G Chir Vol. 35 - n. 3/4 - pp. 61-64
March-April 2014

original article

Endoscopic sclerotherapy for hemostasis of acute esophageal variceal bleeding

G. ROMANO, A. AGRUSA, G. AMATO, G. DE VITA, G. FRAZZETTA, D. CHIANETTA, V. SORCE, G. DI BUONO, G. GULOTTA

SUMMARY: **Endoscopic sclerotherapy for hemostasis of acute esophageal variceal bleeding.**

G. ROMANO, A. AGRUSA, G. AMATO, G. DE VITA, G. FRAZZETTA, D. CHIANETTA, V. SORCE, G. DI BUONO, G. GULOTTA

Introduction. *Currently the most widely used methods for endoscopic control of esophageal varices bleeding are sclerotherapy and rubber band ligation. Although the superiority of band ligation (BL) over endoscopic sclerotherapy (SCL) for the secondary prophylaxis of variceal hemorrhage has been proven, the best approach for acute bleeding remains controversial.*

Patients and methods. *We performed a retrospective study between January 2005 and May 2013. We selected 104 patients with gastrointestinal hemorrhage from rupture of esophageal varices treated with endoscopic sclerotherapy. The sclerosing agent used was 1% polidocanol in 89 cases, butyl-cyanoacrylate in 8 cases and sodium tetradecylsulfate in 4 cases. In 3 cases had not been carried sclerosis because it was not possible to identify the bleeding site.*

Results. *Among the 101 patients who underwent endoscopic sclerotherapy 4 presented re-bleeding within 12 hours from first treatment. Other 10 patients (9.9%) presented re-bleeding within a 5-days period. The most frequent complication was ulceration, observed in 4 cases (3.8%). There was only one case of perforation treated conservatively.*

Conclusions. *The general improvement in the results of the treatment of variceal acute bleeding might be attributed to better clinical management of these patients. In literature no consensus exists regarding the preferred endoscopic treatment. To date, there is no single method applicable to all patients with bleeding esophageal varices, but sclerotherapy is considered effective, safe and repeatable in experienced hands.*

KEY WORDS: Esophageal variceal bleeding - Endoscopic sclerotherapy - Endoscopy - Urgency setting.

Introduction

Ascites, port-caval encephalopathy and bleeding from rupture of esophageal varices are the three most serious complications that can occur in the course of portal hypertension. However, the first two, although quite frequent in the course of the disease, only rarely constitute a cause of life-threatening for the patient. Instead the rupture of varicose veins is a serious and often dramatic event that requires effective rapid and therapeutic choices (1, 2). The endoscopic sclerotherapy is now used to stop acute bleeding from rupture of varices (urgent sclerosis), instead it was put into question the usefulness of this technique in the prevention of first bleeding event (prophylactic sclerosis) and in the prevention of recurrences (elective sclerosis) (3).

The probability that a cirrhotic patient developments esophageal varices varies widely, although in general, it is related to the duration of the disease (4). In a prospective study carried out in 10 years the presence of esophageal varices varies from an average of 8% to 83%, although it has never been demonstrated that incidence follow a linear function (5). The varices progressively increase their size with a variable rate from 5% to 30% for year (6). Patients with endoscopic diagnosis of esophageal varices have, in the 20-28 months following the investigation, the 30% rate of bleeding. Furthermore 70% of survivors has a re-bleeding within a year with mortality rate about 30%. The classification of the Japanese Society for the study of Portal Hypertension allows us to make a more accurate prognosis (7). Varices are defined blue or white according to the color of the mucosa that covers them. For definition of the red marks are identified four sub-

University of Palermo, Palermo, Italy
Department of General Surgery, Urgency and Organ Transplantation

Corresponding author: Giorgio Romano, e-mail: giorgio.romano@unipa.it

groups: 1. dilated venules arranged longitudinally (red wale markings); 2. small patches of redness (cherry red spots); 3. localized blood collections; 4. diffuse redness. In relation to size, esophageal varices are classified as F1, F2 and F3. Other parameters to consider are the extension to the wall (lower third, middle, upper) and the presence of concomitant esophagitis. The cirrhotic patient is very serious, for his poor general condition and the severity of the bleeding itself. He must be treated effectively in the shortest possible time to stop hemorrhage and to prevent early rebleeding (8, 9). It must be remembered furthermore that in 30% of cases the source of bleeding in patients with cirrhosis is represented by a different cause from esophageal varices (varicose veins of the gastric fund, gastropathy, peptic ulcer, antral erosions) (10). Currently the most widely used methods for endoscopic control of esophageal varices bleeding are sclerotherapy and rubber band ligation (3). Although the superiority of band ligation (BL) over endoscopic sclerotherapy (SCL) for the secondary prophylaxis of variceal hemorrhage has been proven, the best approach for acute bleeding remains controversial (11). A recent meta-analysis suggest that sclerotherapy remains the first-choice therapy in the treatment of acute bleeding secondary to esophageal variceal rupture (12).

Patients and methods

Study design

We performed a retrospective study between January 2005 and May 2013 at General Surgery and Emergency Department with Digestive Endoscopic Service of the University Hospital Policlinico "P. Giaccone" in Palermo. We selected 104 patients with gastrointestinal hemorrhage from rupture of esophageal varices treated with endoscopic sclerotherapy. 32 patients were excluded from the study for a number of reasons (Figure 1). In the 104 patients selected in this study a diagnostic endoscopy was performed within six hours from the bleeding. After obtaining informed consent to the procedure (by the patient himself or by the legal representative in case of unconsciousness) we conducted an esophagogastroduodenoscopy (Olympus® GIF-Q145 and GIF-Q160 gastroscope) with the patient in the left lateral decubitus position, with mild sedation (Midazolam® i.v.) and anesthesiologic support (13-15). We identified the site of bleeding and after washing with cold saline solution we performed endoscopic sclerosis. Only in 3 patients (2.9%) we didn't need any hemostasis procedure for spontaneous stop of hemorrhage with inability to recognition of the bleeding site.

Endoscopic technique

Endoscopic sclerotherapy of esophageal varices can be achieved with "overtube" technique or with "freehand" technique. In our experience we always used the freehand technique because the overtube placement is difficult, results in a significant reduction of vision and can cause the rupture of esophageal varices. We used Polidocanol 1% (Ethoxysklerol®) in 89 cases (85.6%), butyl-cyanoacrylate (Histoacryl®) in 8 cases (7.7%) and sodium tetradecyl sulfate 1% (Trombovar®) in 4 cases (3.8 %). Then we abandoned use of sodium tetradecyl sulfate for more difficult control of the bleeding and for the excessive dose of sclerosing useful to obtain haemostasis. Sclerosant agent could be injected into intra- or paravariceal locations. The objective of intravariceal injection is to induce thrombosis and subsequent occlusion of the lumen of the varix. Paravariceal injection, however, occludes the varix by tamponade and induction of submucosal fibrosis of tissue around the varix. Intravariceal injection requires less force but induces more temporary bleeding during the procedure (16).

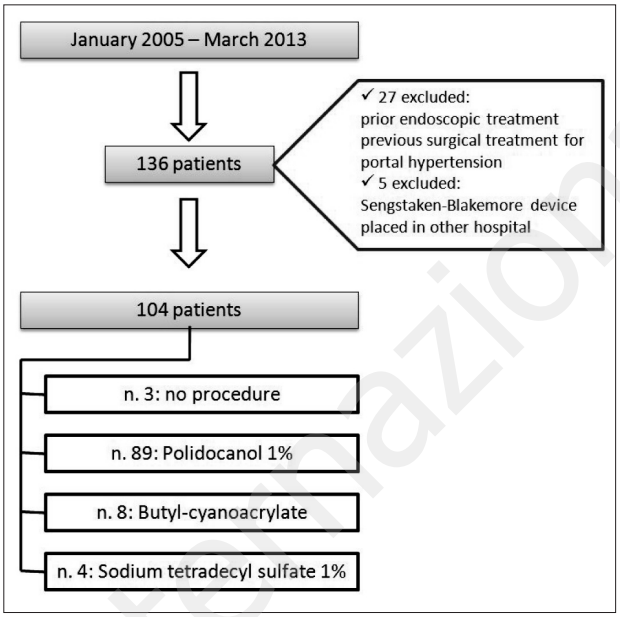

Fig. 1 - Flow chart of patients distribution.

Results

Among the 101 patients who underwent endoscopic sclerotherapy 4 presented re-bleeding within a 12-hours period (early period). In these cases we used butyl-cyanoacrylate (Histoacryl®) with resolution of the hemorrhage. 10 patients (9.9%) instead, presented re-bleeding later than a 5-days period (bleeding from the nasogastric tube and/or decrease in hemoglobin > 3g/dL). In these cases we made a new endoscopic sclerotherapy procedure with polidocanol 1% (17).

The most frequent complication was ulceration, occurred in 4 cases (3.8%). In two patients it was particularly wide, extending circumferentially and distally to the cardia. These patients were treated with endoscopic surveillance. In a case occurred stenosis after 120 days from sclerosis that was treated with mechanical dilation. We observed only a case of perforation (0,96%) of limited clinical entity. CT of the thorax showed small air bubbles localized in the posterior mediastinum without evidence of extraluminal fluid spillage. This patients was treated conservatively with placement of nasogastric tube kept on site for 8 days (18-20). The mortality of these patients

TABLE 1 - PATIENTS CHARACTERISTICS.

Mean age (years)	48 (range 31-74)
Gender	
Male	76
Female	28
Etiology	
Virus (HCV – HBV)	57 (54.8%)
Alcohol	44 (42.3%)
Cryptogenic cirrhosis	3 (2.8%)
Child-Pugh Classification	
Child A	7 (6.7%)
Child B	68 (65.4%)
Child C	29 (27.9%)

is still high: in our series, 14 patients (13.5%) died after sclerosis for the occurrence of hepato-renal and cardio-respiratory complication. 11 were Child-Pugh C patients, confirming the negative progression of prognosis in patients with major deficits of liver function (Table 1) (17, 21).

Discussion

The general improvement in the results of the treatment of variceal acute bleeding might be attributed to better clinical management of these patients. The use of vasoactive drugs (terlipressin) and antibiotic prophylaxis (third generation cephalosporin or quinolone) is currently mandatory for patients with variceal bleeding. Antibiotic therapy reduce the infection rate from 45% to 14%, bleeding recurrence from 44% to 18% and mortality rate from 48% to 15% (22, 23). Although the highest-level recommendation of the use of antibiotics and vasoactive drugs is already established in the literature, no consensus exists regarding the preferred endoscopic treatment in urgency: sclerotherapy or band ligation. Sclerotherapy has proven to be inferior to band ligation for primary and secondary prophylaxis of variceal hemorrhage, but endoscopic sclerotherapy would seem equally effective in the treatment of bleeding in urgency, with the advantages of a simple technique widespread on the territory (24). In clinical practice there are a number of variations in the endoscopic sclerosing technique, including the type of sclerosing agent used, its concentration, injected volume and injection location (intravascular, paravascular or combined), which is reflected in the heterogeneous results of endoscopic sclerotherapy presented in literature (25).

Sclerosis might be achieved, if technically possible, during the bleeding: patients treated in the immediate urgency had better rate of hemostasis and survival and a lower number of re-bleeding. It must be remembered, however, that regardless of the success of sclerotherapy, the high mortality rate is due in large part to the appearance of hepato-renal syndrome and ascites (26). The complication rate of this technique was between 0% and 17.5%. The major complication were stenosis, perforation and ab ingestis pneumonia. Among the minor complications instead we frequently observed the ulcer post-sclerosis (27, 28).

Conclusions

The treatment of acute bleeding from ruptured of esophageal varices has rapidly evolved in the last decades, with the application of new pharmacological protocols (vasoactive drugs and antibiotic prophylaxis), the use of new sclerosant agents and multi-band ligators easier to use, the selective use of trans-iugular portal-systemic shunt (TIPSS) and porto-caval shunt and wider diffusion of liver transplantation (11). There isn't a unique method applicable to all patients with bleeding from esophageal varices. Definitely, an integrated management with initial hemodynamic stabilization of the patient with vaso-active drugs followed by the endoscopic urgent treatment is a satisfactory approach in terms of efficacy and safety in the short and medium term. From analysis of the controversial results of the literature and considering our experience, it appears that endoscopic sclerosis is still a technique of primary importance in the emergency treatment of bleeding from the rupture of esophageal varices. Furthermore, endoscopic sclerotherapy is also widely used in clinical practice and has lower costs. In the overall assessment of the effectiveness of endoscopic sclerosis of esophageal varices in urgent setting, however, these criteria shouldn't be separated from other elements which are also the basis for the success of the technique. In fact, to obtain the better results, it is always necessary the presence of an expert endoscopist who operates in a structure able to fully ensure hepatic and resuscitation management.

References

1. Bosch J, Garcia-Pagan JC. Complications of cirrhosis. I. Portal hypertension. J Hepatol. 2000;32:141-15.
2. Romano G, Agrusa A, Frazzetta G, De Vita G, Chianetta D, Di Buono G, Amato G, Gulotta G. Laparoscopic drainage of liver

abscess: case report and literature review. G Chir. 2013 May-Jun;34(5-6):180-2.

3. Cordon JP, Torres CF, Garcia AB, Rodriguez FG, Suarez de Parga JM. Endosocpic management of esophageal varices. World J Gastrointest Endosc. 2012 16;4(7):312-322.
4. Merli M, Nicolini G, Angeloni S, Rinaldi V, De Santis A, Merkel C, Atili AF, Riggio O. Incidence and natural history of small esophageal varices in cirrhotic patients. J Hepatol. 2003;38:266-22.
5. Czaja AJ, Wolf AM, Summerskill WHJ. Development and early prognosis of esophageal varices in severe chronic active liver disease. Gastroenter. 1979;7:629-633.
6. G DA. Esophageal varices: from aparence to rupture; natural history and prognosis indicators. In: Groszmann RJ BJ, ed. Portal Hypertension in the 21st Century. Dordrecht: Kluwer Academic Publishers; 2004:147-154.
7. Idezuki Y. General rules for recording endoscopic findings of esophagogastric varices (1991). Japanese Society for Portal Hypertension. World J Surg. 1995 May-Jun;19(3):420-2; discussion 423.
8. Abraldes JC, Bosch J. The treatment of acute variceal bleeding. J Clin Gastroenterol. 2007;41 Suppl 3:S312-S317
9. Agrusa A, Romano G, Di Buono G, Dafnomili A, Gulotta G. Laparoscopic approach in abdominal emergencies: a 5-year experience at single centre. G Chir. 2012 Nov-Dec;33(11-12):400-3.
10. Sarin SK, Govil A, Jain AK, Guptan RC, Issar SK, Jain M, Murthy NS. Prospective randomized trial of endoscopic sclerotherapy versus variceal band ligation for esophageal varices: influence of gastropathy, gastric varices and variceal recurrence. J Hepatol. 1997;26:826-832.
11. De Franchis R. Evolving consensus in portal hypertension. Report of the Baveno IV consensus workshop on methodology of diagnosis and therapy in portal hypertension. J Hepatol. 2005;43:167-176.
12. Triantos K, Goulis J, Patch D, Papatheodoridis GV, Leandro G, Samonakis D, Cholongitas E, Burroughs AK. An evaluation of emergency sclerotherapy of varices in randomized trials: looking the needle in the eye. Endoscopy. 2006; 38:797-807.
13. Romano G, Cocchiara G, Cajozzo M, Di Bernardo C, Buscemi G, Agrusa A, Maresi E, Diana G. Endoscopic treatment of gastric carcinoid. Report of a clinical case. Chir Ital. 2003 Jul-Aug;55(4):601-4.
14. Romano G, Cocchiara G, Calderone F, Luna E, Virzì C, Agrusa A, Romano G, Buscemi S, Di Bernardo C, Buscemi G, Maresi E, Gioe' FP, Diana G. Endoscopic treatment of colorectal polyps in a digestive endoscopy outpatient department. Chir Ital. 2004 Sep-Oct;56(5):669-73.
15. Pisano G, Calò PG, Tatti A, Farris S, Erdas E, Licheri S, Dazzi C, Daniele GM. Surgical gastrostomy when percutaneous endoscopic gastrostomy is not feasible: indications, results and comparison between the two procedures. Chir Ital. 2008 Mar-Apr;60(2):261-6.
16. Cardenas A. Management of acute variceal bleeding: emphasis on endoscopic therapy. Clin Liver Dis. 2010;14:251-262.
17. Luz GO, Maluf-Filho F, Matuguma SE, Hondo FY, Ide E, Melo JM, Cheng S, Sakai P. Comparison between endoscopic sclerotherapy and band ligation for hemostasis of acute variceal bleeding. World J Gastrointest Endosc. 2011;3(5):95-100.
18. Lindenmann J, Matzi V, Neuboeck N, Anegg U, Maier A, Smolle J, Smolle-Juettner FM. Management of esophageal perforation in 120 consecutive patients: clinical impact of a structured treatment algorithm. J Gastrointest Surg. 2013;17(6):1036-43.
19. Agrusa A, Romano G, Bonventre S, Salamone G, Cocorullo G, Gulotta G: Laparoscopic treatment for esophageal achalasia: experience at a single center. G Chir. 2013 Jul-Aug;34(7-8):220-3.
20. Gulotta G, Agosta G, Romano G: Perforated duodenal diverticulum: report of a case. Chir Ital. 2001 Jan-Feb;53(2):255-8.
21. Novo G, Corrado E, Tortorici E, Novo A, Agrusa A, Saladino V, Marturana I, Lentini R, Ferrandes M, Visconti C, Massenti F, D'Arienzo M, Vitale F, Gulotta G, Novo S. Cardiac risk stratification in elective non-cardiac surgery: role of NT-proBNP. Int Angiol. 2011 Jun;30(3):242-6.
22. Bernard B, Grangè JD, Khac EN, Amiot X, Opolon P, Poynard T. Antibiotic prophylaxis for the prevention of bacterial infections in cirrhotic patients with gastrointestinal bleeding: a meta-analysis. Hepatology. 1999;29:1655-1661.
23. Hou MC, Lin HC, Liu TT, Kuo BI, Lee FY, Chang FY, Lee SD. Antibiotic prophylaxis after endoscopic therapy prevents re-bleeding in acute variceal hemorrhage: a randomized trial. Hepatology. 2004;39:746-753.
24. Garcia-Tsao G, Sanyal AJ, Grace ND, Carey W. Prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis. Hepatology. 2007;46:922-938.
25. ASGE technology status evaluation report: Sclerosing agents for use in GI endoscopy. Gastrointest Endosc. 2007;66.
26. D'Amico G, De Franchis R. Upper digestive bleeding in cirrhosis. Post-therapeutic outcome and prognostic indicators. Hepatology. 2003;38:599-612.
27. Lee JG, Lieberman DA. Complication related to endoscopic hemostasis techniques. Gastrointest Endosc Clin N Am. 1996;6:305-321.
28. Russo S, Lo Re G, Galia M, Reginelli A, Lo Greco V, D'Agostino T, La Tona G, Coppolino F, Grassi R, Midiri M, Lagalla R. Videofluorography swallow study of patients with systemic sclerosis. Radiol Med. 2009 Sep;114(6):948-59.