Management of Variceal Hemorrhage in Children with Extrahepatic Portal Venous Obstruction-Shunt Surgery Versus Endoscopic Sclerotherapy

Arshad Hussain Wani · Omar Javed Shah · S. A. Zargar

Received: 22 February 2011 / Accepted: 29 September 2011 / Published online: 11 October 2011
© Association of Surgeons of India 2011

Abstract Extrahepatic portal venous obstruction (EHPVO) is a common cause of portal hypertension in children. Esophageal variceal hemorrhage is a major cause of morbidity and mortality in these patients. For many decades, portal systemic shunts were considered as the most effective treatment of variceal hemorrhage. Endoscopic injection sclerotherapy (EIS) was first introduced for emergency management of bleeding varices and subsequently as definitive treatment to prevent recurrent hemorrhage. The purpose of the study was to compare the safety and efficacy of shunt surgery and endoscopic sclerotherapy for patients with proven esophageal variceal bleeding due to EHPVO. The study was a prospective randomized study of 61 children with bleeding esophageal varices due to EHPVO carried out jointly by the department of General Surgery and Gastroenterology at Sher-i-Kashmir Institute of Medical Sciences, Srinagar, between March 2001 and September 2003. Thirty patients received surgery and other 31 patients received EIS. Overall incidence of rebleeding was 22.6% in sclerotherapy group and 3.3% in shunt surgery group. Treatment failure occurred in 19.4% patients in sclerotherapy group and 6.7% in shunt surgery group. The rebleeding rate of sclerotherapy is significantly higher than that of shunt surgery. However, the therapy failure rate of

sclerotherapy is not significantly different from that of shunt surgery.

Keywords Variceal bleeding · Endoscopic sclerotherapy · Shunt surgery · Rebleeding

Introduction

Extrahepatic portal venous obstruction (EHPVO) represents the most frequent cause of portal hypertension in children [1, 2]. It is rare in Western countries, but common in India [2, 3]. Patients with EHPVO have a partial or complete obstruction of their portal trunk; most often secondary to thrombosis of portal vein. The rise in portal venous pressure leads to collateral circulation through portal systemic communications. Varices in the distal esophagus and proximal stomach are a component of the collateral network that divert high-pressure portal venous flow through the left and right gastric veins and short gastric veins to azygos system. Esophageal variceal hemorrhage is a major cause of morbidity and mortality in patients with portal hypertension [4]. It has been suggested that patients with EHPVO either stop bleeding or bleed less frequently as they get older. This is possibly due to new collateral channels opening up as patients get older [5, 6].

The art of managing the patient with recurrent variceal bleeding is to balance the risk of hepatic failure and recurrent bleeding [5]. Operations to prevent recurrent variceal bleeding are directed either to obliterating the varices or reducing portal pressure [5, 7, 8]. Shunts such as end-to-side portocaval, side-to-side portocaval, side-to-side splenorenal and mesocaval direct the blood flow from liver to a systemic vein and in this way decompress the hypertension in the esophageal varices. These are called total shunts and are technically easier. Total diversion was believed to be the major contributing factor in the development of postshunt encephalopathy and late mortal-

A. H. Wani (✉)
Department of Surgery, SD Hospital Kupwara,
Kashmir, India 193222
e-mail: drarshadhwanii@yahoo.co.in

O. J. Shah
Department of Surgical Gastroenterology,
Sher-i-Kashmir Institute of Medical Sciences,
Srinagar, India

S. A. Zargar
Department of Gastroenterology,
Sher-i-Kashmir Institute of Medical Sciences,
Srinagar, India

ity [9, 10]. To avoid these complications, selective decompression of esophageal varices has been explored. The distal splenorenal and coronary vein inferior vena caval shunts decompress the varices without diverting the portal venous blood from liver directly into the systemic circulation. These are called selective shunts. Because of dissatisfaction with portal decompression and its adverse consequences [1, 11], endoscopic sclerotherapy was re-enforced in the 1970's; first for emergency management of bleeding varices and subsequently as definitive treatment to prevent recurrent hemorrhage [12]. Repeated sclerotherapy eradicates esophageal varices in the majority of patients and once the varices have been eradicated, recurrent bleeding is virtually eliminated with adequate follow-up [8].

Aims and Objectives

The purpose of the present study was to compare the safety and efficacy of shunt surgery and endoscopic injection sclerotherapy for patients with proven esophageal variceal bleeding due to EHPVO.

Patients and Methods

Patient Population

This prospective randomized study was carried out jointly by the department of General Surgery and Gastroenterology at Sher-i-Kashmir Institute of Medical Sciences, Srinagar, between March 2001 and September 2003. All consecutive children seen at our institution with proven variceal bleeding due to EHPVO were recruited. A total number of 65 patients were enrolled. Four patients were excluded because of coexisting chronic hepatitis-B cirrhosis in two and refusal of the other two to participate in the study. Patients were accepted for the study if they met the following criteria:- (1) Clinical, endoscopic, and ultrasonographic evidence of EHPVO; (2) Endoscopic evidence of acute or recurrent esophageal variceal bleeding; (3) No evidence of hepatitis B virus or hepatitis C virus infections; (4) Arrest of acute bleeding either spontaneously or by use of one or a combination of transfusion, intravenous octreotide and balloon tamponade, and/or EIS; (5) Patients' willingness to participate in the study; (6) Patients living within 200 km radius of our institute.

Study Design

Patients were either admitted with an acute variceal bleed or were referred following stabilization of such an episode. The diagnosis of EHPVO was made on the basis of history of upper gastrointestinal bleeding, normal liver function, spleno-

megaly, endoscopic evidence of esophagogastric varices, and ultrasonographic findings of blocked or recanalized portal vein with formation of portal cavernoma. Esophageal varices were graded from 1 to 4 using Conn's criteria.

Randomization

All eligible patients with EHPVO were entered into the trial and were randomly assigned by serially numbered sealed envelopes with recurring block size of five to receive sclerotherapy or surgery.

Therapy

Endoscopic procedures were performed using a forward viewing flexible fiberoptic endoscope (Olympus GIF-Q10 Pentax). EIS was performed with 23-gauge transparent Teflon injection using a freehand technique. The injections were given intravariceally and sclerosing agent used was 3% polidocanol (aethoxysklerol^R), Kreussler Germany. Portal systemic shunts were performed by a surgeon with extensive experience in this field. Proximal splenorenal shunts were performed in majority of patients.

Follow-up

Longitudinal follow-up was based on outpatient visits as required.

Definitions

Control of active bleeding was defined as complete cessation of bleeding with stable vital signs for more than 48 consecutive hours after treatment. Variceal eradication was defined as until all visible varices are obliterated or reduced to tiny thrombosed remnants or to grade 1 size. Rebleeding was defined as upper gastrointestinal bleeding that required unscheduled endoscopy or transfusion, or associated with a fall in hemoglobin ≥ 2 g/dl. Treatment failure was defined as (1) ≥ 3 rebleeding episodes that required endoscopic treatment and transfusion, (2) death related to rebleeding or complication, (3) physician's decision to change modality of treatment, and (4) shunt thrombosis.

End Points

The primary end points of the study were the incidence of rebleeding and treatment failure.

Data Management and Statistical Analysis

All data were expressed as mean $\pm$ standard deviation. Quantitative data between two treatment groups were com-

pared using paired or unpaired Student's *t* test. Proportional data were compared with Fischer's exact test and χ^2 test. Kaplan–Meier analysis was used to estimate the time to the first rebleeding episode and variceal recurrence, and log rank test was used to compare the difference between the groups. A two-tailed *P* value of <0.05 was considered significant. Mann–Whitney *U* analysis was used to calculate the difference between the mean units of blood transfused for rebleeds in sclerotherapy and the surgery group.

Result

During the study period, 61 patients underwent randomization to receive EIS or surgery. Thirty patients received surgery and other 31 patients received EIS. The baseline patient characteristics were similar in both groups (Tables 1, 2, 3 and 4). All the patients in both the groups had history of recurrent variceal bleeding. The number of bleeds before enrolment ranged from 1 to 5 (mean 2.9 ± 1.2 units) in the EIS group compared with 1–6 (mean 3.1 ± 1.6 units) in the surgery group. The difference between the two groups was insignificant ($P > 0.05$). No patient had a history of hepatic encephalopathy. Splenomegaly was present in all patients in both the groups.

The percentage of patients who rebled, number of rebleeding episodes, and number of blood transfusions required were all significantly higher in the sclerotherapy group than in surgery group (Table 5, Fig. 1).

Esophageal variceal eradication was achieved in 29 of 31 patients (94.5%) with a mean of 6.2 ± 1.9 sessions (range 3–14). The two remaining patients with bleeding unresponsive to repeated EIS, underwent emergency shunt surgery.

In the sclerotherapy group, treatment failure occurred in 6 (19.4%) patients due to death in 1 patient and change of therapy in 5 patients. The single patient died as a result of exsanguination at home after third session of EIS. Two (6.7%) therapy failures in the shunt group were due to death in one patient and shunt thrombosis in another. The latter patient underwent mesocaval shunt. According to

Table 2 Symptoms and signs of patients

Symptom/sign	Sclerotherapy	Surgery	P value
Recurrent bleeding	31	30	1.0
Mild abdominal pain	19	17	0.79
Anemia	14	15	0.80
Jaundice	2	3	0.67
Splenomegaly	31	30	1.0
Hepatomegaly	7	8	0.77

Kaplan–Meier analysis, there was no statistical difference between the two groups with respect to failure of therapy (Fig. 2).

Discussion

In managing a patient of variceal bleed, blood transfusion alone carries a mortality rate of 20% over a period of few years [7]. Over two-thirds of children treated by direct operation on the varices or their feeding vessels will rebleed [7]. Splenectomy alone is valueless. Attention in recent years has focused on relative merits of portal systemic shunting and endoscopic management.

Early reports on surgical treatment in EHPVO were disappointing; with high rate of morbidity, mortality, and rebleeding [11, 13]. The first series in which surgical treatment was given for EHPVO with encouraging results was reported by Warren and associates in 1988 [1, 12]. They reported 25 patients with EXPVO who had selective shunts with a low postoperative mortality rate (4%) and low rebleeding rate (4%). A subsequent report with longer follow-up of these patients in 1990 reported that the rebleeding rates remained similar, although anastomotic stenosis was identified as a particular problem in these patients [1, 12]. In our series of 30 patients, rebleeding occurred in 1 (3.3%) patient after 28 months of surgery. This patient responded to conservative measures and

Table 1 Clinical data of patients

	Sclerotherapy	Surgery	P value
Number of patients	31	30	—
Sex (male:female)	19:12	20:10	0.79
Age (years) mean $\pm$ SD	11.5 ± 2.7	11.8 ± 3.1	0.69
Age at first bleed	7.5 ± 2.6	6.8 ± 2.4	0.28
Mean number of bleeds before treatment	2.9 ± 1.2	3.1 ± 1.6	0.58
Mean number of transfusions	3.7 ± 1.4	3.1 ± 1.4	0.58

Table 3 Endoscopic findings in both the groups

Endoscopic finding	Sclerotherapy	Surgery	P value
Esophageal varices	31	30	1.0
Grade-2	2	1	0.57
Grade-3	11	9	0.78
Grade-4	18	20	0.60
Gastric varices	11	9	0.78
Portal hypertensive gastropathy	10	11	0.79
Duodenal ulcer	1	1	1.0

Table 4 Hematological and biochemical indices in both groups

Investigation	Sclerotherapy (n=31)	Surgery (n=30)	P value
Hemoglobin			
Mean	8.1±2.1	8.4±1.8	0.55
Range	6–13	5.5–13.5	
Platelet count (mm ³)	145,000±85,700	138,430±83,660	0.76
Total leukocyte count (mm ³)	4,820±0.9	4,735±2,370	0.68
Albumin (g/dl)	3.5±0.9	3.4±1.0	N.S.
Bilirubin			
<1 mg	21	22	0.78
1.1–2 mg	7	4	0.51
>2 mg	3	4	0.70

needed two blood transfusions. According to Kaplan–Meier estimates, the 1, 2, and 3 year cumulative rebleeding was 26%, 28%, and 30%, respectively in the EIS and 0%, 0%, and 6% in the surgery group. Two (6.7%) therapy failures in the shunt group were due to death in 1 patient and shunt thrombosis in another. The latter was successfully treated with mesocaval shunt. The low rebleeding rate after shunt indicates the ability of this operation to prevent recurrent variceal bleeding in children with EHPVO.

Since its introduction, more than half a century ago, injection sclerotherapy has proven to be an effective method for controlling recurrent hemorrhage from esophageal varices [7]. It was first reported as successful technique in children in 1959. From January 1980 to December 1984, Cello et al. [14] enrolled 64 adults with Child class C cirrhosis and actively bleeding esophageal varices. Thirty-two patients were randomly assigned to sclerotherapy and 32 to portocaval shunt. In their preliminary report, sclerotherapy was better than surgical shunting in terms of both total costs and transfusion requirements. With longer follow-up, the short-term advantage of sclerotherapy over

Table 5 Bleeding in sclerotherapy and shunt groups

	Sclerotherapy	Surgery	P value
Number of patients with rebleeds	7 (22.6%)	1 (3.3%)	0.026
Rebleeds before variceal eradication	6	–	0.011
Rebleeds after variceal eradication or surgery	1	1	1.0
Total episodes of rebleeds	8	1	0.02
Mean units transfused for rebleeds	0.8±1.61	0.64±0.36	0.018

Fig. 1 Kaplan–Meier curve showing the probabilities for the absence of recurrent bleeding in patients treated by sclerotherapy or surgery

portocaval shunt surgery disappeared as more patients treated with sclerotherapy rebled. In our study, overall incidence of rebleeding in sclerotherapy group was 22.6%. Of the 7 patients who rebled in the sclerotherapy group, 6 (85.7%) patients rebled while undergoing EIS and included two treatment failures. The remaining rebleeding episodes were successfully controlled with conservative treatment and EIS. One patient, who rebled after variceal eradication,

Fig. 2 Kaplan–Meier curve showing the probabilities for the absence of treatment failure in patients treated with sclerotherapy or surgery

had bleeding from portal hypertensive gastropathy. This bleeding episode ceased spontaneously with conservative measures. Treatment failure occurred in 6 (19.4%) patients due to death in 1 patient and change of therapy in 5 patients. The single patient died as a result of exsanguination at home after third session of EIS. Shunt surgery was required in 2 patients because of recurrent bleeding. These 2 patients received a mean of 3.5 sessions and each had three rebleeding episodes requiring a mean of 5.5 units of blood transfusion. In the remaining 3 patients, shunt surgery was necessitated after variceal obliteration for biliary obstruction due to portal biliopathy. These 3 patients had coexisting bile duct stones. Endoscopic sclerotherapy is associated with a variety of complications [7], in particular esophageal ulceration and stricture formation. In our study, all ulcers were asymptomatic and were only detected because of regular endoscopies. There were no cases of esophageal perforation in our series. Other serious complications, such as spinal cord paralysis, mediastinitis, bronchoesophageal fistula, and cardiac tamponade that have been rarely reported [7], did not occur in our series.

To conclude, the rebleeding rate of sclerotherapy (22.6%) is significantly higher than that of shunt surgery (3.3%). However, the therapy failure rate of sclerotherapy (19.4%) is not significantly different from that of shunt surgery (6.7%). Thus, sclerotherapy is an acceptable alternative to shunt surgery for treatment of variceal hemorrhage in children with EHPVO.

References

- Orozco H, Takahashi T, Mercado MA, Prado E, Chan C (1994) Surgical management of extrahepatic portal hypertension and variceal bleeding. *World J Surg* 18:246–250
- Kagzi RS, Nadkarni KM, Jahangirdar RR, Pinto AC, Bhalariao RA (1982) Evaluation of the surgical treatment of extrahepatic portal hypertension. *Indian J Surg* 44:420–426
- Pande GK, Reddy VM, Kar P, Sahni P, Berry M, Tandon BN (1987) Operation for portal hypertension due to extrahepatic obstruction: result and 10 year follow-up. *Br Med J* 295:1115–1117
- Garg PK, Joshi YK, Tandon RK (1999) Comparison of endoscopic variceal sclerotherapy with sequential endoscopic band ligation plus low-dose sclerotherapy for secondary prophylaxis of variceal hemorrhage: a prospective randomized study. *Gastrointest Endosc* 50:369–373
- Hill TD, Bowle MD (1991) Endoscopic sclerotherapy for control of bleeding varices in children. *Am J Gastroenterol* 86:472–476
- Mitra SK, Rao KLN, Narasinhham KL, Dilawari JB, Batra YK, Chawla Y et al (1993) Side-to-side lienorenal shunt without splenectomy in noncirrhotic portal hypertension in children. *J Pediatr Surg* 78:398–402
- Howard ER, Stringer MD, Mowat AP (1998) Assessment of injection sclerotherapy in the management of 152 children with oesophageal varices. *Br J Surg* 75:404–408
- Stringer MD, Howard ER (1994) Long-term outcome after injection sclerotherapy for oesophageal varices in children with extrahepatic portal hypertension. *Gut* 35:257–259
- Alvarez F, Bernard O, Brunelle F, Hadchouel P, Odièvre M, Alagille D (1983) Portal obstruction in children. Clinical investigations and hemorrhage risk. *J Pediatr* 103:696–702
- Jean-Bernard OHC, Reynaert M, De Hemptine B (1982) Arterialization of the portal vein in conjunction with a therapeutic portal shunt. *Ann Surg* 196:656–662
- Webb IJ, Sherlock S (1979) The etiology, presentation and natural history of extrahepatic portal venous obstruction. *Q J Med* 48:627–639
- Gimson AE, Ramage JK, Panos MZ, Hayllar K, Harrison PM, Williams R (1993) Randomized trial of variceal banding ligation versus injection sclerotherapy for bleeding oesophageal varices. *Lancet* 342:391–394
- Langer B, Taylor BR, Mackenzie DR, Gilas T, Stone RM, Blendis L (1985) Further report of a prospective randomized trial comparing distal splenorenal shunt with end-to-side portocaval shunt. *Gastroenterol* 88:424–429
- Cello JP, Grendell JH, Crass RA, Weber TE, Trunkey DD (1987) Endoscopic sclerotherapy versus portocaval shunt in patients with severe cirrhosis and acute variceal hemorrhage. *N Engl J Med* 316:11–15