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Endoscopic band ligation followed by sclerotherapy: Is it superior to sclerotherapy in children with extrahepatic portal venous obstruction?

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Abstract

Background and Aim: There is scarcity of data about children on a combination of endoscopic variceal ligation (EVL) and endoscopic sclerotherapy (EST). We assessed the efficacy of EVL followed by EST and EST alone in children with extrahepatic portal venous obstruction (EHPVO).

Methods: From January 2000 to March 2007, 186 consecutive children (mean age 6.3 ± 4.2 years, 82% boys) with EHPVO with variceal bleeding were included. EVL followed by EST (Group I, $n = 101$) or EST alone (Group II, $n = 60$) was carried out at 3-weekly intervals until eradication. Surveillance endoscopy was done at 3 to 6-monthly intervals. In all cases, the number of sessions required to eradicate the esophageal varices, the volume of sclerosant, the complications and the endoscopic outcome on follow up were recorded.

Results: Eradication was achieved in 158 of 161 (98%) children and 25 were lost to follow up. Group I required significantly fewer sessions (5.2 ± 1.8 vs 6.8 ± 2.8, $P < 0.005$), less sclerosant (13 ± 8.2 mL vs 30 ± 20 mL, $P < 0.001$) and had fewer complications (7% vs 28%, $P < 0.001$) as compared with Group II. On follow up (33 ± 17.6 months in Group I and 43 ± 16.7 months in Group II), there was a significant increase in the prevalence of portal hypertensive gastropathy as well as isolated gastric varices in both the groups. However, the prevalence of gastroesophageal varices decreased.

Conclusions: EVL followed by EST is better than EST alone in children with EHPVO as it requires fewer sessions and has fewer complications. However, following eradication, evolution of gastric varices and portal hypertensive gastropathy was similar in the two groups.

Introduction

The commonest cause of portal hypertension in children in developing countries continues to be extrahepatic portal venous obstruction (EHPVO), with variceal bleeding and splenomegaly as the most common presentation.[1–3] Variceal bleeding contributes to mortality and morbidity in children with EHPVO.[4] Esophageal varices can be tackled either endoscopically or by doing a surgical shunt. Endoscopic procedures like sclerotherapy (EST) or band ligation (EVL) are established methods of treatment of variceal bleeding in adults. Although EST has become an accepted and highly successful technique for controlling variceal bleeding and achieving eradication in children,[5–7] experience of EVL in children is limited.[8–10] In view of the wide spectrum of complications with EST, there is a need for alternative methods. Endoscopic variceal ligation (EVL) has been shown to eradicate varices faster with lesser complication rates but with increased rates of variceal recurrence and it is difficult to ligate smaller varices.[11,12]

So the new concept of combining the best of both endoscopic modalities by using EVL followed by low-dose EST was introduced.[13–15] Although a combination of EVL and EST has been shown to be superior to any individual method in adults,[14,15] there is scarcity of data in children.[10] There is no study in children that has looked into the long-term effect of this combination technique of tackling esophageal varices. In this prospective endoscopic outcome audit, we therefore studied the combination of EVL followed by EST and compared this with EST alone, both in terms of efficacy and the long-term post-eradication follow up in children with EHPVO.

Methods

From January 2000 to March 2007 consecutive children (<16 years of age) with a diagnosis of EHPVO with variceal bleeding were included in this study. Diagnosis of EHPVO was made by demonstration of portal vein obstruction with or without splenic

vein block by Doppler ultrasonography with normal liver function tests. In the first three years of our study EST alone was used as EVL was not readily available at our center. In the latter half of the study, EVL followed by EST was used in all except in very young children (<2 years of age) due to technical difficulties. Informed consent was obtained from parents before each session of endoscopy. The procedure was carried out under ketamine sedation. Endoscopy was performed using a flexible pediatric forward-viewing video endoscope (GIF-XP-20; Olympus Corporation, Tokyo, Japan). Esophageal varices were graded (I–IV) according to the classification of Conn.[16] Also, assessment was made about the status of gastric varices and portal hypertensive gastropathy (PHG). Gastric varices were classified according to Sarin's classification.[17] These were divided into two types: gastroesophageal varices (GOV) (GOV1 [extension of esophageal varices into stomach along the lesser curvature] and GOV2 [extension along the greater curvature]) and isolated gastric varices (IGV). If the patient had more than one type of gastric varix, we labeled them by choosing the largest type of gastric varix observed. Grading of PHG was nil, mild or severe according to the description given by Taor *et al*.[18] Scarlatina rash, superficial reddening, and fine white reticulate pattern separating the areas of raised red erythematous mucosa resembling snake skin were classified as mild; and cherry red spots and diffuse hemorrhagic pattern were graded as severe PHG.

Sclerotherapy was carried out with an indigenously made 23G sclerotherapy needle. Each variceal column was injected with 0.5–2 mL of sclerosant (1% polidocanol), depending on the size of the variceal column. EVL was carried out with a multiband ligation device manufactured by either Boston Scientific International, La Garenne Colombes, Cedex, France (Speed band) or Wilson Cook Medical, Winston Salem, NC, USA (Sayed's six shooter). After attaching the device to the endoscope, bands were applied during a single intubation, the first band was placed just proximal to the esophagogastric junction, with subsequent bands placed in a cephalad direction in a slightly spiral pattern; bands were applied to all visible varices. All children (both the EVL and EST groups) received endotherapy sessions every 3 weeks until eradication. A switch from EVL to EST was done when the grade of varices were reduced to grade II or less.

Eradication was defined as the absence of any varices at the lower end of the esophagus. After achieving eradication, surveillance endoscopy was done at 3 months and then at 6-monthly intervals. Recurrent varices were treated with EST only when they were more than Grade II.

A detailed record of each patient pertaining to the number of sessions required to eradicate the esophageal varices, the volume of sclerosant injected, the number of bands applied, any complication encountered, recurrence of varices and evolution of gastric varices and PHG was maintained. The institutional ethical committee's approval was provided for this audit.

Statistical analysis

Statistical analysis was carried out using SPSS 13.0 software (SPSS, Chicago, IL, USA). The results were expressed as mean ± standard deviation. The comparison between the two groups (EVL + EST and EST alone) for quantitative variables was carried out using the Student's *t*-test and for categorical variables using the χ^2-test and Fisher's exact test. A *P*-value < 0.05 was taken as significant.

Results

During the study period a total of 186 children with EHPVO were managed at our center, 25 of whom were lost to follow up after 2.3 ± 1.4 endotherapy sessions but before eradication and hence were excluded. Of the remaining 161 children, EVL followed by EST was carried out in 101 children (Group I) and EST alone was carried out in 60 children (Group II). Eradication was achieved in all children in Group I (100%) while it was not achieved in three children in Group II (95%). For the final analysis we included only those children who had achieved eradication and thus Group II comprised of 57 children. The mean age of children in Group I was 8 ± 3 years while it was 7 ± 4.5 years in Group II with male-to-female ratios being approximately 4:1 in both the groups. A drop-out analysis was done comparing participants ($n = 158$) and non-participants (lost-to-follow-up cases, $n = 25$) to rule out selection bias. There was no significant difference between them as far as baseline characteristics are concerned. Table 1 shows the baseline characteristics of Group I, Group II and Group III (lost-to-follow-up cases). All three groups were comparable for all characteristics (Table 1).

During the study period, 39 children underwent shunt surgery and their indications were: large fundal varices in 13; massive splenomegaly with hypersplenism and growth failure (all together) in 15; massive splenomegaly with splenic infarct in two; portal biliopathy in four; portal colopathy with lower gastrointestinal bleeding in three; and poor compliance to endotherapy in two.

The comparison between Group I and Group II is given in Table 2. In Group I, the mean number of EVL sessions was 2 ± 0.3 and the mean number of bands applied per session was 2 ± 0.5 (range, 2 to 6). The total number of sessions of EVL and EST required in this group was significantly less than in Group II ($P < 0.005$). Similarly, the volume of sclerosant required in Group I was significantly less than in Group II ($P < 0.001$).

Table 1 Baseline characteristics of children with extrahepatic portal venous obstruction (EHPVO) in Groups I, II and III

Parameter*	Group I (EVL + EST) $n = 101$	Group II (EST alone) $n = 57$	Group III (Lost to follow up), $n = 25$
Age (year)	8.19 ± 3.8	7.09 ± 4.69	8.09 ± 4.16
M : F	4:1	4.7:1	4:1
Large varices	96 (95.3%)	43 (76.8%)	23 (92%)
PHG—mild	14 (13.9%)	9 (15.74%)	7 (28%)
PHG—severe	2 (1.98%)	1 (1.75%)	1 (4%)
GOV1	57 (56.4%)	25 (43.1%)	14 (56%)
GOV2	10 (9.9%)	5 (8.62%)	4 (16%)
IGV	3 (2.9%)	2 (3.44%)	0

**P*-value is not significant of any of these parameters.
EVL, endoscopic variceal ligation; EST, endoscopic sclerotherapy; GOV1, gastroesophageal varices along lesser curve; GOV2, gastroesophageal varices along greater curve; IGV, isolated gastric varices; PHG, portal hypertensive gastropathy.

Table 2 Comparison of follow up and endoscopic details between Groups I and II

Parameter	Group I (EVL + EST) $n = 101$	Group II (EST alone) $n = 57$	*P*-value
Follow up (in months)	33 ± 17.6	43 ± 16.7	<0.01
Number of sessions (total)	5.24 ± 1.8	6.85 ± 2.8	<0.005
Sclerosant volume	13 ± 8.25 mL	30 ± 20 mL	<0.001
Esophageal stricture	7 (6.93%)	16 (28.07%)	<0.001
Esophageal ulcer	8 (7.92%)	6 (10.53%)	NS
Rebleeding	4 (3.97%)	6 (10.53%)	NS
Recurrence of esophageal varices	26 (25.74%)	22 (38.59%)	NS

Values are expressed as mean ± standard deviation. EVL, endoscopic variceal ligation; EST, endoscopic sclerotherapy; NS, not significant.

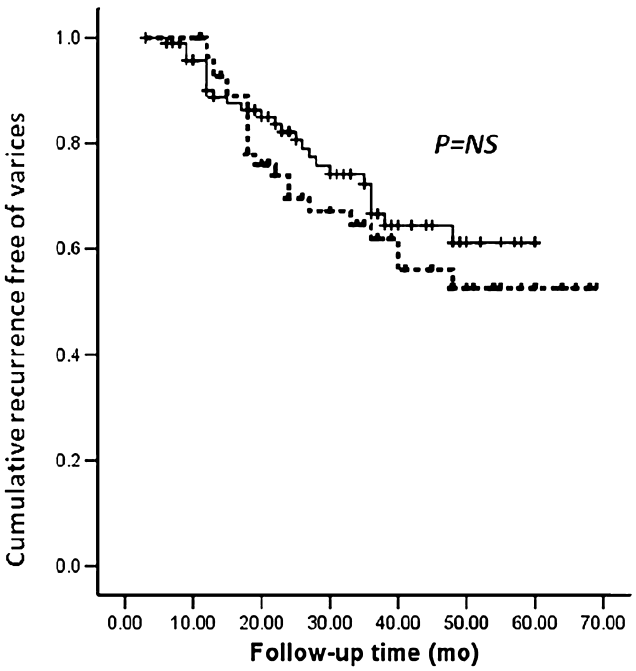

Figure 1 Kaplan–Meier curve to show recurrence of varices in two groups. - - - RxMethod ESTalone; — EVLEST; ✣ ESTalone censored; + EVLEST-censored.

The follow-up duration after eradication was significantly longer in Group II than in Group I as children in Group II were recruited earlier than children in Group I. Complication in the form of esophageal stricture was significantly more common in Group II than in Group I ($P < 0.001$). Comparing the children who developed stricture in Group I and Group II, it was found that the volume of sclerosant used was significantly higher (45.6 ± 23.7 vs 24.3 ± 12.0, $P < 0.04$) and the number of dilation sessions required was significantly more (2.4 ± 1.6 vs 0.9 ± 0.7, $P < 0.03$) in Group II children with stricture than in Group I children with stricture. However, there was no difference in age and sex distribution between the two groups of children with stricture. Nevertheless, ulcers were seen equally in both the groups. Rebleeding rates between the two groups were not significantly different. Similarly there was no difference in the rate of recurrence of varices between the groups. A life table analysis (Kaplan–Meier curve) (Fig. 1) also showed that there was no difference in recurrence of varices between the two groups. There was no mortality in the study group.

Table 3 Comparison of prevalence of pre- and post-eradication portal hypertensive gastropathy and gastric varices between Group I and Group II

Parameters	Group I* $n = 101$	Group II† $n = 57$	*P*-value
Mild PHG			
Pre-eradication	14 (13.9%)	9 (15.74%)	NS
Post-eradication	47 (46.54%)	26 (45.61%)	NS
Severe PHG			
Pre-eradication	2 (1.98%)	1 (1.75%)	NS
Post-eradication	8 (7.92%)	11 (19.29%)	<0.05
GOV1			
Pre-eradication	57 (56.4%)	25 (43.1%)	NS
Post-eradication	34 (33.67%)	13 (22.81%)	NS
GOV2			
Pre-eradication	10 (9.9%)	5 (8.62%)	NS
Post-eradication	21 (20.79%)	14 (24.56%)	NS
IGV			
Pre-eradication	3 (2.9%)	2 (3.44%)	NS
Post-eradication	11 (10.84%)	7 (12.28%)	NS

*Within Group I, $P < 0.001$ between pre and post eradication for mild PHG, severe PHG, GOV2, IGV and $P = 0.002$ for GOV1.

†Within Group II, $P < 0.001$ between pre and post eradication for PHG (both mild and severe), GOV1, GOV2 and IGV.

GOV1, gastroesophageal varices along lesser curve; GOV2, gastroesophageal varices along greater curve; IGV, isolated gastric varices; NS, not significant; PHG, portal hypertensive gastropathy.

The outcome of PHG and gastric varices in Groups I and II is given in Table 3. Following eradication of esophageal varices, there was significant increase in the prevalence and the severity of PHG in both the groups ($P < 0.001$). Although there was significant increase in the prevalence of GOV2 and IGV in both the groups following eradication of esophageal varices, the prevalence of GOV1 decreased significantly following eradication. Nevertheless, there was no significant difference in the prevalence of PHG or GOV between Group I and Group II, except post-eradication severe PHG, which was significantly more prevalent in Group II compared to Group I ($P < 0.05$). Thus the pattern of changes in gastric varices between pre- and post-eradication was similar in the two groups.

Discussion

This is the first long-term follow-up study on EVL followed by EST in children. The study gives a long-term insight into EVL followed by EST as a treatment modality for varices in children with EHPVO. We have shown that EVL followed by EST is superior to EST alone as it takes fewer sessions to eradicate esophageal varices with fewer complications. However, on

long-term follow up of 3 years, the outcome of gastric varices and PHG is similar with both the modalities.

Randomized trials comparing EVL with EST in adults[19–21] as well as in children[9] have shown that EVL is superior to EST as it eradicates varices faster with fewer complications. In fact EVL has become the preferred mode of treatment of variceal bleeding in adults. Nevertheless, EST cannot be totally ruled out as a therapeutic modality, especially in children. EST remains the only therapeutic option in children younger than 2 years of age due to insertion difficulty with a comparatively larger banding cylinder and in many developing countries EST is still preferred over EVL due to the higher cost of the latter. Although the number of studies in children on EVL is limited,[8–10] there are many on EST.[5–7] Our present study, like the only RCT on EVL and EST in children,[9] has also substantiated the fact that EVL eradicates varices faster with fewer complications.

Despite having many advantages, when used alone, there is a high risk of recurrence of varices with EVL, as it is difficult to ligate smaller varices and perforators and paraesophageal collaterals remain patent after EVL.[8,11,12,22] To overcome these problems, adjuvant sclerotherapy once varices become smaller with EVL has been suggested.[13] The idea of taking the advantages of both modalities (EVL and EST) for variceal eradication was first suggested by Sarin *et al*.[13] By using EVL as primary treatment, we can achieve rapid eradication with fewer complications and by using a low volume of sclerotherapy following EVL, we can block the perforators and paraesophageal collaterals and thereby reduce the risk of recurrence.

Previous studies[14,15,23] have clearly shown EVL followed by EST as a superior modality compared with EST alone. Like the present study, the only study so far about children on EVL followed by EST[10] has shown a 100% eradication rate. The number of sessions required to eradicate esophageal varices, the volume of sclerosant used, and the complication rates in the EVL-followed-by-EST group are significantly less compared with the EST-alone group and these results are comparable with a previous study.[10] However, the long-term effect of EVL plus EST on PHG and gastric varices has not yet been studied.

In our study, on long-term follow up there was a significant increase in the frequency and severity of PHG as well as IGV in both the groups. Nevertheless, there was a significant reduction in the prevalence of GOV1. There was no significant difference in the evolution of gastric varices and PHG between the groups. Sarin *et al*.[19] have shown that the frequency and severity of PHG is much more with EST than with EVL (20.5% vs 2.3%, $P < 0.001$) and it has been postulated that EVL blocks the esophageal veins only in the mucosa and submucosa, leaving the perforators to drain the paraesophageal collaterals with resultant lesser congestion of the gastric microcirculation. However in EST, sclerosant may flow into the deeper layers of the esophageal wall and block the collateral vessels. Hence, more profound congestion of the gastric microcirculation is expected following EST, compared with EVL, and that may have a more marked effect on PHG.[19] In our study, at the end both the groups have received EST, thereby nullifying the effect of EVL. Our findings of the effects of endotherapy on PHG and gastric varices are similar to those reported by Itha *et al*.[24] and Poddar *et al*.[25] in their studies with EST as a treatment modality.

The distribution of gastric varices in our study is similar to that of previous pediatric[24,25] studies. The commonest type of gastric varices are GOV1 and this type of varices usually disappears with endotherapy (EST or EVL).[17] On the other hand the least common type of gastric varices is IGV and most of these appear after endotherapy.[17,25] In our study also, almost half of the GOV1 disappeared with endotherapy and the rate of disappearance was similar in both the groups. However, the majority (72%) of IGV appeared after endotherapy. The same was true for GOV2. Itha *et al*.,[24] in their study of 183 children with EHPVO, and Poddar *et al*.,[25] in their study of 274 children with EHPVO, have shown similar types of evolution of gastric varices following EST.

Our results of EST alone are comparable to the previously published studies.[4,5] In view of rapid eradication with EVL followed by EST, fewer children had rebleeding before eradication. The main limitation of our study was that cases were not randomized. The other limitation is that we do not have information about 25 (13%) patients who were lost to follow up before the eradication of varices.

In conclusion, EVL followed by EST is better than EST alone in children with EHPVO as it requires fewer sessions, has fewer complications and less recurrence. However, following eradication, evolution of gastric varices and PHG was similar in the two groups. We therefore recommend EVL followed by EST as an effective endoscopic modality in treating children with bleeding esophageal varices.

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