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Original Article

A controlled trial of early versus delayed feeding following ligation in the control of acute esophageal variceal bleeding

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Abstract

Background: The impact of feeding after endoscopic treatment of gastroesophageal varices has rarely been thoroughly investigated. We conducted a controlled study to evaluate whether delayed feeding causes a reduced incidence of rebleeding on patients receiving emergency endoscopic therapy for bleeding gastroesophageal varices.

Methods: Cirrhotic patients presenting with acute esophageal variceal bleeding were provided critical treatment through emergency endoscopic variceal ligation. After bleeding from the varices had been arrested, the eligible participants were randomized to two groups. The early-feeding group and the delayed-feeding group were asked to fast for 4 hours and 48 hours, respectively, after endoscopic therapy. The primary end points were initial hemostasis, very early rebleeding, and ulcer-bleeding rates.

Results: There were 36 patients enrolled in the early-feeding group and 34 patients in the delayed-feeding group. Both groups were comparable in baseline data. Initial hemostasis was achieved in 100% in both groups, and very early rebleeding was not encountered in either group. The incidence of adverse events was similar between both groups. The mean hospitalization days were 6.0 ± 2.4 days (range: 2–17 days) in the early-feeding group, and 7.5 ± 3.1 days (range: 3–22 days) in the delayed-feeding group ($p < 0.05$).

Conclusion: Early feeding with liquid diet after a successful endoscopic therapy of bleeding varices did not have any impact on hemostasis.

Keywords: banding ligation; early feeding; variceal bleeding

1. Introduction

Acute esophageal variceal hemorrhage is a formidable complication of portal hypertension, although its management has evolved rapidly in recent years.[1,2] Vasoconstrictors are generally used as a first-line therapy. Following the use of a vasoconstrictor, endoscopic therapy is often employed to arrest the bleeding varices as well as to prevent early rebleeding. A meta-analysis showed that the combination of vasoconstrictor and endoscopic therapy is superior to endoscopic therapy alone in the control of acute esophageal variceal hemorrhage.[3] Previous studies showed that endoscopic variceal ligation (EVL) is superior to endoscopic injection sclerotherapy (EIS) in the control of active variceal hemorrhage.[4,5] It is thus recommended that EVL is the endoscopic treatment of choice for acute esophageal variceal bleeding.[5] Moreover, apart from the control of acute variceal bleeding, the use of prophylactic antibiotics has been proven to be helpful in the prevention of bacterial infection as well as early variceal rebleeding.[6] Currently, the combination of vasoconstrictors, prophylactic antibiotics, and EVL has become the standard of therapy for patients with acute esophageal variceal bleeding.

On the other hand, a high incidence of early rebleeding may be encountered after combination therapy. It is estimated that

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40% of early rebleeding occurs within 5 days of initial bleeding, which in turn leads to a high mortality rate.[7,8] The impact of feeding after endoscopic treatment of gastroesophageal varices has rarely been well investigated. It is still unknown whether those early rebleeding events have any relation to the feedings of patients with acute esophageal variceal bleeding treated with EVL. It is customary for clinicians to institute absolute fasting for 2 or 3 days after an emergency EVL. This may presumably be a safe approach to guard against the occurrence of early rebleeding. However, prolonged fasting may be unethical to patients who have a low risk of rebleeding. Moreover, prolonged fasting may lead to impaired nutrition and development of ascites in cirrhotic patients, possibly resulting in an increased length of hospitalization. Thus, we conducted a controlled study to evaluate whether delayed feeding has a reduced incidence of rebleeding on patients receiving emergency endoscopic therapy for bleeding gastroesophageal varices.

2. Methods

Between March 2011 and December 2012, patients presenting with acute gastroesophageal variceal bleeding proven by emergency endoscopy within 12 hours were considered for enrollment. Other enrolled criteria were (1) the etiology of portal hypertension was cirrhosis; (2) patients between 20 and 80 years of age; (3) EVL was performed after confirmation of acute esophageal variceal bleeding, and Histoacryl injection was performed if acute gastric variceal bleeding was diagnosed; and (4) variceal bleeding was arrested on the spot by emergency endoscopic therapy.

Acute esophageal variceal bleeding was defined as (1) when blood was directly seen by endoscopy to issue from an esophageal varix (active bleeding), or (2) when patients presented with red color signs or blood clots on their esophageal varices with blood in the esophagus or stomach, and no other potential site of bleeding has been identified (inactive bleeding).[8] *Gastric variceal bleeding* was defined as active spurting from a gastric varix or the presence of red spots and erosions on a gastric varix.[9] The diagnosis of cirrhosis was based on history, physical examinations, liver histology, or image studies. Our methods of emergency EVL and Histoacryl injection have been described previously in detail.[8–10] Briefly, ligation was initiated at the bleeding point, hematocystic spots or white nipple signs if present, or at gastroesophageal junction, and advanced proximally. The obturation agent for gastric varices was 0.5 mL *n*-butyl-2-cyanoacrylate (Histoacryl; B. Braun Melsungen AG, Melsungen, Germany) mixed with 0.5 mL Lipiodol Ultra-Fluide (Guerbet, Bois Cedex, France). The injection sites were focused at either the bleeding site or the hematocystic spots, or the erosive spots on the culprit varix. After completion of EVL or gastric variceal obturation, water irrigation was performed to ensure hemostasis was achieved.

The exclusion criteria were (1) association with a severe systemic illness, such as sepsis, uremia, advanced hepatocellular carcinoma (HCC), and HCC staging > Barcelona-Clínic Liver Cancer B; (2) failure to control variceal bleeding by emergency endoscopic therapy; (3) uncooperative or on endotracheal intubation; (4) ever received EIS or EVL within 1 month prior to index bleeding; (5) Child–Pugh's scores >13; (6) deep jaundice (serum bilirubin >10 mg/dL) and presence of encephalopathy > stage II or massive ascites; and (7) refusal to participate.

The eligible participants continued to receive vasoconstrictor for 3 days (either terlipressin or somatostatin) and prophylactic antibiotics for 5 days (cefazolin or cefotaxime). Lactulose was administered to patients with blood or coffee-ground-like materials in the stomach. The eligible participants were randomized to two groups: the early-feeding group and the delayed-feeding group. Randomization was based on a table of random numbers in a sealed envelope. Enrollment was done immediately after endoscopic treatment was completed and variceal bleeding was arrested. Patients in the early-feeding group were asked to fast for only 4 hours following endoscopic treatment. Subsequently, a liquid diet (fruit juice, soybean juice, milk, rice in liquid form) was instituted for 3 days. Additionally, <500 cc intravenous fluid with proper electrolyte supplement per day was administered. Thereafter, a soft diet was provided for 3 days, after which a regular diet was resumed since the seventh day after endoscopic treatment. Patients in the delayed-feeding group were asked to absolutely fast for 48 hours after endoscopic treatment, and 1500 cc/day intravenous fluids (normal saline or glucose water) with proper electrolytes were administered for 2 days. After 2 days of fasting, a liquid diet was given for 1 day, and subsequently, a soft diet was given for 3 days, and then a regular diet was instituted on the seventh day after endoscopic treatment. If rebleeding occurred within 7 days of endoscopic therapy, patients in both groups were again asked to fast for 48 hours, and then put on a liquid diet for 1 day followed by a soft diet for 4 days.

The definitions of treatment failure, very early rebleeding, initial hemostasis, and 5-day hemostasis were similar to those described previously.[11]

Treatment failure was defined as failure to control acute bleeding episodes or very early rebleeding or death within 5 days. *Failure to control acute variceal bleeding* was defined as the occurrence of any of the following events within 48 hours of enrollment, based on the modified criteria of the Baveno III consensus:[11] (1) fresh hematemesis after enrollment; (2) sudden onset of reduction in blood pressure of ≥20 mmHg and/or an increase in pulse rate of ≥20 beats/minute with 2 g drop in hemoglobin; (3) transfusion of four units of blood required to increase the hematocrit to above 27% or hemoglobin to above 9 g/dL; and (4) death. *Very early rebleeding* was defined as when the criteria for failure to control acute variceal bleeding occurred between 48 hours and 120 hours after enrollment in patients achieving control of acute bleeding. *Control of acute bleeding* (initial hemostasis) was defined as when the criteria for failure did not occur within 48 hours of enrollment. A *5-day hemostasis* was defined as when the criteria for failure to control acute variceal bleeding and very early rebleeding did not occur within 5 days of enrollment. A nasogastric tube was not routinely inserted after initial endoscopy. However, a nasogastric tube was inserted in cases of failure to control