Complications of Sclerotherapy for Esophageal Varices in Liver Transplant Candidates

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ENDOSCOPIC sclerotherapy as the initial form of therapy for bleeding esophageal varices is considered to be the treatment of choice in many centers. While bleeding is usually effectively controlled,[1,2] the long-term prognosis for such patients remains poor[3,4] since progressive hepatic deterioration often precipitated by the bleeding episode frequently leads to an early death.

In an attempt to prevent the onset of future bleeding episodes in cirrhotic patients prophylactic sclerotherapy has become popular. The disappointing results of various prophylactic surgical procedures for bleeding varices have encouraged further the widespread use of prophylactic sclerotherapy. Nonetheless, recent randomized controlled studies have not supported the universal use of prophylactic sclerotherapy.[5,6]

The advent of orthotopic liver transplantation (OLT) as an effective means of treating end-stage liver disease (ESLD) has altered the long-term prognosis for many cirrhotic patients.

A recent report from this center has reported that sclerotherapy for bleeding varices followed by OLT significantly improved survival of cirrhotic patients.[3] The complications associated with sclerotherapy in potential liver transplant candidates and the effect of such complications on the outcome of OLT have not been addressed. This report indicates that sclerotherapy is associated with significant morbidity that can influence the outcome of OLT.

MATERIALS AND METHODS

Part of the evaluation of all transplant candidates includes an upper gastrointestinal endoscopy at which time any varices identified are graded.

The varices were graded as follows: grade I, varices filling 25% or less of the air-distended lumen of the esophagus; grade II, varices filling 26% to 50% of the air-distended lumen of the esophagus; grade III, varices filling 51% to 75% of the air-distended lumen of the esophagus; and grade IV, varices filling more than 76% of the air-distended lumen of the esophagus.

Those with grade III or IV varices seen between July 1985 and December 1988 were included in this study as this group was enrolled in a study assessing the role of sclerotherapy in the management of esophageal varices. The technique employed for variceal sclerosis and the method of injection utilized have been described previously.[7] Briefly, all procedures were performed under conscious sedation using intravenous (IV) midazolam (2 to 10 mg) and meperidine (50 to 200 mg). An Olympus 2T fiberoptic endoscope was used and 4 mL of 5% sodium morrhuate was injected per injection using a free hand technique. Prophylactic sclerotherapy was performed on a fixed schedule on days 1, 4, 7, 14, 21, and 28 and then weekly until all of the varices were obliterated and/or OLT was performed. Emergent sclerotherapy was undertaken only if the patients were: (1) acutely bleeding from varices and required more than 4 U of blood to maintain hemodynamic stability or (2) continuing to bleed despite IV Pitressin. The clinical and biochemical paremeters for patients on the medical and surgical service based on Childs criteria were evenly matched (Table 1).

The chi-square test was used to determine the statistical significance of differences in proportions. A P value of $<.05$ was considered to be significant.

RESULTS

During the 3.5-year period encompassing patient accrual for this study, a total of 1314 patients with grade III or grade IV varices were seen by the combined medical-surgical transplant services. This group represented 44% of the total 2988 adult patients who were seen, evaluated, and ultimately accepted for OLT at this institution during the study period.

Prophylactic sclerotherapy was performed on 648 of 686 (95.0%) patients admitted to the medical service while emergency sclerotherapy was performed on the remaining 38 cases (5.0%). Of 628 patients admitted to the surgical services, 134 (21%) underwent emergent sclerotherapy based on the above criteria for an emergent procedure. The remaining 494 patients (79%) had no bleeding and received no sclerotherapy despite having endoscopically demonstrated grade III/IV esophageal varices.

A comparison of the important features of the two groups of patients studied is shown in Table 2. Eighty-five percent (583) of the patients on the medical service and

Table 1. Childs Criteria

Childs criteria	Medical (%)	Surgical (%)
A	10	12
B	72	63
C	18	25

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Table 2. Outcome of Sclerotherapy in Medical and Surgical Patients

Total Number*	Medical No. (%)†	Surgical No. (%)‡
Prophylactic sclerotherapy	648 (94)	0
Emergency sclerotherapy	38 (5.5)	134 (21.3)§
No sclerotherapy	0	494 (78.7)
Survival to OLT	583 (85)	509 (81)
Death before OLT	97 (14)	119 (19)
Death due to bleeding	18 (2.7)	89 (14)§
Other deaths (multiorgan, hepatic failure, sepsis)	79 (11.5)	30 (4.7)

*Total number, 1314 patients.
†Medical Service, 686 patients admitted.
‡Surgical service, 628 patients admitted.
§$P < .05$.

81% (509) on the surgical service survived to receive transplants while 14% (97) of the patients on the medical service and 19% (119) of the patients on the surgical service died before OLT. A greater proportion of the surgical patients (21.3%) had emergent sclerotherapy than did those on the medical service (5.5%) ($P < .01$). The policy was to admit patients who presented with bleeding to the surgical service because of heavier staff coverage of this service and the greater availability of intensive care beds. On either the medical or surgical service, the sclerotherapy was provided by the same gastroenterologists.

The complications of sclerotherapy experienced in both the prophylactic and emergent sclerotherapy groups are shown in Table 3. A significantly higher complication rate was noted for emergent sclerotherapy than for prophylactic sclerotherapy ($P < .01$). However, the total number of patients with complications in the prophylactic sclerotherapy group was 81 (12.5%) of the patients so treated. It must be noted also that the sclerotherapy performed in the emergently treated group occurred under the difficult circumstances of active bleeding with poor visualization in desperately ill patients.

The single most important factor that emerged from an analysis of the factors predisposing to complications was the presence of repeated injections over 36 to 48 hours. All patients in the emergent sclerotherapy group who perforated had a minimum of three sclerotherapy sessions over a period of 72 hours. Three esophageal perforations also occurred in the prophylactic sclerotherapy group. However, when the number of procedures, rather than the number of patients treated is considered, a much higher complication rate was apparent for the emergent sclerotherapy group (96 of 490 procedures, 19.6%) as compared with the prophylactic sclerotherapy group (58 of 3468 procedures, 1.7%) ($P = <.001$).

Table 3. Major Complications of Prophylactic and Emergency Sclerotherapy

	Prophylactic (648)	Emergency (172)
Esophageal stricture	58 (9%)	96 (56%)
Bleeding esophageal ulcers	20 (3.1%)	18 (10.5%)
Esophageal perforation	3 (0.5%)	5 (2.9%)
Total	81 (12.5%)	119 (69.4%)

The development of a sclerotherapy complication in either group often resulted in a delay in OLT or death. In three cases, OLT was performed within 24 to 48 hours after emergent sclerotherapy. A high gastric perforation was discovered at the time of laparotomy in one of these patients. In the other two, an esophageal perforation contributed to the death of each but was not detected until the postmortem examination.

Strictures and bleeding esophageal ulcers, occurring as a result of sclerotherapy, were treated conservatively with excellent results in most cases. Often bougienage was required for esophageal strictures. Sucralfate therapy was universally administered for esophageal ulcers. Hemorrhage from esophageal ulcers usually responded to nonsurgical treatment. However, formal esophago-gastrectomy to arrest bleeding was required in two cases following a successful liver transplant and one of these patients died. The other had a total esophogectomy and colon interposition performed 6 months later.

DISCUSSION

Endoscopic sclerotherapy has been recommended as the treatment of choice for bleeding esophageal varices[2,7] but the long-term survival of such patients is dependent on their hepatic reserve as stratified by Childs classification and perhaps on the severity of the initial episode of variceal bleeding.[7]

The majority of trials regarding the benefits of sclerotherapy have been undertaken at centers where OLT is not available. Garrett et al[3] from this institution have reported that sclerotherapy followed by OLT significantly improves overall patient survival. However, the complications associated with sclerotherapy were not reported.

Patients with ESLD who bleed often decompensate rapidly. Traditionally they are admitted to an intensive care unit and are treated by volume replacement to maintain hemodynamic stability. A Pitressin infusion is administered followed by emergent endoscopy both for diagnostic and therapeutic purposes. These patients are often irrational with hepatic encephalopathy or alcohol withdrawal symptoms combined with vomiting or retching and excessive coughing. Visualization of the esophagus and the source of bleeding is typically not easy. While precise identification of the source of the bleeding may be achieved, precise injection of the sclerosant is not. Thus, intramural injections are common and as a result the complication rate of emergent sclerotherapy is greater than that seen with elective sclerotherapy.

If emergent sclerotherapy has a greater morbidity than prophylactic sclerotherapy in OLT patients, then what might be an alternative solution for such cases? The Sengstaken-Blakemore (S-B) tube is effective in controlling hemorrhage in 95% of cases, with only a few compli-

cations that are avoidable, if appropriate precautions and monitoring are utilized.[8] Based on the experience at the University of Pittsburgh, we would suggest that emergent sclerotherapy be avoided for patients who are obvious candidates for OLT and who are admitted to the hospital with major variceal bleeding. Instead, a S-B tube should be inserted to control the hemorrhage and an immediate alert for a donor organ should be put in effect. OLT should be performed within 48 to 72 hours. This action avoids the need to carry out aggressive emergent sclerotherapy and provides a solution for the underlying cause of the variceal hemorrhage. This approach has been utilized in six patients at this institution recently with an excellent outcome in all six. Clearly the limiting factor for such a course of action is the availability of suitable donor organs. At centers where OLT is routinely performed, such as the University of Pittsburgh, an appropriate donor organ is essentially always found within 72 hours. In earlier cases seen at this institution, OLT was carried out within 24 to 48 hours after emergent sclerotherapy was performed for acute variceal bleeding. Excellent results were obtained from the OLT but important morbidity including esophageal perforation, esophageal ulcers, and stricture formation were seen frequently. Clearly, not all centers have either the facilities or staff to perform OLT within 48 hours of a bleeding episode. Under the proper circumstances, however, temporary control with the S-B tube would appear to be a better solution than emergent sclerotherapy.

Repeated sclerotherapy sessions (mean 3 to 4) performed over a short period of time were found to be the single most important contributing factor to the subsequent development of sclerotherapy complications. Ulcerations occur within a few hours of variceal injections and are fully established by 7 to 10 days.[9] Thus, frequent reinjections of the same or nearby sites often result in extensive transmural injury.

The role of prophylactic sclerotherapy in patients selected for OLT also requires reassessment. In particular, 494 patients (79%) admitted to the surgical service did not require any sclerotherapy. Thus, a substantial proportion of the patients who were treated prophylactically probably would not have bled and therefore do not require sclerotherapy. It must be remembered that patients treated prophylactically had no bleeding to begin with, and yet experienced a complication rate of approximately 13%.

In the present study, the frequency of subsequent hemorrhage in patients who were not bleeding at the time of transplant evaluation was the same in the patients who had prophylactic sclerotherapy as in those who did not. The size of the varices in the two groups was similar. Nonetheless, a greater number of emergency bleeding episodes (134 of 628) occurred in those not receiving prophylactic sclerotherapy compared with those who did (34 of 686). This was because patients who presented with bleeding were usually admitted to the service not systematically providing prophylactic sclerotherapy.

In conclusion, the widespread use of prophylactic sclerotherapy for varices irrespective of varix size or the state of the patient's liver disease requires careful reassessment before its universal acceptance. Even in expert hands, a substantial complication rate is experienced.

Similarly, the role of emergency sclerotherapy under the difficult conditions of acute variceal hemorrhage also requires reassessment. Alternative forms of treatment with an S-B tube followed by early OLT rather than emergent sclerotherapy for patients with poor hepatic reserve is advised.

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