

OUTCOME AFTER INJECTION SCLEROTHERAPY FOR ESOPHAGEAL VARICEAL BLEEDING IN PATIENTS WITH LIVER CIRRHOSIS & COPD

Rukhsana Javed Farooqi, Javed Iqbal Farooqi,
Masood-ur-Rehman, Hameed Ahmad,
Farooq Ahmad, Sultan Gul

Department of Pulmonology , Khyber Teaching Hospital, Peshawar
Department of Medicine, PGMI, Lady Reading Hospiatl, Peshawar

ABSTRACT

Objective: to find out the outcome after variceal bleeding in patients with liver cirrhosis and COPD.

Material and Methods: This retrospective study was conducted in Gastroenterology Unit, HMC Peshawar & Saidu Group of Teaching Hospitals Swat, from June 1998 to December 2002. The study group comprised cirrhotic & COPD patients treated with endoscopic sclerotherapy for esophageal bleeding.

Results: Twenty-seven patients, 22 men and 5 women, with a mean (SD) age of 47.4 (4.2) years (range 34-53 years), were studied. Out of 27 patients, bleeding was successfully controlled in 25 patients (92.59%), whereas 02 (07.40%) died within 48 hours, despite the therapy. Seven (25.92%) patients developed complications, including encephalopathy (n=5) and renal failure (n=2).

Conclusion: We conclude that occurrence of variceal bleeding is associated with high morbidity and the frequent development of life-threatening complications in patients with liver cirrhosis and COPD. Hepatic encephalopathy, rebleeding, renal failure, and hepatocellular carcinoma are the main risk factors.

Key words: Cirrhosis, COPD, Variceal Bleeding.

INTRODUCTION

Acute variceal bleeding ranges amongst the most common causes of morbidity and mortality during the clinical course of liver cirrhosis¹⁻⁴. Severity, presentation and source of bleeding, degree of liver dysfunction, and presence of underlying conditions (like in COPD patients) are the possible factors, which determine the morbidity and mortality of such cases^{3,5,6}. A retrospective analysis was done, of cirrhotic patients with COPD, who were admitted to the hospital with variceal bleeding, to find out the outcome.

MATERIAL AND METHODS

Twenty-seven cirrhotic patients with COPD presenting with variceal bleeding, admitted to hospitals where one of the authors worked (Hayatabad Medical Complex Peshawar & Saidu Group of Teaching

Hospitals / Shifa Medical Center Swat) from June 1998 to December 2002, were included in this retrospective study. The clinical condition of the patients at the time of bleeding was graded according to the Child-Pugh classification⁷. Co-morbid conditions were classified according to the index developed by Charlson, et al⁸. Laboratory investigations at the time of hospital admission included serum albumin, prothrombin time, serum total bilirubin, and platelet count. An episode of bleeding was assessed regarding its severity⁹ (mild, moderate, severe), presentation (hematemesis and/or melena), endoscopic intervention and its findings^{10,11}, associated conditions like ingestion of NSAIDs, spontaneous bacterial peritonitis, hepatocellular carcinoma, etc. The outcome of bleeding was analyzed according to the following parameters:

1. Successful control of bleeding defined as

absence of rebleeding, stable pulse rate, blood pressure, and hematocrit.

2. Rebleeding defined as, new episode of bleeding developing 6 hours after the initial episode has been successfully controlled¹².
3. Complications like encephalopathy, ascites, Hepatorenal syndrome, and spontaneous bacterial peritonitis.
4. Mortality divided as immediate, within first 48 hours, within the next 6 weeks, death up to the end of follow-up.

Statistical analysis:

Statistical analyses were carried out by using Chi-square test for the comparison of proportions, and Student's t-test for the comparisons of means.

RESULTS

Baseline characteristics:- Twenty-seven patients with liver cirrhosis & COPD, 22 men and 5 women, with a mean (\pm SD) age of 47.4 \pm 4.2 years (range 34 - 53 years), were studied. Nineteen (70.37%) patients were anti-HCV positive and 8 (29.63%) patients were HBs-Ag positive. Majority of the patients belonged to Child class B & C, with moderate severity of bleeding, presenting with hematemesis and melena, and bleeding from esophageal varices (Table-1).

□ **Outcome and its prognostic factors:-** Outcome parameters included the following:

□ **Successful control of bleeding:** Out of 27 patients, bleeding was successfully controlled in 25 patients (92.59%). Control

Baseline characteristics of the patients

CHARACTERISTICS	NO OF PATIENTS (n=27)
Sex distribution (M/F)	(22/05)
Age distribution (Mean SD)	47.4 \pm 4.2 years
Virology of cirrhosis:	
● Anti-HCV positive	19 (70.37%)
● HBsAg positive	08 (29.63%)
Child-Pugh grade:	
● A	03 (11.11 %)
● B	05 (18.51%)
● C	19 (70.38%)
Severity of bleeding:	
● Mild	02 (07.40 %)
● Moderate	16 (59.26%)
● Severe	09 (33.34%)
Type of bleeding:	
● Hematemesis	02 (07.40%)
● Melena	09 (33.34%)
● Hematemesis & melena	16 (59.26%)
Endoscopic findings:	
● Esophageal varices	23 (85.18%)
● Gastric varices	04 (14.82%)
Associated conditions:	
● Ingestion of NSAIDs	03 (11.11 %)
● Spontaneous bacterial peritonitis	05 (18.52 %)
● Hepatocellular carcinoma	01 (03.70 %)

Table-1

of bleeding was significantly associated with Child-Pugh classification (all patients [100 %] in grade A & B, whereas 17 patients [89.47%] in grade C, ($p < 0.05$); and severity of bleeding (all patients [100 %] in mild & moderate episodes, whereas 7 patients [77.77%] in severe episodes, ($p < 0.05$).

- Re-bleeding:- Out of 25 patients in whom acute variceal bleeding was successfully controlled, rebleeding occurred in 4 patients (16.00%). Rebleeding was significantly associated with Child-Pugh classification (none of the patients [0%] in grade A or grade B, all 4 patients [21.05%] in grade C, ($p < 0.05$); and severity of bleeding (none of the patients [0%] in mild episodes, 1 patients [06.25%] in moderate episodes, and 3 patients [33.33%] in severe episodes, ($p < 0.05$).
- Other Complications:- Out of 25 patients in whom acute variceal bleeding was successfully controlled, 7 patients (25.92%) patients developed complications, including encephalopathy ($n=5$) and renal failure ($n=2$). Complications were significantly associated with Child-Pugh classification (none of the patients [0%] in grade A, 1 patients [20.00%] in grade B, and 6 patients [31.58%] in grade C, ($p < 0.05$); and severity of bleeding (none of the patients [0%] in mild episodes, one patient [06.25%] in moderate episodes, and 6 patients [66.67%] in severe episodes, ($p < 0.05$).
- Mortality:- Out of 27 patients, 2 patients (07.40%) died within 48 hours, despite the therapy, because of irreversible shock. Both the patients were in elderly age group ($p < 0.05$), in Child-Pugh C grade ($p < 0.005$), and with very severe episode of bleeding ($p < 0.005$).

DISCUSSION

Occurrence of an episode of acute variceal bleeding worsens the natural history of compensated cirrhosis¹³⁻¹⁶. The aim of the present study was to find out the outcome in terms of control of bleeding, occurrence of rebleeding, complications and mortality survival after acute variceal bleeding in a high-risk group of cirrhotic patients like those with COPD. It should be noted, however, that

results should be interpreted with caution because of the retrospective design of the study and relatively small number of patients studied.

Regarding epidemiological aspects, we found a tendency towards decreasing age at the time of presentation of the bleeding episode throughout the observation period. We also found a decrease in the percentage of patients in whom upper GI bleeding was the first presentation of cirrhosis. Our observations are comparable with others⁹.

Regarding the possible predisposing factors of acute variceal bleeding, NSAIDs ingestion was noted in only 3 patients [11.11%], similar to other studies¹⁷⁻²¹. Predominant source of bleeding was esophageal varices, followed by gastric varices; also comparable with other studies^{3,17,18,22}.

Acute variceal bleeding was successfully controlled in 25 patients (92.59%), by injection sclerotherapy with absolute alcohol in case of esophageal varices and diathermy electrodiathermy-coagulation in case of gastric varices. Out of these, complications like encephalopathy & renal failure occurred in 7 patients (25.92%). Two patients (7.41%) died within 48 hours, despite the therapy, because of irreversible shock. Child-Pugh class C and severe attack of bleeding were associated with increased risk of failure of control of bleeding, occurrence of rebleeding, development of encephalopathy & renal failure, and mortality; comparable with other studies²²⁻²⁸. Factors significantly affecting the mortality were advanced age ($p < 0.05$), Child-Pugh C grade ($p < 0.005$), and severity of bleeding ($p < 0.005$). There is a large variation in mortality rates among studies^{2,4,29-31}, mainly in relation to the periods of time in which studies were conducted since the management of variceal bleeding has shown a substantial change in recent years. Other possible factors include differences in the interpretation of time 'zero' i.e. the time of beginning of the bleeding episode, study population, outcome parameters, etc.

We conclude that occurrence of variceal bleeding is associated with high morbidity and the frequent development of life-threatening complications in patients with liver cirrhosis and COPD. Hepatic

encephalopathy, rebleeding, renal failure, and hepatocellular carcinoma are the main risk factors. Long-term survival needs to be determined in such cases in prolonged studies.

REFERENCES

1. Franco D, Durandy Y, Deporte A, Bismuth H. Upper gastrointestinal hemorrhage in hepatic cirrhosis: causes and relation to hepatic failure and stress. *Lancet* 1977; 80:218-20.
2. Graham DY, Smith JL. The course of patients after variceal hemorrhage. *Gastroenterology* 1981; 80:800-9.
3. Christensen DY, Krintel JJ, Meltofte HS, et al. Prognosis after the first episode of gastrointestinal bleeding or coma in cirrhosis: Survival and prognosis. *Scand J Gastroenterol* 1989; 24:999-1006.
4. Burroughs AK, Mezzanotte G, Phillips A, et al. Cirrhotics with variceal hemorrhage: the importance of the time interval between admission and the start of analysis for survival and rebleeding rates. *Hepatology* 1989; 9:801-7.
5. Garden OJ, Motyl H, Gilmour WH, et al. Prediction of outcome following acute variceal hemorrhage. *Br J Surg* 1985; 72:91-5.
6. De Franchis R, Pascal JP, Ancona E, et al. Definitions, methodology and therapeutic strategies in portal hypertension. *J Hepatol* 1992; 15:256-61.
7. Pugh RN, Murray-Lyon IM, Dawson JL, et al. Transaction of the esophagus for bleeding esophageal varices. *Br J Surg* 1973; 60:646-9.
8. Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987; 40:373-83.
9. Juan A O, Andres P, Miguel A S, Abdallah H W, Adolfo B, Jose M R. Predictors of morbidity and mortality after the first episode of upper GI bleeding in liver cirrhosis. *J of Hepatol* 2000; 32:19-24.
10. Paquet KJ, Mercado-Diaz M, Kalk JF. Frequency, significance and therapy of the Mallory-Weiss syndrome in patients with portal hypertension. *Hepatology* 1990; 11:879-83.
11. Tabibian N, Graham DY. Source of upper gastrointestinal bleeding in patients with esophageal varices seen at endoscopy. *J Clin Gastroenterol* 1987; 9:279-82.
12. Fleischer D. Etiology and prevalence of severe persistent upper gastrointestinal bleeding. *Gastroenterology* 1983; 84:538-43.
13. Saunders JB, Walters JRF, Davies P, et al. A 20-year prospective study of cirrhosis. *Br Med J* 1981; 282:263-6.
14. D'Amico G, Morabito A, Pagliaro L, et al. Survival and prognostic indicators in compensated and decompensated cirrhosis. *Dig Dis Sci* 1986;31:468-75.
15. Gines P, Quintero E, arroyo V, et al. Compensated cirrhosis: natural history and prognostic factors. *Hepatology* 1987;7: 122-8.
16. Gentini P, Laffi G, La Villa G, et al. Long course and prognostic factors of virus-induced cirrhosis of the liver. *Am J Gastroenterol* 1997; 92:66-72.
17. Poynard T, Chaput JC, Mary JY, et al. Analyse critique des facteurs lies a late mortalite au trentieme jours dans les hemorrhagies digestive hautes du cirrhotique (Eng. Trans). *Gastroenterol Clin Biol* 1980; 4:655-65.
18. Gatta A, Merkel C, Amodio P, et al. Development and validation of a prognostic index predicting death after upper gastrointestinal bleeding in patients with liver cirrhosis: a multicenter study. *Am J Gastroenterol* 1994; 89: 1528-36.
19. Wilcox CM, Shalek KA, Cotsonis G, et al. Striking prevalence of over-the-counter NSAID use in patients with upper gastrointestinal bleeding. *Arch Intern Med* 1994; 154:42-6.
20. De Ledinghen V, Heresbach D, Fourdan O, et al. Anti-inflammatory drugs and variceal bleeding: a case-control study. *Gut* 1999; 44:270-3.
21. Corely DA, Stefan AM, Wolf M, et al. Early indicators of prognosis in upper gastrointestinal bleeding. *Am J Gastroenterol* 1998; 93:336-40.

22. Koff RS. Benefit of endoscopy in upper gastrointestinal bleeding in patients with liver disease. *Dig Dis Sci* 1981; 26(suppl):125-6.
23. Bernard B, Cadranel JF, Valla D, et al. Prognostic significance of bacterial infection in bleeding cirrhotics patients: a prospective study. *Gastroenterolgy* 1995; 108:1828-34.
24. Castera L, Pauwels A, Levy VG, et al. Indicateurs pronostiques chez les malades atteints de cirrhosis admis en service de reanimation(Eng. Trans). *Gastroenterol Clin Biol* 1996; 20:263-8.
25. Melchior JC, Poupon RE, Verrier J, et al. Analyse des facteurs lies la mortalite precoce au cours des hemorragies digestives dues 1'hypertention portale(Eng. Trans). *Gastroenterol Clin Biol* 1987; 11:402-8.
26. Hsieh WJ, Lin HCH, Hawng SJ, et al. The effect of ciprofloxacin in the prevention of bacterial infection in patients with cirrhosis after upper gastrointestinal bleeding. *Am J Gastroenterol* 1998; 93:962-6.
27. Goulis J, Armonis A, Patch D, et al. Bacterial infection is indepently associated with failure to control bleeding in cirrhotic patients with gastrointestinal bleeding. *Hepatology* 1998; 27:1207-12.
28. Pauwels A, Mostefa-Kara N, Debenes B, et al. Systemic antibiotic prophylaxis after gastrointestinal bleeding in cirrhotic patients with a high risk of infection. *Hepatology* 1996; 24:802-6.
29. Thomas E, Rosenthal WS, Rymer W, et al. Upper gastrointestinal bleeding in patients with alcoholic liver disease and esophageal varices. *Am J Gastroenterol* 1979; 72:623-9.
30. Heresbach D, Bretagne JF, Raoul JL, et al. Prognostic et facteurs pronostiques de l'hemorragie par rupture de varice chez le cirrhotique a l'ere de la sclerose endoscopique (Eng. Trans). *Gastroenterol Clin Biol* 1991; 12:838-44.
31. Merkel C, Gatta A, Bellumet A, et al. optimizing the time-frame for the definition of bleeding related death after acute variceal bleeding in cirrhosis. *Eur J Gastroenterol hepatol* 1996; 8:75-9.

Address for correspondence:

Rukhsana Javed Farooqi
 Department of Pulmonology ,
 Khyber Teaching Hospital, Peshawar