A transparent cap assisted endoscopic injection sclerotherapy for the treatment of patients with esophageal varices

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Abstract

Aim: The aim of this study was to compare the efficacy and safety of cap assisted endoscopic injection sclerotherapy (EIS) versus direct endoscopic injection sclerotherapy (EIS) in the management of patients with cirrhosis after esophageal variceal bleeding.

Methods: Patients with cirrhosis suffering from esophageal variceal bleeding who underwent EIS with or without the help of a transparent cap in Shandong Provincial Hospital between November December 2014 and April 2017 were included in this retrospective study. All of the cases included in the study were divided into two groups: Group A (EIS with a transparent cap, n=50), Group B (direct EIS, n=45). Data collected included patients’ demographics, details of the procedure, variceal eradication, variceal rebleeding, variceal recurrence and survival during the follow-up period. All data were expressed as mean ± SD. Quantitative variables were compared by Student t test, and qualitative variables were compared by the Fisher exact test or the chi-square test. A P value less than 0.05 was considered significant.

Results: The mean duration of follow-up was similar in both groups (16.3±10.2 mo and 15.5±9.5 mo, respectively). To achieve the eradication of varices, the volume of sclerosant (64.86±10.62 ml vs 104.73±21.25 ml, P =0.044), the mean number of sessions (2.37±1.15 times vs 5.70±1.57 times, p =0.042), the time required to perform endoscopic treatment (6.57±1.50 minutes vs 11.22±2.29 minutes, P =0.049) and the time for the initial esophageal varices eradication were significantly reduced in the cap assisted EIS group than in the direct EIS group (5.43±1.38 weeks vs 8.93±1.5 weeks, P =0.041). The probability of variceal recurrence and rebleeding was significantly higher in the direct EIS group than in cap assisted EIS group. Only 22 patients (44%) developed complications in the cap assisted EIS group as compared to 30 patients ( P =0.039) in the EIS group. The
probability of survival was similar in both groups (P =0.133).

Conclusion: EIS with a transparent cap is an effective and safe treatment for esophageal varices.

Background

Esophageal variceal bleeding is a major cause of morbidity in patients with cirrhosis. Endoscopic variceal ligation (EVL) and endoscopic injection sclerotherapy (EIS) were widely used to treat esophageal variceal bleeding. Because of the lower rebleeding and complication rates of ligation, EVL has been recommended as the optimum endoscopic treatment to prevent recurrent bleeding from esophageal varices\(^1,2\). However, ligation is not without drawbacks due to a higher tendency to variceal recurrence\(^3\). EIS was superior to EVL in preventing variceal recurrence\(^4\) and is still widely used to control acute esophageal variceal bleeding as well as to eradicate varices to prevent recurrent bleeding. The main reason why EIS is not generally recommended is because of the higher rate of complications and lower effect in reducing mortality\(^5\).

In 1980s, Kitano et al designed a transparent tube to facilitate the accurate sclerosant injection and there were a series of studies showed that over-tube assisted EIS was easier, safer, more rapid in sclerosing esophageal varices with less complications than direct EIS\(^6-8\). However, in this technique, the patients had to swallow a fifty centimeters transparent tube, and this technique was not widely accepted because the uncomfortability and pain after the procedure.

EIS includes two methods-the intravariceal injection and the paravariceal injection. It is difficult to perform pure intravariceal injection, especially if the varices are small or in recurrent cases following EIS or EVL. We tried intravariceal injection sclerotherapy with a transparent cap(Figure 1).
The present study was therefore conducted to compare the efficiency and safety of both methods (cap assisted or direct EIS) in the management of patients with cirrhosis after esophageal variceal hemorrhage. To our knowledge, at the time of writing, no other report in English literature has compared the two procedures in the treatment of esophageal variceal hemorrhage.

Methods

Patients

The subjects were patients with cirrhosis suffering from esophageal variceal bleeding who underwent EIS with a transparent cap (Group A) or direct EIS (Group B) in Shandong Provincial Hospital between December 2014 and April 2017. The inclusion criterial were:

1. Diagnosis of liver cirrhosis by biopsy or clinical examination and imaging, including ultrasound, computed tomography (CT), or magnetic resonance imaging;
2. Patients suffered from bleeding within 6 months before being admitted;
3. The degree of esophageal varices was F2 of F3 in these patients, as revealed by gastroscopy. Patients were excluded if they presented with one or more of the following items: (1) Hepatocellular carcinoma or other malignancies; (2) A history of gastric variceal bleeding; (3) A history of EIS, EVL, or portal systemic anastomosis; (4) Complete obstruction of the portal vein due to thrombosis; (5) Infection.

All cases were performed by one or two endoscopic experts. Informed written consent was obtained from each patient. Shandong Provincial Hospital ethics committee approval was obtained for the chart review.

For intravariceal injection, an indigenously designed transparent cap, a teflon injector with a 21 gauge needle (Olympus) and a therapeutic gastroscope (Olympus GIF Q260J) were used.
Treatment Procedures And Follow-up

In group A, a transparent cap (MAJ-290, Olympus) was fixed in front of the gastroscope, which could afford an accurate injection of sclerosant into the varcies. Lauromacrogol was used as a sclerosant. The injection needle was pre-filled with lauromacrogol. The procedure was given starting from the lower end of the variceal columns near the cardia with 5–7 ml per injection according to the diameter of the varices, totally less than 40 ml. If bleeding occurred at puncture sites, the transparent cap was pressed onto the bleeding point until the bleeding stops. In group B, EIS was operated without the help of transparent cap, so both intravariceal and paravariceal sclerotherapy were applied.

The endoscope was withdrawn after achieving haemostasis and decompressing the stomach. In both groups, sclerotherapy was done on a regular 2–4 weeks, until variceal eradication was achieved. Once varices were eradicated, repeat endoscopy was performed at 3–6 months intervals to check for recurrent varices.

Variceal eradication was defined as non-visualization of varices, or less than grade F2 varices, or varices that could not be injected. Recurrence of varices was defined as appearance or an increase in the grade of varices after achieving successful obliteration. The final decision between varices eradication or recurrence had to be agreed upon by two experienced endoscopists.

Rebleeding was defined as a new onset of hematemesis, coffee-ground vomitus, hematochezia, or melena with an increasing pulse rate over 110 beats per minute, and decreasing blood pressure below 90 mmHg. Complications were determined by questionnaire. Patients were questioned before any kind of treatment as well as after and complications were only those symptoms which appeared after the commencement of both methods. Post-treatment Esophageal ulcers and stricture were usually diagnosed during the endoscopic follow-up of the patients.
Statistical analysis

All data were expressed as mean ± SD. Quantitative variables were compared by Student t test, and qualitative variables were compared by the Fisher exact test or the chi-squared test (with Yates correction) wherever appropriate. The Kaplan-Meier estimation was used to examine recurrence and rebleeding of esophageal varices and rate of survival. Comparisons were performed using the log-rank test. A P value < 0.05 was considered significant. Statistical analyses were performed by use of SPSS 20.0 software.

Results

Demographics

Between November 2014 and March 2017, EIS with transparent cap or direct EIS was performed in a total of 115 cirrhotic patients with a history of esophageal varices bleeding. Of the 115 patients, 6 had previously received treatment for esophageal varices either with EIS, EVL, or portal systemic anastomosis, 10 had hepatocellular carcinoma, 4 had a history of gastric variceal bleeding; these were excluded. In the remaining 95 patients, 50 patients were treated with cap assisted EIS (Group A) and 45 patients were treated with direct EIS (Group B) (Fig. 2). The clinical characteristics of the 95 patients in the two groups were retrospectively reviewed from a computerized database of our hospital, the severity of liver disease was assessed by Child-Pugh criteria[9], the size of the esophageal varices was graded according to Beppu’s criteria[10].As shown in Table 1, patients in the two groups were comparable for age, sex, aetiology of cirrhosis, Child’s grade, and variceal size. The median follow-up period was 15.5 ± 9.5 months in group A and 16.3 ± 10.2 months in group B.

Obliteration And Recurrence Of Esophageal Varices

As shown in Table 2, there were no significant difference in initial obliteration of varices
concerning between group A and group B (44/50 vs 39/45, p > 0.05). However, the mean
time necessary to achieve obliteration was 5.43 ± 1.38 weeks and 8.93 ± 1.5 weeks for
group A and group B, respectively. Furthermore, the probability of variceal recurrence was
significantly lower in group A than in group B (P = 0.014; Fig. 3). In 17 of the 23 patients
(5 in group A and 12 in group B), variceal recurrence presented as an episode of bleeding
from ruptured esophageal varices. 6 patients (2 in group A and 4 in group B) had a
recurrence diagnosed at routine follow-up examination. Recurrent varices were obliterated
in 10 (43.5%) of the 23 patients treated with cap assisted EIS or direct EIS and in 6(26%)
of 23 treated with EVL. In the remaining patients, recurrent varices were not obliterated
because they either died (5 patients) or were lost to follow-up (2 patients).

Rebleeding

Upper gastrointestinal tract rebleeding from all sources occurred in 10 patients (10/50) in
group A and 18 patients (18/45) in group B during the follow-up period (P = 0.033;
Fig. 4A). When considering only rebleeding from esophageal varices, 5 patients rebled in
group A and 12 in group B. The probability of rebleeding from esophageal varices was
significantly lower in group A than in group B (P = 0.034, Fig. 4B). The incidence of
bleeding from gastric varices was not significant between the two groups.

Complications

The complications in both group are shown in table 3. A lower proportion of patients in the
cap assisted EIS group experienced complications than in the direct EIS group (P = 0.039).
Seven patients in group A and 16 patients in group B suffered from fever (P = 0.017).
Chest pain was encountered in 9 patients in group A and 16 patients in group B (P > 0.05).
The patients were treated with conventional medical therapy, with fever and abdominal
pain usually being alleviated within 1 week. Four patients in group A developed mucosal
ulceration at the site of a previous injection. The corresponding number in group B was 11, and this difference was significant (P = 0.046). Esophageal stricture was found in 3 patients in a group A and 6 in group B who complained of dysphagia after sclerotherapy. Most of the procedure-related complications were mild in the two groups. There was no complication-related death in either group.

Survival

There were 7 deaths in group A and 11 in group B. The etiologies of the death are shown in Fig. 2. The Kaplan-Merier survival curve is shown in Fig. 5. Survival in the two groups was not significantly different (P = 0.133, Fig. 5). Two patients in group A and 3 patients in group B died of variceal bleeding. Four patients in group A and 6 patients in group B died of hepatic failure.

Discussion

Bleeding from esophageal varices is a life-threatening condition with an incidence of 5%-15% in patients with liver cirrhosis and mortality rates of at least 20%[11, 12]. The therapeutic methods for esophageal varices include EIS, EVL, nonselective β-blockers, TIPS, shunt surgery, and so on[13-16]. EVL is increasingly used because of its safety and simplicity and because no sclerosant is required. However, EVL only achieves local eradication, but does not completely disrupt the interconnecting perforating and feeder vessels[17]. Accumulated evidence suggests that the patency of feeder vessels of varices, such as paraesophageal varices and periesophageal varices, predisposes to variceal recurrence[15, 18-20]. These feeder vessels are occluded more efficiently by sclerotherapy than ligation, which is usually confined to the mucosal and submucosal collaterals. Hou et al and Shiv et al found that the early recurrence and multiple recurrence of esophageal varices are more likely in
patients undergoing endoscopic ligation, compared to sclerotherapy\textsuperscript{21, 22}. So, although EVL is widely accepted as the optimum endoscopic treatment for esophageal variceal, EIS was superior to EVL in preventing esophageal variceal recurrence\textsuperscript{4} and is still widely used to control acute esophageal variceal bleeding as well as to eradicate varices to prevent recurrent bleeding. EIS can be accomplished by either intravarical EIS or paravariceal EIS. However, like EVL, paravariceal EIS also only achieves local eradication, but does not completely disrupt the interconnecting perforating and feeder vessels\textsuperscript{3}. Paravariceal injection technique is not effective and early recurrences have been reported \textsuperscript{23}.

We observed a lower recurrence of esophageal varices and a lower rebleeding rate in the cap assisted EIS group than in the direct EIS group. Variceal eradication could be achieved significantly early with cap assisted sclerotherapy. The number of sessions required and the time of injections per session were also significantly reduced in the cap assisted group. The smaller volume of sclerosant was require to eradicate esophageal varices in the cap assisted EIS group.

In the treatment of esophageal varices, intravariceal EIS obliteration both interconnecting perforating veins and feeding veins of esophageal varices. However, EIS is associated with high incidences of local and systemic complications. Several study showed that dysphagia and esophageal stricture formation after EIS up to 59\% of patients.

Our study shows that a lower proportion of patients in the cap assisted EIS group experienced complications than in the direct EIS group (\(P = 0.039\)). Four patients in the cap assisted EIS group developed mucosal ulceration at the site of a previous injection. The corresponding number in the direct EIS group was 11 and this difference was significant (\(P = 0.046\)). Esophageal stricture was found in 3 patients in a group A and 6 in
group B who complained of dysphagia after sclerotherapy. It was usually a transient phenomenon and no patient required esophageal dilatation for the relief of symptoms. The benefits of transparent cap application in the operation of EIS are as fellow:

(1) Maintaining a clear field of vision; (2) The cap can fairly compress and immobilize the targeted varices, which enable the accurate injection of sclerosant and reduce sclerosant leaking in the injection site and reducing complications; (3) Reducing patients discomfort.

There was no significant difference in the mortality rates between the two groups. However, our study is a retrospective single-center study and has included limited cases. In the future, a prospective, randomized, and controlled trial is required to further testify our conclusion.

In conclusion, with the auxiliary of a transparent cap, the modified EIS, compared with direct EIS, has lower esophageal variceal recurrence, rebleeding and complications. It is a promising modality for the treatment of esophageal varices.

Abbreviations

Endoscopic injection sclerotherapy (EIS); Endoscopic variceal ligation (EVL).

Declarations

**Ethics approval and consent to participate:** The study was approved by Shandong Provincial Hospital ethics committee. Written informed consent for participating was obtained from all participants.

**Consent for publication:** Written informed consent for publication was obtained from all participant.

**Availability of data and material:** We declared that materials described in the manuscript, including all relevant raw data, will be freely available to any scientist wishing to use them for non-commercial purposes. **Competing interests:** The authors
declare no competing interest

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**Authors' contributions** ZSL proposed the study. ZSL, WJ, ZXH performed the research and wrote the first draft. ZSL and WJ collected and analyzed the data. All authors contributed to the design and interpretation of the study and to further drafts. ZSL is the guarantor.

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Tables

| Table 1 Demographics of the patients included in the two groups. |
|---------------------------------------------------------------|
| Group | Age (years) | Male/female | Etiology of cirrhosis | Child-Pugh classification | Variceal size | Duration of follow-up (mo) |
|-------|-------------|-------------|------------------------|---------------------------|--------------|--------------------------|
| A     | 49.23±7.12  | 29/21       | NR                     | NR                        | F2           | 16.3±10.2                |
| B     | 53.10±9.05  | 26/19       | NR                     | NR                        | F3           | 15.5±9.5                 |

P value: NS
|                                | Group A | Group B | P value |
|--------------------------------|---------|---------|---------|
| Varices eradication            | 44/50   | 39/45   | NS      |
| Number of sessions until eradication | 2.37±1.15 | 5.70±1.57 | 0.042 |
| Time for eradication(weeks)    | 5.43±1.38 | 8.93±1.5 | 0.041 |
| Time for per treatment (minutes) | 6.57±1.50 | 11.22±2.29 | 0.049 |
| Amount of lauromacrogol(ml)    | 64.86±10.62 | 104.73±21.25 | 0.044 |
| Recurrence of varices          | 7/44    | 16/39   | 0.014   |
| UGI rebleeding                 | 10      | 18      | 0.049   |
| Esophageal varices             | 5       | 12      | 0.034   |
| Gastric varices                | 2       | 2       | NS      |
| Esophageal/gastric ulcer       | 1       | 2       | NS      |
| Portal hypertensive gastropathy | 2       | 1       | NS      |
| Undetermined                   | 0       | 1       | NS      |
### Table 3 Complications in the two groups.

|                          | Group A N=50 | Group B N=45 | P value |
|--------------------------|--------------|--------------|---------|
| No. of patients with complications | 22           | 30           | 0.039   |
| Fever                    | 7            | 16           | 0.017   |
| Chest pain               | 9            | 15           | NS      |
| Ulcer                    | 4            | 11           | 0.046   |
| Esophageal stricture     | 3            | 10           | 0.034   |

### Figures

![Figure 1](image1.png)

**Figure 1**

The procedure of cap assisted EIS. A. The transparent cap used in the procedure of EIS; B. Cap assisted intravariceal injection; C. The transparent cap was pressed onto the bleeding point after injection.
Figure 2

Flow diagram of rebleeding and death after EIS in the two groups.
Figure 3

Probability of being free of variceal recurrence after initial esophageal varices eradication in the two groups.
Figure 4

Probability of being free from rebleeding in the two groups. A. Probability of being free from rebleeding from the upper gastrointestinal tract in the two groups. B. Probability of being free from esophageal variceal rebleeding in the two groups.
Figure 5

Probability of survival in the two groups.