Gut and Gastroenterology

RESEARCH ARTICLE

Medical Versus Endoscopic Treatment of Oesophageal Varices in Liver Cirrhosis

Hanno AF[1],Aboelkheir HF[1], Alwazzan DA[1], Abdelrahman MI[1]*

[1]Tropical Medicine Department, Faculty of Medicine, Alexandria University, Egypt

Abstract

Introduction: Portal hypertension is the most common complication of liver cirrhosis. It may be complicated by gastrointestinal bleeding from oesophageal or gastric varices. Treatment of varices can be medical by using non-selective beta blockers (as propranolol or cavedilol), or endoscopic (endoscopic variceal ligation EVL, endoscopic injection sclerotherapy EIS), or both.

Aims & Methods: This study was conducted on 80 patients with liver cirrhosis and oesophageal varices (O.V.) grade III and IV, who were classified into five groups. Group I, 20 patients were subjected to EVL alone, group II, 20 patients received carvedilol alone(6.25 mg once daily, then increased to 6.25 mg twice daily after 1 week), group III received propranolol alone (20 mg three times daily), group IV, 20 patients who were subjected to EVL combined with carvidolol (6.25 mg once daily, then increased to 6.25 mg twice daily after 1 week)and group V, 20 patients who were subjected to EVL combined with propranolol(20 mg three times daily). All patients were followed up by doppler study of portal vein and upper G.I. endoscopy.

Results: Upper G.I. endoscopy was done for all patients every 3 months up to 12 months. In the 1st visit, 95% of group I patients had O.V. grade IV and 5% had grade III O.V., by the 4th visit 80% had O.V. grade I and 20% had no O.V. in the same group. In group II, in the 1st visit 90% of patients had O.V. grade IV and 10% had O.V. grade III, in the 4th visit 60% had O.V. grade I and 40% had no O.V., In group III, in the 1st visit 95% of patients had O.V. grade IV and 5% had O.V. grade III, in the 4th visit 50% had O.V. grade I and 30% had no O.V., In group IV, in the 1st visit 20% of patients had O.V. grade IV and 80% had O.V. grade III, in the 4th visit 40% had O.V. grade I and 60% had no O.V., regarding group V, in the 1st visit, 75% had grade IV O.V. and 5% had O.V. grade III, while in the 4th visit 60% had O.V. grade I and 40% had no varices.

Conclusion: The combination of carvedilol and EVL is more effective in treating medium and large sized O.V. than EVL alone or EVL combined to propranolol.

Introduction

Portal hypertension is responsible for the majority of complications of patients with liver cirrhosis, such as, development of oesophageal varices (OV), ascites, hepatorenal syndrome and hepatic encephalopathy.(1) OV are found in between 39 and 50% of cirrhotic patients; approximately half of them bleed at some point, and rebleeding occurs in up to two-thirds of the patients [1,2] .

Almost 25% of patients with variceal bleeding (VB) die, with the associated mortality rate depending on several factors, including the severity of the underlying liver disease, the treatment received during the acute episode [3], the size of the varices and the presence of red spot signs. [2] Up to 30% of these patients also develop gastric varices, which on bleeding result in an even higher mortality [4,5].

Non-selective beta blockers (NSBB) and endoscopic variceal ligation (EVL) has been the mainstay of primary prophylaxis and reduce the risk of bleeding from 50 to 15 % for large varices. [6,7] NSBB are a class of drugs with effects on the sympathetic nervous system [8]. NSBB have beta-1 receptor blocking effects that reduce cardiac output and portal venous inflow and beta-2 receptor blocking effects that lead to splanchnic vasoconstriction. Both the reduced cardiac output and the reduced portal venous inflow will reduce portal pressure [8,9].

NSBB are cost-effective [10], and may be also used in the prevention of other complications of cirrhosis and portal hypertension, including bleeding from portal hypertensive gastropathy [11]. However, other studies do not recommend the use of NSBB in patients with decompensated cirrhosis [12,13] ,in addition, they have some side effects that lead to treatment discontinuation in approximately in 15% of patients [14] such as depression, fatigue, sexual dysfunction, bradycardia and even heart block [15,16]. Therefore further

Correspondence to: Abdelrahman MI, Department of Tropical Medicine, Faculty of Medicine, Alexandria University, Alexandria, Egypt, Tel: +203 5410338, E-mail: marwaibrahim90@yahoo.com

Received: July 15, 2018; **Accepted:** July 18, 2018; **Published:** July 20, 2018

researches are needed regarding the appropriate use of NSBB in patients with cirrhosis.

NSBB used in clinical practice are propranolol, nadolol, and timolol [17], and recently, carvedilol that represents a promising drug that needs to be explored further [18]. Carvedilol is a racemic mixture that possesses both non-selective β2-antagonist and α1-receptor antagonist activity. Given its combined mechanism of action, carvedilol may have a greater potential for lowering portal pressure than propranolol [19].

The concept of EVL was based upon the treatment of varices with rubber band ligation. EVL obliterates varices by capturing all or part of a varix with rubber bands, resulting in mechanical strangulation and occlusion from thrombosis. The tissue then necrotizes and sloughs off in a few days to weeks, leaving a superficial mucosal ulceration, which rapidly heals [5].

It was documented that there was no difference in survival between EVL and NSBB for treating patients with high-risk OV, EVL showed the same efficacy or even better than the NSBB in preventing a first bleed[20] .But the recurrence of esophageal varices after EVL was more than 50% within 2 years[21]. This is because persistence of high portal pressure after EVL results in reformation of OV [22]. So the addition of NSBB to reduce portal pressure has been proved to decrease OV recurrence [23].

Patients and Methods

This study was conducted on 100 patients with liver cirrhosis and esophageal varices (O.V.) Liver cirrhosis was diagnosed on clinical, biochemical and radiological basis then patients were selected after upper GIT endoscopy screening for esophageal varices of grade III and IV.

Patients were classified into five groups. Group I, 20 patients were subjected to EBL alone, group II, 20 patients received carvedilol alone(6.25 mg once daily, then increased to 6.25 mg twice daily after 1 week), Group III received propranolol alone (20 mg three times daily), group IV, 20 patients who were subjected to EBL combined with carvedilol (6.25 mg once daily, then increased to 6.25 mg twice daily after 1 week) and group V, 20 patients who were subjected to EBL combined with propranolol(20 mg three times daily).

All patients were followed up by doppler study of portal vein and upper G.I. endoscopy.

Aim of the work

The aim of this work was to compare between medical treatment and band ligation in the treatment of oesophageal varices secondary to liver cirrhosis.

Results

Patient demographic data:

Regarding sex, the majority of patients were males consisting of 55%, 75%, 80%, 65% and 60% respectively. There was no statistical significance between the studied groups regarding sex (p= 0.189)

Regarding to age, patient's ages ranged from 40 to 72 years in group I, 45 to 65 years in group II, 36 to 70 in group III, 35 to 60 in group IV and 41 to 66 in group IV. [Table 1].

Endoscopic follow up of the studied groups

Upper G.I. endoscopy was done for all patients every 3 months up to 12 months. In the 1st visit, 95% of group I patients had O.V. grade IV and 5% had grade III O.V., by the 4th visit 80% had O.V. grade I and 20% had no O.V. in the same group.

In group II, in the 1st visit 90% of patients had O.V. grade IV and 10% had O.V. grade III, in the 4th visit 60% had O.V. grade I and 40% had no O.V., In group III, in the 1st visit 95% of patients had O.V. grade IV and 5% had O.V. grade III, in the 4th visit 50% had O.V. grade I and 30% had no O.V.,

In group IV, in the 1st visit 20% of patients had O.V. grade IV and 80% had O.V. grade III, in the 4th visit 40% had O.V. grade I and 60% had no O.V., regarding group V, in the 1st visit, 75% had grade IV O.V. and 5% had O.V. grade III, while in the 4th visit 60% had O.V. grade I and 40% had no varices [Figure 1].

Doppler follow up of portal vein:

Regarding the percentage of change between the first and fourth visit, in group I mean value of 18.54 % was achieved. While in group II it was 11.06%, 10.8% in group III, 22.35 in group IV and 20.56% decrease in portal vein diameter after the fourth visit. There was a statistical significance between the five groups regarding the percentage of change between the first and the fourth visit. ($p < 0.001$*) [Figure 2].

	group I (n=20)		group II (n=20)		group III (n=20)		group IV (n=20)		group V (n=20)		Test of sig	p value
	No.	%	No.	%	No.	%	No.	%	No.	%		
SEX												
Male	11	55	15	75	16	80	13	65	12	60	x^2=3.33	p=0.189
female	9	45	5	25	4	20	7	35	8	40		
AGE												
Min-Max	40.0-72		45-65		36-70		35-60		41-66		f=3.614	p=0.033*
Mean±SD	50.85±8.65		57.10±6.07		55.90±8. 42		47.5±8.2		53.3±			
Sig.bt.gps	p^1= 0.014*		p^2= 0.045*		p^3= 0.629		p^4= 0.497		p^5= 0.342			

Table 1: different studied groups according to patient's demograph.

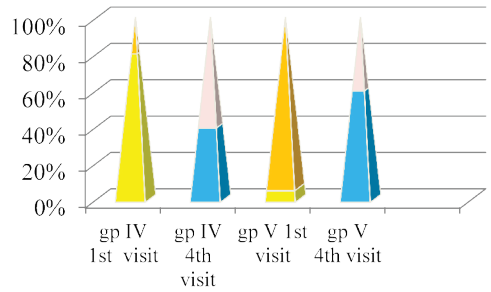

Figure 1: Grades of esophageal varices in group IV and V in the first and fourth visit during therapy.

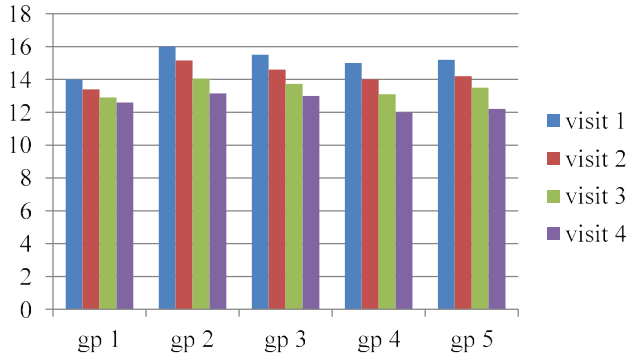

Figure 2: Comparison between the different studied groups according to the Doppler study of the portal vein.

Discussion

Portal hypertension (PHT) is responsible for the majority of complications of patients with liver cirrhosis, for example, the development of oesophageal varices, ascites, hepatorenal syndrome, hyperdynamic circulation and hepatic encephalopathy. [1] Patients with oesophageal varices are at risk of variceal bleeding, especially if varices are large or with red spot signs. [24, 25] Despite advances in the management of acute variceal bleeding the in hospital mortality is still as high as 20% [26]

Earlier studies have already shown that achieving a haemodynamic response to non-selective β-blockers (NSBB) (defined as a decrease in hepatic venous pressure gradient (HVPG) of ≥20% compared to baseline values or to absolute values <12 mm Hg) treatment may protect from variceal bleeding. [27,28] consequently, current guidelines [29] suggest pharmacological treatment with NSBB or endoscopic band ligation (EBL) for the prevention of the first variceal bleeding episode.

Nadolol and propranolol have traditionally been used for prophylaxis of variceal bleeding, [30-32] while carvedilol represents a promising drug that needs to be explored further. [29] Carvedilol is a racemic mixture that possesses both non-selective β1/2-antagonist and α1-receptor antagonist activity. Given its combined mechanism of action, carvedilol may have a greater potential for lowering portal pressure than propranolol [1].

This study was conducted on 100 patients with liver cirrhosis and esophageal varices (O.V.) Liver cirrhosis was diagnosed on clinical, biochemical and radiological basis then patients were selected after upper GIT endoscopy screening for esophageal varices of grade III and IV.

Patients were classified into five groups. Group I, 20 patients were subjected to EBL alone, group II, 20 patients received carvedilol alone(6.25 mg once daily, then increased to 6.25 mg twice daily after 1 week), Group III received propranolol alone (20 mg three times daily), group IV, 20 patients who were subjected to EBL combined with carvedilol (6.25 mg once daily, then increased to 6.25 mg twice daily after 1 week) and group V, 20 patients who were subjected to EBL combined with propranolol(20 mg three times daily).

Regarding the diameter of the portal vein it was significantly smaller in the fourth visit than the first visit in the five studied groups, the percentage of change between the first and fourth visits in patients who received a combined treatment of oesophageal varices by band ligation and carvedilol was significantly higher than other groups ($p < 0.001$) this is in agreement with Reiberger T [33], et al. Who found that Carvedilol had significantly greater effects on portal pressure than propranolol (−19% vs −12%),

William F [34] et al, in Canada conducted a study on sixty patients suffering from liver cirrhosis and bleeding oesophageal varices found a positive correlation between the diameter of portal vein and grade of varices.

In the present study combination of carvedilol and EVL was found to be significantly effective (0.001*) in treating medium and large sized O.V.(on the 4 th visit 60% had no esophagreal varices) than EVL alone(20% no varices by 4th visit) or EVL combined to propranolol(40% no varices), this is in agreement with Abid S et al, [35]who found that when Carvedilol was compared to EBL showed a significantly lower rate of first variceal bleeding , however Shah et al, [36] suspected that carvedilol is not superior to EBL for primary prophylaxis of esophageal varices.

In the present study propranolol combined with EVL was significantly associated with a better outcome (40% no varices by 4th visit) than using either propranolol alone (30% no varices by 4th visit) or EVL alone (20% no varices by 4th visit) but Abid S et al, [35] found that Propranolol decreases risk of variceal bleeding. EBL superior to propranolol in prevention, but propranolol is easier to use.

Conclusion

The combination of carvedilol and EVL is more effective in treating medium and large sized O.V. than EVL alone or EVL combined to propranolol.

References

1. Bosch J, García-Pagán JC (2000) Complications of cirrhosis. I. Portal hypertension. *Journal of Hepatology* 32:141-56 [View Article]

2. Ferlitsch M, Reiberger T, Hoke M, *et al*. (2012) Von Willebrand factor as new non-invasive predictor of portal hypertension, decompensation and mortality in patients with liver cirrhotic. *Hepatology* 124: 395-402[View Article]

3. Cerqueira RM, Andrade L, Correia MR, Fernandes CD, Manso MC (2012) Risk factors for in hospital mortality in cirrhotic patients with oesophageal variceal bleeding. *Eur J Gastroenterol Hepatol* 24:551–7[View Article]

4. Merli M, Nicolini G, Angeloni S, et al. (2003) Incidence and natural history of small esophageal varices in cirrhotic patients. *J Hepatol* 38: 266-72. [View Article]

5. Dell'Era A, Iannuzzi F and de Franchis R. (2015) Endoscopic management of variceal haemorrhage. Journal of Gastroenterology and Hepatology Research 4: 1507-14. [View Article]

6. Bernard B, Lebrec D, Mathurin P, et al. (1997) Propranolol and sclerotherapy in the prevention of gastrointestinal rebleeding in patients with cirrhosis: a meta-analysis. J Hepatol. 26:312–24. [View Article]

7. Khuroo MS, Khuroo NS, Farahat KLC, Khuroo YS, Sofi AA et al. (2005) Meta-analysis: endoscopic variceal ligation for primary prophylaxis of oesophageal variceal bleeding. *Aliment Pharmacol Ther*.21:347–61[View Article]

8. Garcia-Tsao G, Sanyal AJ,Grace ND, Carey W (2007) Prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis. *Hepatology (Baltimore, Md.)* 46:922-38. [View Article]

9. Garcia-Tsao G, Bosch J,Groszmann RJ (2008) Portal hypertension and variceal bleeding - unresolved issues. Summary of an American Association for the Study of Liver Diseases and European Association for the Study of the Liver single-topic conference. *Hepatology* 47:1764-72. [View Article]

10. Imperiale TF, Klein RW, Chalasani N (2007) Cost-effectiveness analysis of variceal ligation vs. beta-blockers for primary prevention of variceal bleeding. *Hepatology* 45: 870-8. [View Article]

11. Abraldes JG, Tarantino I, Turnes J, Garcia-Pagan JC, Rodés J et al. (2003) Hemodynamic response to pharmacological treatment of portal hypertension and long-term prognosis of cirrhosis. *Hepatology*. 37: 902-8. [View Article]

12. Serste T, Melot C, Francoz C, Durand F, Rautou PE et al. (2010) Deleterious effects of beta-blockers on survival in patients with cirrhosis and refractory ascites. *Hepatology* 52: 1017-22. [View Article]

13. Serste T, Francoz C, Durand F, Rautou PE, Melot C et al. (2011) Beta-blockers cause paracentesis-induced circulatory dysfunction in patients with cirrhosis and refractory ascites: a cross-over study. *J Hepatol*.; 55: 794-9. [View Article]

14. Garcia-Tsao G and Lim JK. (2009) Members of Veterans Affairs Hepatitis CRCP. Management and treatment of patients with cirrhosis and portal hypertension: recommendations from the Department of Veterans Affairs Hepatitis C Resource Center Program and the National Hepatitis C Program. *Am J Gastroenterol* 104: 1802-29. [View Article]

15. Rosen RC, Kostis JB and Jekelis AW (1988) Beta-blocker effects on sexual function in normal males. *Arch Sex Behav* 17: 241-55. [View Article]

16. Ko DT, Hebert PR, Coffey CS, Curtis JP, Foody JM et al. (2004) Adverse effects of beta-blocker therapy for patients with heart failure: a quantitative overview of randomized trials. *Arch Intern Med*. 164: 1389-94. [View Article]

17. De Franchis R. (2010) Revising consensus in portal hypertension: report of the Baveno V consensus workshop on methodology of diagnosis and therapy in portal hypertension. *J Hepatol* 53:762-8. [View Article]

18. Lo GH, Chen WC, Chen MH, Hsu PI, Lin CK et al. (2002) Banding ligation versus nadolol and isosorbide mononitrate for the prevention of esophageal variceal rebleeding. *Gastroenterology* 123:728–34. [View Article]

19. Bosch J (2010) Carvedilol for portal hypertension in patients with cirrhotic. *Hepatology* 51:2214-8. [View Article]

20. Gluud LL, Klingenberg S, Nikolova D, Gluud C (2007) Banding ligation versus beta-blockers as primary prophylaxis in esophageal varices: systematic review of randomized trials. *Am J Gastroenterol*. 102:2842-8. [View Article]

21. Hou MC, Lin HC, Lee FY, Chang FY, Lee SD (2000) Recurrence of esophageal varices following endoscopic treatment and its impact on rebleeding: comparison of sclerotherapy and ligation. *J Hepatol*. 32:202-8. [View Article]

22. Lo GH, Liang HL, Lai KH, Chang CF, Hwu JH et al (1996) The impact of endoscopic variceal ligation on the pressure of the portal venous system. *J Hepatol*. 1:74-80. [View Article]

23. Sarin SK, Wadhawan M, Agarwal SR, Tyagi P, Sharma BC (2005) Endoscopic variceal ligation plus propranolol versus endoscopic variceal ligation alone in primary prophylaxis of variceal bleeding. *Am J Gastroenterol*. 100:797-804. [View Article]

24. Garcia-Tsao G, Groszmann RJ, Fisher RL, Conn HO, Atterbury CE et al (1985) Portal pressure, presence of gastroesophageal varices and variceal bleeding. *Hepatology* 5:419-24. [View Article]

25. Groszmann RJ, Bosch J, Grace ND, Conn HO, Garcia-Tsao G et al (1990) Hemodynamic events in a prospective randomized trial of propranolol versus placebo in the prevention of a first variceal hemorrhage. *Gastroenterology* 99:1401-7. [View Article]

26. Cerqueira RM, Andrade L, Correia MR, Fernandes CD, Manso MC (2012) Risk factors for in-hospital mortality in cirrhotic patients with oesophageal variceal bleeding. *Eur J Gastroenterol Hepatol* 24:551-7. [View Article]

27. Abraldes JG, Tarantino I, Turnes J, Garcia-Pagan JC, Rodés J et al (2003) Hemodynamic response to pharmacological treatment of portal hypertension and long-term prognosis of cirrhotic. *Hepatology* 37:902-8. [View Article]

28. D'Amico G, Garcia-Pagan JC, Luca A, Bosch J (2006) Hepatic vein pressure gradient reduction and prevention of variceal bleeding in cirrhotic: a systematic review. *Gastroenterology* 131:1611-24. [View Article]

29. de Franchis R. (2010) Revising consensus in portal hypertension: report of the Baveno V consensus workshop on methodology of diagnosis and therapy in portal hypertension. *J Hepatol* 53:762-8. [View Article]

30. Lo GH, Chen WC, Chen MH, Hsu PI, Lin CK et al (2002) Banding ligation versus nadolol and isosorbide mononitrate for the prevention of esophageal variceal rebleeding. *Gastroenterology* 123:728-34. [View Article]

31. Garcia-Pagan JC, Morillas R, Banares R, Albillos A, Villanueva C et al (2003) Propranolol plus placebo versus propranolol plus

isosorbide-5-mononitrate in the prevention of a first variceal bleed:a double-blind RCT. *Hepatology* 37:1260-6. [View Article]

32. Schepke M, Kleber G, Nurnberg D, Willert J, Koch L et al (2004) Ligation versus propranolol for the primary prophylaxis of variceal bleeding in cirrhotic. *Hepatology* 40:65-72. [View Article]

33. Reiberger T, Ulbrich G, Ferlitsch A, Payer BA, Schwabl P et al (2013) Carvedilol for primary prophylaxis of variceal bleeding in cirrhotic patients with haemodynamic non-response to propranolol *Gut* 62:1634-34. [View Article]

34. William F, Loran T. (2010) Assessment of success rate of treatment of bleeding esophageal varices in cirrhotic liver patients. *Hepatology J* 30:70-8[View Article]

35. Abid S Saadat Ali, Muhammad Asif Baig, and Anam Akbar Waheed (2015) Carvedilol vs propranolol for portal hypertension *WJGE* May 7: 532-539. [View Article]

36. ShahShah HA, Azam Z, Rauf J Abid S, Hamid S et al (2014) Carvedilol vs.esophageal variceal band ligation in the primary prophylaxis of variceal hemorrhage: a multi centre randomized controlled trial. *J Hepatol* 60: 757-64. [View Article]

Citation: Hanno AF, Aboelkheir HF, Alwazzan D, Abdelrahman MI (2018) Medical Versus Endoscopic Treatment of Oesophageal Varices in Liver Cirrhosis. Gut Gastroenterol 1: 001-005.

Copyright: © 2018 Abdelrahman MI et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.