Effect of Endoscopic Variceal Sclerotherapy on Esophageal Motor Functions and Gastroesophageal Reflux

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Sclerotherapy results in significant local complications, both immediate and delayed. This study was designed to examine the esophageal pathophysiology underlying these complications. **Methods:** We prospectively evaluated esophageal transit, motility abnormalities and gastroesophageal reflux (GER) with barium studies and esophageal functional scintigraphy in 24 patients (20 men, 4 women; mean age 33 ± 12.4 yr) before sclerotherapy (Phase I), after two sessions (Phase II), following variceal eradication (Phase III) and 4 wk later (Phase IV). **Results:** Varices were obliterated after 5.6 ± 1.9 sessions of intravariceal sclerotherapy performed weekly with 1% polidocanol (17.3 ml per session). There was no baseline Phase I dysmotility or reflux. Phase II studies recorded a marked delay of esophageal global and segmental (mid and distal) transit time in 98.2% of patients by scintigraphy and 90% by barium studies. Incoordinate contractions and aperistalsis were observed in 0, 66.7%, 58.3% and 33.8% of patients from Phases I–IV studies, respectively. Barium studies revealed tertiary waves and reverse peristalsis in 0, 50%, and 75% of patients from Phases I–III; strictures were observed in 0, 1, and 3 patients during Phases I–III. GER was detected scintigraphically in 0, 58.3%, 25% and 16.6% during Phases I–IV sequentially. In contrast, barium studies grossly underestimated GER (0, 5% and 15% at phases I–III). **Conclusion:** There was strong concordance between esophageal symptoms, transit, motillity abnormalities and GER ($p < 0.05$). Variceal eradication (Phases III and IV) was associated with a gradual recovery of esophageal symptoms, ulcers and all abnormal scintigraphic parameters. Sclerosant-induced chemical esophagitis in association with peptic esophagitis due to gross reflux following sclerotherapy possibly can explain the symptoms in most patients.

Key Words: variceal sclerotherapy; esophageal motor functions; gastroesophageal reflux; barium studies

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Endoscopic variceal sclerotherapy is an emergent and definitive therapy for bleeding esophageal varices that occur in cirrhosis (*1,2*), noncirrhotic portal fibrosis and extrahepatic portal venous obstruction (*2–4*). The overall efficacy of endoscopic variceal sclerotherapy is associated with a wide range of local complications, some of which occur at the beginning of the therapeutic course, for example, esophageal ulceration, substernal pain, pyrosis and motor dysphagia, all of which resolve rapidly (*5*). Later in the course, 2% to 50% of patients are afflicted by esophageal strictures (*6–8*), requiring repetitive bougienage. Hence, there is a strong need to evaluate the esophageal pathophysiology following endoscopic variceal sclerotherapy. The final aim is to devise a treatment policy to avert or treat endoscopic variceal sclerotherapy-induced morbidity, which is especially required for patients with extrahepatic portal venous obstruction, noncirrhotic portal fibrosis and cirrhosis (child A class), who have a good life expectancy because of normal or near-normal liver function. Patients with these disorders account for 50% of those who present with bleeding esophageal varices in India (*9,10*).

Our study evaluates, prospectively and sequentially, the changes in esophageal function following endoscopic variceal sclerotherapy in patients with cirrhosis, extrahepatic portal venous obstruction and noncirrhotic portal fibrosis, who presented with esophageal varices.

MATERIALS AND METHODS

Patients

Twenty-four consecutive patients (Table 1) underwent intravariceal endoscopic variceal sclerotherapy effecting total variceal obliteration, including five patients who presented with bleeding esophageal varices. Endoscopic variceal sclerotherapy was carried out weekly with a forward-viewing pan endoscope and needle injector. The varices were obliterated after a mean 5.6 ± 1.9 session of endoscopic variceal sclerotherapy using a mean volume of 17.3 ml 1% Polidocanol per session. The pre-endoscopic variceal sclerotherapy baseline motility data were recorded for 19 of these patients; this cohort served as an ideal control group for the sequential study.

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TABLE 1
Demographic and Clinical Indices of Patients Who Underwent Esophageal Variceal Sclerotherapy (EVS)

Sex (M/F)	20/4
Age (yr) ($\mu \pm$ s.d.)	33 ± 12.4
Etiology (total n = 24)	
Cirrhosis*†	9 (37.5%)
NCPF	6 (25%)
EHO	8 (33.3%)
HVOTO	1 (4.2%)
Variceal grade (at onset of EVS)	
Grade IV/III	16/8
EVS sessions/patient ($\mu \pm$ s.d.)	5.6 ± 1.9
Mean sclerosant vol./session	17.3 ml

*Alcoholic (four patients), posthepatitis (four patients), Wilson's disease (one patient).

†Child score: A/B/C-3/5/1 patients, respectively.

NCPF = noncirrhotic portal fibrosis; EHO = extrahepatic portal venous obstruction; HVOTO = hepatic venous outflow tract obstruction.

Study Protocol

Prospective sequential assessment was conducted in four phases: before endoscopic variceal sclerotherapy (Phase I), within 24 hr of the second endoscopic variceal sclerotherapy session (Phase II), on completion of endoscopic variceal sclerotherapy (Phase III) and 4 wk after variceal eradication (Phase IV). Gastroesophageal reflux (GER) scintigraphy was usually performed after 3 days of transit studies, and no H_2 blockers or prokinetic agents were administered during the study period. At each phase, the patients answered a standard questionnaire of symptoms (retrosternal pain, pyrosis, dysphagia, cough, wheezing and fever). Endoscopic mucosal abnormalities (ulcers, strictures) were recorded simultaneously. Barium studies (swallow and GER) and esophageal functional scintigraphy were conducted at each phase in a random fashion within 4 days of each session. Each investigator—the clinician administering the questionnaire, the endoscopist, the radiologist and the nuclear medicine physician—was blinded to the results of the others throughout the study.

Barium Studies

Bolus transit (supine, erect) was monitored under fluoroscopy after patients swallowed the barium solution (95% weight per volume). In addition, motility abnormalities such as aperistalsis, tertiary waves, reverse peristalsis and irregularities of esophageal outline were also recorded. Gastroesophageal reflux was studied in the left anterior oblique position after swallowing 300 ml of barium solution.

Esophageal Functional Scintigraphy

In accordance to Russell et al.'s technique (*11*), the patient was placed in the supine position and a 10-ml homogeneous bolus of water and 0.5 mCi (18.5 mBq) ^{99m}Tc-phytate was ingested with a single swallow. Double-swallow studies were eliminated. Studies were repeated in the erect position if the first bolus failed to enter the stomach. Acquisition frames were recorded at intervals of 0.5 sec/frame for 120 frames. The microprocessor electronically divides the esophageal zone into three equal segments by area normalization (proximal, middle, distal). Bolus transit is plotted graphically: radioactivity representing volume on the vertical axis and time in seconds on the horizontal axis. The global transit time (GTT) and the segmental transit time (proximal, middle, distal: PTT, MTT and DTT, respectively) are thus accurately quantified. Motility abnormalities are classified into incoordinate contraction and aperistalsis in case of prolonged transit.

Gastroesophageal Reflux Scintigraphy

Gastroesophageal reflux scintigraphy was performed 3 days after transit studies using a modified Fisher's technique (*12*). A capsule containing 0.5 mCi (18.5 MBq) ^{99m}Tc-phytate was swallowed along with 300 ml of plain water. The patient was then placed under the detector in the supine position. On dissolution of the capsule (approximately 3–4 min), data acquisition started with a frame rate of 16 sec/frame for 32 min. The GER index was then computed. The reflux index was defined as the background-corrected esophageal count divided by total gastric counts at time zero multiplied by 100.

Statistical Analysis

All values were expressed as mean ± s.d. Paired t-tests were used to assess the significance of difference between various phases of the study. Associations between esophageal symptoms and motility data in each phase were assessed by the paired chi-square (McNemar) test.

RESULTS

Clinical Symptoms and Esophageal Mucosal Changes

Before endoscopic variceal sclerotherapy (*1*), none of the patients had any esophageal symptoms. Endoscopy showed no esophageal ulcers or strictures other than varices. Thereafter, early assessment (Phase II) revealed the presence of symptoms in 23/24 (95.8%) patients: retrosternal pain and pyrosis in 21 patients, dysphagia in 19, cough/wheeze in 4 and fever in 5. Concurrently, 22/24 (91.7%) patients developed esophageal ulcers [17 superficial and 5 deep (>2 cm) ulcers] viewed on esophagoscopy. At this time, there was a marked increase in symptoms and ulcers ($p < .001$). During Phase III, however, 16/24 (66.7%) patients had persistent symptoms: dysphagia in eight patients, pyrosis in six and retrosternal pain in two. While the patients experienced pain for a brief period, the dysphagia persisted. Simultaneously, in eight patients esophageal narrowing developed—five of these had minimal inflammatory stenosis, and a passage of the endoscope restored full luminal patency. These patients had definite fibrotic stricture that required frequent dilation with Savary-Gilliard dilators. Delayed assessment (Phase IV) showed that these patients had persistent dysphagia along with marked overall reduction in symptoms (Phase I vs. Phase II: ($p < 0.001$; Phase I vs. Phase III: $p < 0.01$).

Barium Studies

Baseline barium studies (Phase I) were normal in all patients. There was a distinct change during Phase II—delayed transit occurred in 18 (90%) patients (Phase I vs. Phase II: $p < 0.01$). Similarly, peristaltic wave disturbances were recorded in 10/20 (50%) patients (tertiary waves in eight, reverse peristalsis in three). Lower end outline irregularities were observed in five patients and funneling was noted in one. For Phase III, all 20 patients studied had delayed transit (Phase II vs. Phase III: p = ns; Phase I vs. Phase III: $p < 0.001$). Motility abnormalities

TABLE 2
Scintigraphic Evaluation of Esophageal Transit (Segmental and Global) Alterations, Motility Abnormalities and Gastroesophageal Reflux Following EVS

Parameters	Evaluation phase			
	I (n = 19)	II (n = 24)	III (n = 24)	V (n = 18)
Mean esophageal transit time (sec)				
Segmental: μ and s.d.				
Proximal	0.7 (0.3)	0.9 (0.6)	0.8 (0.4)	0.8 (0.5)
Middle	1.4 (0.4)	4.0 (4.1)	2.3 (1.9)	2.2 (1.2)
Distal	3.6 (2.5)	6.1 (4.6)	3.2 (2.0)	3.1 (1.5)
Global	5.7 (2.5)	11.0 (7.7)	6.3 (3.5)	6.1 (2.4)
Motility abnormalities (%)				
Incoordinate	0	41.6	16.6	22.2
Aperistalsis	0	25.0	41.6	11.1
Overall abnormalities	0	66.7	58.3	38.9
GER index: μ and (s.d.)	0.7 (0.7)	14.1 (17.4)	4.3 (6.9)	5.1 (11.0)

were noted in 15 (75%) patients, tertiary waves in 10 and reverse peristalsis in 9 during Phase III (Phase II vs. Phase III: p = ns; Phase I vs. Phase III: $p < 0.001$). We also observed stricture of the distal esophagus in three patients, lower end irregularities in five and pseudodiverticulum in two. Gastroesophageal reflux was noted in only one and three patients at intervals of Phases II and III, respectively. Further barium studies (Phase IV) were abandoned due to its poor sensitivity for GER during Phases II and III.

Esophageal Functional Scintigraphy

Segmental Transit Times. Mid and distal transit times at Phase II were distinctly prolonged [compared to (ct) Phase I: MTT ($p < 0.01$); DTT ($p < 0.05$). Distal transit times subsequently declined in Phases III and IV (ct II; $p < 0.05$) (Table 2; Fig. 1). The PTT was unaltered throughout the study.

Global Transit Time. Basal GTT (5.7 ± 2.5 sec) was normal; it was prolonged in Phase II (11.0 ± 7.7 sec) (ct I: $p < 0.01$), but thereafter declined in Phases III and IV (ct II: $p < 0.05$), approximating Phase I (p = ns).

Motility Disturbances. There was no basal (Phase I) motility abnormality. During Phase II, motility abnormalities developed in 16 (66.7%) patients (ct I, $p < 0.001$). Incoordinate contractions were seen in 10 patients and aperistalsis (mostly affecting the distal esophagus) was seen in six. Maximally observed during Phase II, these disturbances decreased by Phase IV (ct II and III; $p < 0.05$), but normal conditions did not return (ct I, $p < 0.01$) (Table 2; Fig. 2).

Gastroesophageal Reflux Scintigraphy after Endoscopic Variceal Sclerotherapy

Gastroesophageal reflux was detected in 0/19, 14/24 (58.3%), 6/24 (25%) and 3/18 (16.6%) patients during Phases I–IV sequentially. Correspondingly, the mean (s.d.) GER index in Phases I–IV were 0.7 ± 0.7, 14.1 ± 17.4, 4.3 ± 6.9 and 5.1 ± 11.0 sequentially (Table 2; Fig. 3). The mean basal GER index was normal (<4.0). The index was maximal during Phase II (ct I, III, IV: $p < 0.001$, $p < 0.05$, $p < 0.05$) and thereafter declined gradually.

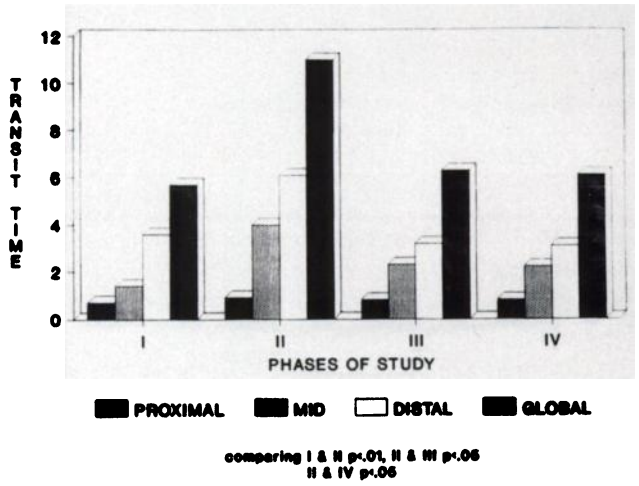

FIGURE 1. Esophageal transit following endoscopic sclerotherapy.

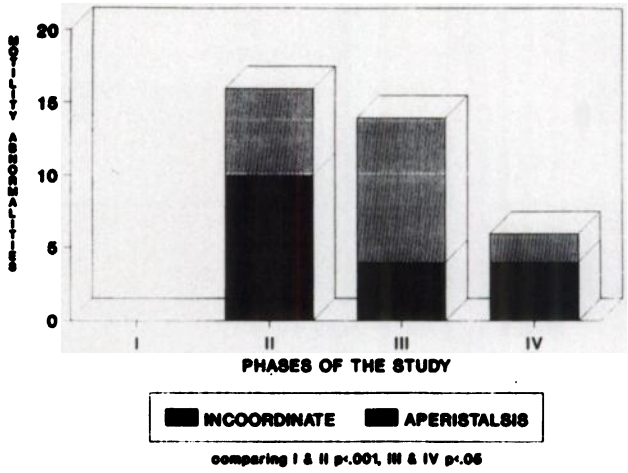

FIGURE 2. Motility abnormalities following endoscopic sclerotherapy.

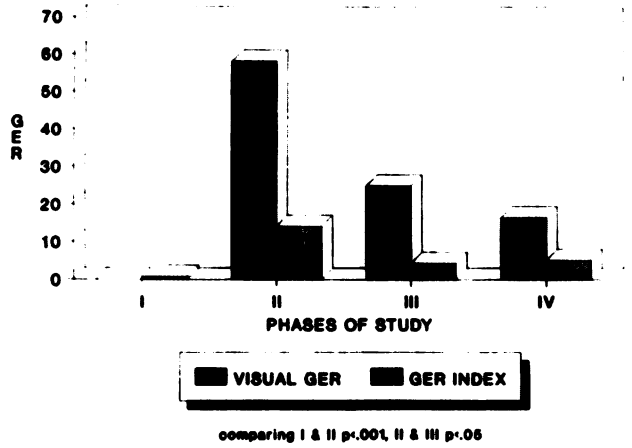

FIGURE 3. Gastroesophageal reflux following endoscopic sclerotherapy.

Esophageal Symptom and Function Correlates after Endoscopic Variceal Sclerotherapy

There was a marked concordance in the deterioration of esophageal symptoms and motor function in Phase II with subsequent recovery in Phases III and IV. During Phases II and III, symptoms were associated with delayed global segmental esophageal transit, increased motility abnormalities and GER as depicted in Table 3 (Phase III, $p < 0.05$).

DISCUSSION

Several attempts have been made to understand the pathophysiology of local complications of endoscopic variceal sclerotherapy. Serious problems, however, afflict most of the research done so far, either in design or in technique. The evaluation of dysmotility in different patients, before and after endoscopic variceal sclerotherapy (*13,14*) represents a defective study design. Other investigators have evaluated esophageal dysmotility in the early period of endoscopic variceal sclerotherapy and its phasic correlation with esophageal symptoms. Very few sequential (manometric) studies (*17–19*) involving small numbers of patients have been performed. Furthermore, only three radionuclide studies have evaluated esophageal motility following endoscopic variceal sclerotherapy (*14,15,20*); unfortunately, all three are monophasic post-endoscopic variceal sclerotherapy studies with either incongruous baseline data (in a different set of patients) (*14*) or none at all (*15,20*). Our prospective investigation is a sequential study of endoscopic variceal sclerotherapy-induced motility alterations in 24 patients with cirrhosis, noncirrhotic portal fibrosis and extrahepatic portal venous obstruction. An attempt was made to rectify the flaws noted in previous studies. The barium study provided a rapid screening test for esophageal dysmotility (*21*). Esophageal functional scintigraphy is a simple, noninvasive, quantitative and highly sensitive test for esophageal transit, dysmotility (*11,12*) and GER (*12*) evaluation. Esophageal functional scintigraphy has equal (*23*) or greater sensitivity than manometry for diagnosing motility abnormalities (*11*). Although supposedly the most accurate tool for ascertaining esophageal motility, manometry is expensive, technically demanding and uncomfortable for the patient. Serious disagreement is found in most reports of manometric motility parameters following endoscopic variceal sclerotherapy; for example, lower esophageal sphincter pressure (LESP) is variously reported as decreasing (*13*), increasing (*15*) or constant (*16,17,20,24*). Similarly, confusing findings are reported for decreased peristaltic wave amplitude (*13,15,19*) versus constant amplitude, duration or velocity (*17,20*). An increase in nonpropagated contractions in the distal esophagus, however, has been uniformly recorded (*18–20,24*).

A sudden spurt of self-limited esophageal symptoms (retrosternal pain, pyrosis and dysphagia) and mucosal ulcers were noted immediately after the second session of endoscopic variceal sclerotherapy. Subsequently, the overall symptoms declined sharply, although dysphagia was recorded in eight patients at the end of endoscopic variceal sclerotherapy, five of whom had, probably minor, esophageal inflammatory stenosis that subsided spontaneously (recorded on follow-up endoscopic examinations). Chronic fibrotic strictures occurred in 3/24 (12.5%) patients

TABLE 3
Esophageal Symptom and Functional Correlation with Scintigraphy and Barium Studies

Parameters	Evaluation phase			
	I (n = 19)	II (n = 24) (%)	III (n = 24) (%)	IV (n = 18) (%)
Clinical symptoms	0	95.8	66.7	15
Scintigraphic observation				
Transit	0	98.2	72.5	28.6
MA	0	66.7	58.3	33.8
GER	0	58.3	25.0	16.6
Barium studies				
MA	0	50.0	75.0	—
GER	0	5.0	15.0	—
Stricture	0	4.2	12.5	—

MA = motility abnormalities; GER = gastroesophageal reflux.

who required frequent bougienage to restore luminal patency. Barium studies showed delayed esophageal transit, motility abnormalities such as tertiary waves and reverse peristalsis following endoscopic variceal sclerotherapy, but no significant GER was noted (a reflection of the insensitivity of barium versus reflux scintigraphy). These data indicate a poor correlation between symptoms of GER and barium studies.

Radionuclide studies showed a marked delay in segmental and global transit, increased motility abnormalities (incoordinate contractions and aperistalsis) and GER in the early phase of endoscopic variceal sclerotherapy. As varices were eradicated, most of the abnormal scintigraphic parameters returned to normal. This reversible trend compares well with manometric studies (increased incidence of nonpropagated contractions in the distal esophagus with delayed acid clearance) in the early phase of endoscopic variceal sclerotherapy followed by partial recovery (*17–19*).

Currently, GER after endoscopic variceal sclerotherapy remains a contentious issue. Earlier researchers did not report an increased incidence of GER (*6,15,18,19*). On the contrary, two recent studies (*25,26*) have recorded significant GER following paravariceal endoscopic variceal sclerotherapy.

CONCLUSION

Finally, it appears that endoscopic variceal sclerotherapy induces an acute chemical esophagitis with mucosal necrosis, esophageal dysmotility, delayed transit and peptic esophagitis as a consequence of severe GER. There is sound correlation between esophageal symptoms, transit, motility abnormalities and GER throughout the phases of endoscopic variceal sclerotherapy. Variceal eradication was associated with a gradual recovery of all clinical and esophageal functional abnormalities and gastroesophageal reflux. Persistent GER at the end of endoscopic variceal sclerotherapy undoubtedly contributes to aggressive fibrosis and esophageal stricture. Intensive antireflux treatment with Omeprazole may reduce the incidence of local complications, especially strictures, following endoscopic variceal sclerotherapy.

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