# Chapter 21
# Endoscopic Treatment of Esophageal Varices: Obara Method

**Katsutoshi Obara**

**Abstract** Endoscopic treatment is the first choice for treating esophageal varices in Japan. In particular, the Obara method, which is known as the ethanolamine oleate (EO)-Aethoxysklerol (AS) combination method, is widely performed as it contributes to a low risk of recurrence. Inject 5% EO into all the esophageal varices and their feeding veins under fluoroscopy until they can be imaged on a fluoroscopy monitor. After the esophageal varices are obliterated using the EO method, inject 1% AS into the obliterated varices and their surrounding mucosa so that shedding of the obstructed esophageal varices and sclerosis of the esophageal wall by fibrosis can be expected. The Obara method is an extremely useful procedure for preventing recurrence by completely eradicating esophageal varices.

**Keywords** Esophageal varices · Obara method · EO-AS combination method
Ethanolamine oleate · Aethoxysklerol

## 21.1 Introduction

A variety of treatment methods have been adopted for the endoscopic treatment of esophageal varices. Ethanolamine oleate (EO) was first employed in the treatment of esophageal varices in 1946 by Trolle et al. [1], and in Japan, Takase et al. introduced endoscopic injection sclerotherapy (EIS) using 5% EO (the EO method or the Takase method) in 1978 [2]. And Suzuki et al. established a unique intra- and paravariceal combined injection technique with 1% Aethoxysklerol (AS), the so-called Suzuki method, in 1981 [3]. In those days, the Takase method was validated as effective; however, it was associated with a number of complications, while the Suzuki method was found to be safer but

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less effective than the Takase method. Therefore, in 1987, Obara et al. introduced the EO-AS combination method, the so-called Obara method, in 1987, which adopted the advantages of both of these previous methods in order to enhance their efficacy and safety [4].

Evidence-based guidelines for liver cirrhosis 2015 recommend that EIS should be used for the treatment of esophageal varices because both recurrence rates and bleeding (including rebleeding) rates are lower in patients treated with EIS compared with those in patients treated with endoscopic variceal ligation (EVL) resulting in the effective prevention of recurrence of esophageal varices (Recommendation grade 1, Evidence level A) [5–7].

This chapter describes the action mechanisms of sclerosing agents used in the Obara method and its treatment procedures.

## 21.2 Action Mechanism of Sclerosing Agents

### *21.2.1 Ethanolamine Oleate (EO)*

EO is an anionic surfactant that was originally used as a leather-softening agent. In our institute in the 1980s, the action mechanism of EO was intensively studied using a dog so that it could be clinically applied in an optimal manner [8]. EO poses vascular endothelial cell damaging action [9–11], thrombus formation action [12–14], hemolytic action [15–18], tissue-damaging action [19], and/or effects on the circulatory system such as lowering the blood pressure or shock, the main mechanism for which has traditionally been thought to be a decline in cardiac output coupled with bradycardia.

### *21.2.2 Aethoxysklerol (AS)*

AS is a 1% solution of the anionic surfactant polidocanol. In our institute, AS was injected around the auricular veins of a rabbit, and changes in the tissue were studied over time [8]. Injection of AS on the periphery of small veins results in ulceration due to AS's tissue-damaging action. This causes the small veins to develop necrosis and fall off together with the ulcer or the periphery of the small veins to develop a dense coating of fibrous tissues. As the ulcer produced by AS is shallower than that formed by EO or absolute ethanol (ET) [19], there is little risk of perforation. Moreover, the fibrosis occurs very quickly and is similar in degree to EO and ET. This makes AS the optimum sclerosing agent for injection on the periphery of esophageal varices [20].

### *21.2.3 Efficacy of EO Method*

Histological examination of an autopsied esophagus (Fig. 21.1) [8] in a patient with terminal hepatocellular carcinoma and imminent signs of esophageal variceal rupture 1 week after treatment using the EO method showed that the two varices

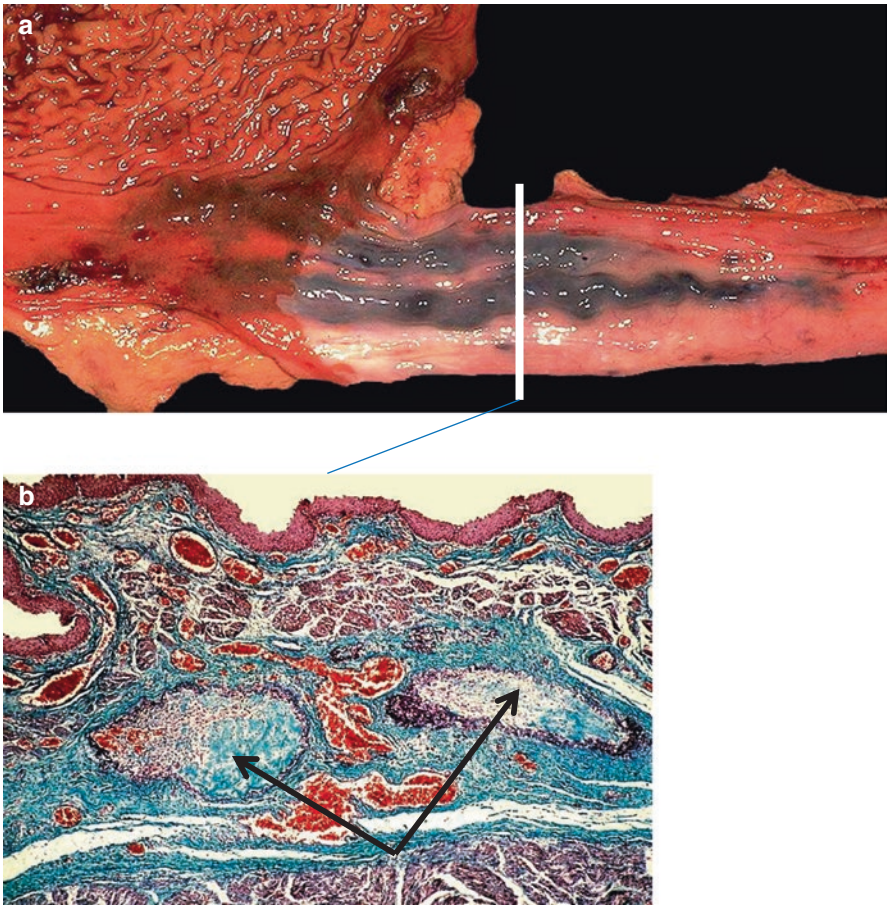


**Fig. 21.1** Pathological findings 1 week after the treatment with the EO method (autopsied case). (**a**) This image shows the autopsied esophagus and stomach of a terminal HCC case 1 week after a procedure using the EO method. Two lines of esophageal varices exhibiting thromboses are visible macroscopically. *HCC* hepatocellular carcinoma, *EO* ethanolamine oleate. (**b**) This is a histopathological image of the lower esophagus. Totally occluded thromboses are observed in two esophageal varices in which EO was injected, showing the effects of the EO method (black arrows). However, the growth of small recurrence-prone blood vessels of various sizes is observed in the surrounding region

into which EO had been injected had developed totally obliterated thrombi, indicating the efficacy of the EO method. However, the growth of small blood vessels of various sizes was observed in their vicinity. These vessels are called recurrence-prone vessels due to the high likelihood of their giving rise to a recurrence. In order to prevent a recurrence, it is useful to eliminate these vessels by employing the AS method after completing the EO method [4].

## 21.3 Obara Method Procedures

The Obara method is the EIS treatment for recurrence prevention, in which the Takase method and the Suzuki method are applied (Fig. 21.2) [4].

### *21.3.1 EO Method*

This technique is employed to obliterate the esophageal varices and their blood supply routes by tracing them under fluoroscopy. With intravenous injection, a puncture is started in the largest varix. If the sizes of the varices are similar, the puncture is started in the varix that displays the most advanced red color (RC) signs [21, 22]. If a clear red plug or white plug is found with an elective case, that

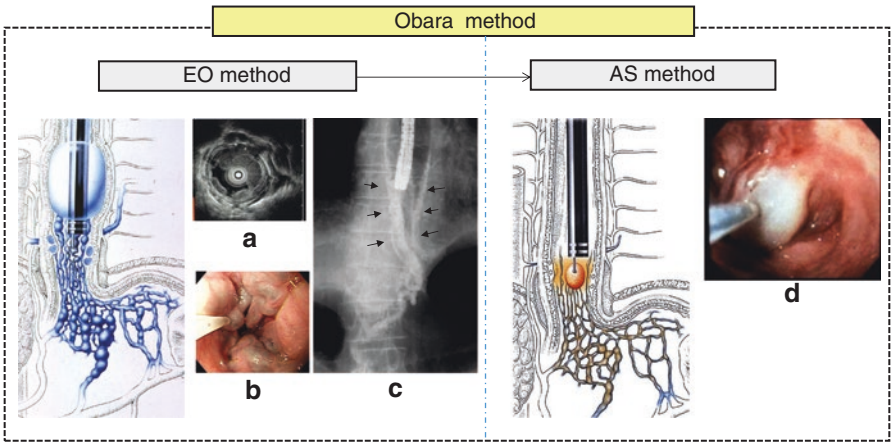


**Fig. 21.2** Obara method (EO-AS combination method). (**a**) EUS findings. The varices are observed as low-echoic lumen images in the submucosal layer. (**b**, **c**) Puncture from the 7 o'clock direction, inject enough 5% EO into the esophageal varices and the blood supply route to produce an occlusive thrombosis. *EUS* endoscopic ultrasonography, *EO* ethanolamine oleate, *AS* aethoxysklerol. (**d**) Inject 1% AS into the mucosa surrounding the small blood vessels that remain after the EO method has been performed in order to completely eradicate the varices by necrosis and drop-off

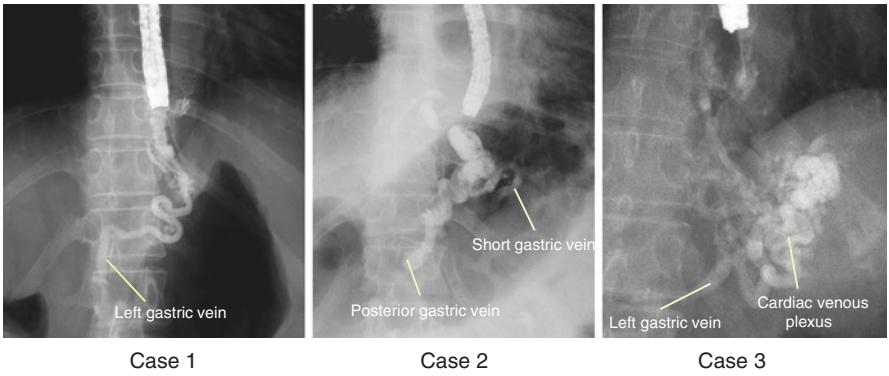


**Fig. 21.3** Blood supply routes observed during injection sclerotherapy

specific varix must be treated first. When enough EO has been injected, EO injection should be stopped while confirming that the blood supply routes are being imaged (Fig. 21.3) [4, 8, 23].

#### 21.3.1.1 Pipeline Varix

Kumagai et al. [24] proposed that a giant esophageal varix connected to a cardiac varix should be called a "giant-tree-type varix," while Toyonaga [25] suggested the term "pipeline varix" based on portal vein contrast imaging. As blood flows directly from the left gastric vein (LGV) to the varix without passing through the palisade veins, a large volume of blood flows rapidly, with the result that the high frequency of extraesophageal shunt complications makes such varices even more resistant to treatment.

Block the blood flow securely with a 6 cm balloon, and confirm the presence of a shunt and the quantity of blood flow by means of variceal contrast imaging using a contrast agent. If the contrast imaging is successful enough that the LGV can be imaged, inject EO into the LGV. If the contrast imaging is unsuccessful and a shunt is present, refer to the Sect. 21.3.1.2. "Giant-tree"-type pipeline varices are generally difficult to treat with just one EO session; therefore, a second EO session is often performed 1 week later in order to achieve complete obliteration.

#### 21.3.1.2 Esophageal Varices with a High-Risk Extraesophageal Shunt

When performing the EO method, make sure that EO flows into the blood supply routes and not into the lung, the heart, or the whole body. Should this occur, stop the EO injection immediately, taking into account the presence of high-risk shunts, which are portopulmonary shunts in the portopulmonary venous anastomosis (PPVA) and the inferior vena cava (IVC) (Fig. 21.4) [26–29]. EO flowing from the

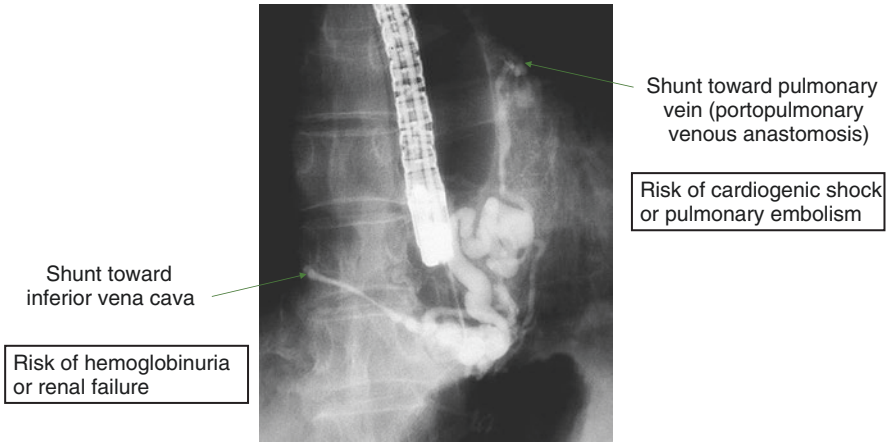


**Fig. 21.4** A high-risk extraesophageal shunt case

PPVA into the pulmonary veins could cause a shock or a pulmonary embolism, and EO flowing into the IVC poses the risk of inducing hemoglobinuria or renal failure.

Image the shunt with a contrast agent, and, if the contrast imaging is defective, administer 0.5–1 mL of ET intermittently (total dose, 3 mL or less); wait for 1–2 min, and reattempt contrast imaging (the ET method) [10, 26]. If it can occlude the shunt and the blood supply routes are imaged, inject EO into the blood supply routes. If the blood supply routes cannot be imaged by contrast imaging, withdraw the needle, and, if bleeding occurs, pressurize the bleeding point for 2–3 min with a 6 cm balloon for hemostasis. After hemostasis, apply the EO method to the other varices. Try to treat the problematic varices again after 1 week. If the ET method conducted 1 week later is still ineffective, confirm the shunted vessel with a 20 MHz ultrasonic miniprobe (UMP), and ligate the perforating section with a rubber O-ring. Then puncture the varix on the anal side of the ligated lesion, and obliterate the blood supply routes with EO (the selective EVL-EO combination method) [30].

UMP findings are useful for identifying high-risk shunts before treatment. If the diameter of the perforating vein observed with a UMP is smaller than 3 mm, the EO method is effective. If it is 3–5 mm, ET is effective (Fig. 21.5). However, if the diameter is bigger than 5 mm, the ET method is ineffective; therefore, the selective EVL-EO combination method should be used [26].

### *21.3.2 AS Method*

The aims of the AS method are to cause the thrombosed esophageal varices produced by the EO method to fall off and to eliminate any remaining small blood vessels (recurrence-prone vessels). It is effective to inject 2 mL of AS per point so

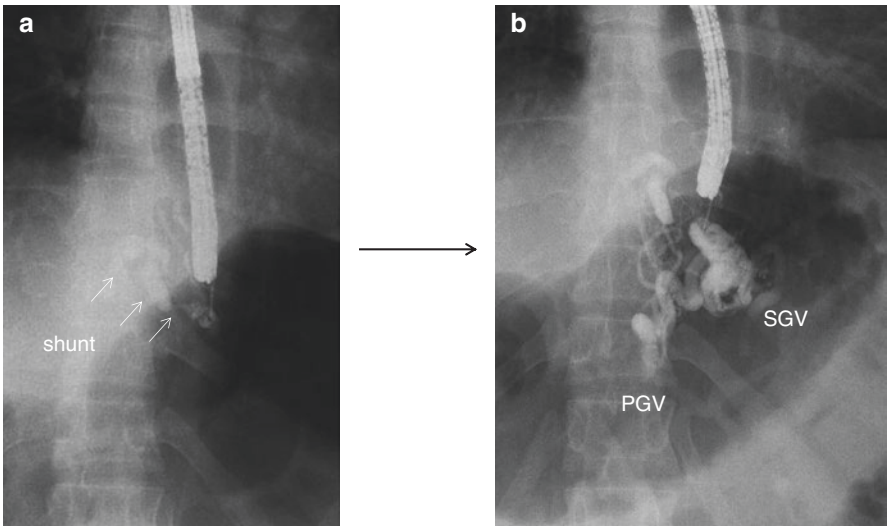


**Fig. 21.5** Treatment procedures for esophageal varices with an extraesophageal shunt. (**a**). The shunt diameter of this varix as measured with EUS was 4.2 mm. As the injected contrast agent flowed out to the shunt (inferior vena cava), the blood supply routes were not imaged. *EUS* endoscopic ultrasonography. (**b**) After injecting 1 mL of ET and waiting for 2 min, contrast imaging was reattempted. As this succeeded in imaging the blood supply routes, EO was injected until the blood supply routes (PGV and SGV) were obliterated. *ET* absolute ethanol, *EO* ethanolamine oleate, *PGV* posterior gastric vein, *SGV* short gastric vein

that it bulges from inside the mucosa. Injection in the submucosa is ineffective because AS spreads widely, and injection of a large amount in the muscle layer poses a risk of mediastinitis or esophageal perforation. The total amount of AS should be limited to within 20 mL [23].

## 21.4 Treatment Outcomes

With the Obara method, the accumulated nonrecurrence rates were 83.2% after 1 year, 68.1% after 3 years, and 66.0% after 5 years. The recurrent cases were F1–F2 esophageal varices with RC-positive, and bleeding occurred in about 10% of these cases (Fig. 21.6) [4, 8, 31]. All recurrent cases required inpatient treatment. Deguchi et al. compared the cumulative recurrence rates between the EO-AS combination method (the Obara method) only and EO-AS combination method followed by APC consolidation and reported that the recurrence rates were 29.0% after 1 year and 34.7% after 2 years in cases without the consolidation method and 9.7% after 1 year and 11.3% after 2 years in cases with the consolidation method ($p = 0.013$) [32]. Accordingly, the Obara method has been shown to be effective in preventing recurrence, and applying the mucosal fibrosis method (consolidation

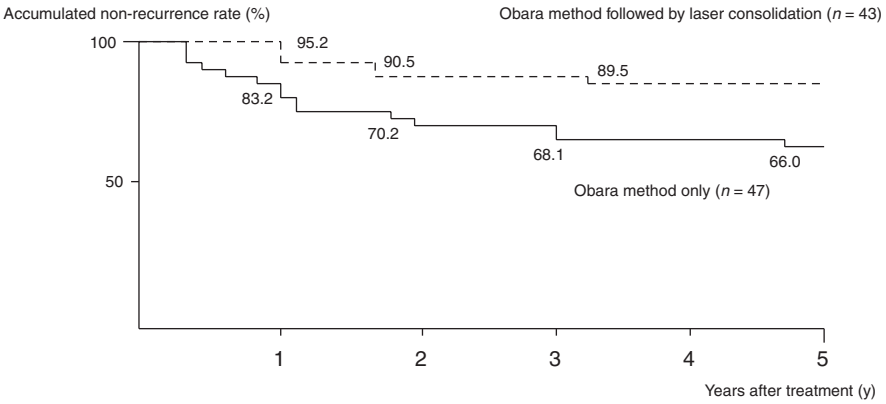


**Fig. 21.6** Cumulative nonrecurrence rates in patients treated using the Obara method followed by laser consolidation. Quoted from: Obara K [31]

method) has been shown to further reduce the recurrence rates (please see Chap. 25).

## 21.5 Complications

The precautions to be taken when employing the EO method are to avoid allowing EO to flow into the portal vein (the inflow of a large amount of EO carries with it the risk of portal vein thrombus or hepatic failure due to endothelial cell damage), limit the total EO injection amount to within 0.4 mL/kg (excessive administration may induce cardiogenic shock) [26], minimize the outflow to the rest of the body (otherwise, the hemolysis action of EO may cause hemoglobinuria or renal failure), and reduce extravascular EO leaks outside the blood vessel to 2 mL or less (otherwise, the strong tissue-damaging action of EO may cause esophageal ulceration and/or perforation).

As action mechanisms of EO are well known these days, critical complications are rarely found, while the AS method was originally a safe procedure with few complications [26, 31].

## 21.6 Conclusion

With the EO method only, recurrence of the varices cannot be prevented in a satisfactory manner. Therefore, it is extremely important to additionally apply AS method after the esophageal varices and their feeding veins have been obliterated. The Obara method for treating esophageal varices is a basic procedure of EIS

requiring comparatively more skill and experience than those required for EVL. However, with experienced endoscopists it is an essential treatment method on account of its improved patient safety and its efficacy in preventing recurrence for a long time.

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