meta-analytic review. Hepatology 1995;22:332-54.
7. Abraldes JG, Villanueva C, Bañares R, et al; Spanish Cooperative Group for Portal Hypertension and Variceal Bleeding. Hepatic venous pressure gradient and prognosis in patients with acute variceal bleeding treated with pharmacologic and endoscopic therapy. J Hepatol 2008;48:229-36.
8. Lebrec D, Nouel O, Corbic M, Benhamou JP. Propranolol--a medical treatment for portal hypertension? Lancet 1980;2:180-2.
9. Tripathi D, Hayes PC. Beta-blockers in portal hypertension: new developments and controversies. Liver Int. 2014;34:655-67.
10. Pagliaro L. Lebrec D, Poynard T, Hillon P, Benhamou J-P. Propranolol for prevention of recurrent gastrointestinal bleeding in patients with cirrhosis: a controlled study N Engl J Med 1981; 305: 1371-4.
11. Pascal JP, Cales P. Propranolol in the prevention of first upper gastrointestinal tract hemorrhage in patients with cirrhosis of the liver and esophageal varices. N Engl J Med 1987;317:856–61.
12. Poynard T, Calès P, Pasta L, Ideo G, Pascal JP, Pagliaro L, Lebrec D. Beta-adrenergic-antagonist drugs in the prevention of gastrointestinal bleeding in patients with cirrhosis and esophageal varices: an analysis of data and prognostic factors in 589 patients from four randomized clinical trials. Franco-Italian Multicenter Study Group. N Engl J Med 1991;324:1532-8.
13. Garcia-Tsao G, Bosch J. Management of varices and variceal hemorrhage in cirrhosis. N Engl J Med 2010;362:823-32.
14. Abraldes JG, Tarantino I, Turnes J, Garcia-Pagan JC, Rodés J, Bosch J. Hemodynamic response to pharmacological treatment of portal hypertension and long-term prognosis of cirrhosis. Hepatology 2003;37:902-8.
15. Senzolo M, Cholongitas E, Burra P, Leandro G, Thalheimer U, Patch D, Burroughs AK. beta-Blockers protect against spontaneous bacterial peritonitis in cirrhotic patients: a meta-analysis. Liver Int 2009;29:1189-93.
16. Frishman WH. Carvedilol. N Engl J Med 1998;339:1759–65.
17. Abraldes JG, Tarantino I, Turnes J, Garcia-Pagan JC, Rodes J, Bosch J. Hemodynamic response to pharmacological treatment of portal hypertension and long-term prognosis of cirrhosis. Hepatology 2003; 37(4):902-8.
18. Gupta V, Rawat R, Shalimar, Saraya A. Carvedilol versus propranolol effect on hepatic venous pressure gradient at 1 month in patients with index variceal bleed: RCT. Hepatol International 2017; 11(2): 181-7.
19. Hamal AB, KC S, Thapa P, Sharma D, Karki N, et al. Carvedilol versus propranololol for secondary prophylaxis of variceal hemorrhage in patients with liver cirrhosis. Adv Res Gastroentero Hepatol 2020;15(4): 555920.
20. Afzal MY, Haq MI, Javed S. Comparison of carvedilol and propranolol for secondary prophylaxis of varicealbleed in cirrhotic patients. J Fatima Jinnah Med Univ 2018; 12(3): 106-9.
21. Reiberger T, Ulbrich G, Ferlitsch A, Payer B A, Trauner M, et al. Carvedilol for primary prophylaxis of variceal bleeding in cirrhotic patients with hemodynamic non-response to propranolol. Gut 2013; 62(11): 1634-41.
22. Lo GH, Chen WC, Wang HM, Yu HC. A randomized, controlled trial of carvedilol vs. nadolol plus isosorbide mononitrate for the prevention of variceal rebleeding. J Gastroenterol Hepatol 2012; 27(11): 1681-7.
23. Mandorfer M, Bota S, Schwabl P, Bucsics T, Pfisterer N, Kruzik M, Hagmann M, Blacky A, Ferlitsch A, Sieghart W, et al. Nonselective β blockers increase risk for hepatorenal syndrome and death in patients with cirrhosis and spontaneous bacterial peritonitis. Gastroenterology 2014;146:1680-90.
24. Sersté T, Melot C, Francoz C, Durand F, Rautou PE, Valla D, Moreau R, Lebrec D. Deleterious effects of beta-blockers on survival in patients with cirrhosis and refractory ascites. Hepatology 2010;52:1017–1022.
25. Sinagra E, Perricone G, D'Amico M, Tine F, D'Amico G.Systematic review with meta-analysis: the haemodynamic effects of carvedilolcompared with propranolol for portal hypertension in cirrhosis. Alimentary Pharmacol Ther 2014; 39(6):557-68.