Foam Sclerotherapy with other Gases

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Introduction

Foam Sclerotherapy is becoming more widely accepted by the international vascular community for treating varicose veins. Foam can be used to treat saphenous trunks, varicose tributaries, perforating veins and venous malformations. Many feel that foam is the treatment of choice for: neovascularization after previous surgery, recurrent varicose veins, sciatic nerve varices, the distal GSV after thermal ablation or stripping to the knee, and very tortuous internal varicosities. When treating these true medical conditions, it is best to use the term Endovenous Chemical Ablation (ECA), rather than sclerotherapy, to distinguish it from a cosmetic treatment.¹ It is important to recognize that ECA is quite different from sclerotherapy of reticular and telangiectatic vessels, and requires significantly more training by the administering physician.

For many years, conventional sclerotherapy has utilized liquid sclerosants very effectively in the treatment of smaller vessels.² Foam sclerotherapy is a variant of conventional sclerotherapy. Instead of injecting a liquid sclerosant solution into the vein, the sclerosant solution is transformed into foam by forcibly mixing it with air or other physiologic gases. Only detergent-type sclerosants can be foamed by this method. Foam, in contrast to liquid, makes better contact with the endothelium of the vein wall and will remain in the vein for a longer period of time; thus increasing the efficacy of this procedure, while allowing the treatment of larger veins.

History of Foam

The first detergent sclerosant, sodium morrhuate, was introduced in 1930. In 1939, Stuart McAusland ³ used sodium morrhuate as foam to inject telangiectatic veins. This foam was obtained by shaking up the bottle of sodium Morrhuate and aspirating the “soapy froth” into a syringe. It is here that the foam era begins. Robert Foote, in 1944, described making his soapy froth by shaking 1 ml of Ethamoline (ethanolamine oleate) in a 2 ml syringe. Karl Sigg, in 1949, described using Orbach’s air-block technique; but instead of air, he injected Foote’s froth, thus achieving better results. In 1990, Hess suggested the possibility of using other gases instead of air, stating that oxygen and carbon dioxide would be better because of their greater solubility in blood.⁴ The field of therapeutic medical ECA changed dramatically in 1995 when Juan Cabrera
published his results of using a microfoam produced with CO₂ as the carrier gas.⁵ Today, mainly sodium tetradecyl sulfate and polidocanol are used as sclerosant foams.

**Efficacy of Foam Treatment**

The efficacy of foam versus liquid sclerotherapy has been investigated in two randomized, controlled trials.⁶,⁷ Patients with incompetent great saphenous veins (GSV) were injected with either 3% polidocanol liquid, or foam, under ultrasound guidance. There were less treatment sessions required in the foam group, when compared to the liquid group.⁶ Occlusion of the GSV was more than twice that in the foam group, when compared to the liquid group.⁶,⁷ The secondary endpoints of reflux time, refilling time and patient satisfaction also improved significantly in the foam group.⁶ At a 2 year re-evaluation, 53% of foam-treated verses 12% of liquid-treated patients had successful obliteration of the GSV.⁷ These randomized controlled trials clearly show the superiority of foam over its liquid counterpart, at equal concentrations, for the treatment of the GSV.

Juan Cabrera published a clinical series of 500 legs treated with foam sclerotherapy. He reported that after 3 years, 81% of treated great saphenous veins remained closed, and 97% of superficial varicosities disappeared. No deep vein thrombosis or pulmonary embolisms were encountered in this series. These results were achieved with only one treatment session in 86% of patients, two sessions in 11%, and three sessions in 3% of patients.⁸

Another study demonstrated that foam sclerotherapy was also very effective in patients with severe venous disease and ulceration. In this study, 109 limbs with C4-C6 were compared to 76 limbs with C1-C3 disease. Six months after treatment, 75% of patients in both groups had occluded saphenous trunks. The investigators concluded that foam sclerotherapy was equally effective in both complicated and uncomplicated chronic venous disease.⁹

Two large meta-analyses¹⁰,¹¹ have shown that endovenous thermal ablation is more effective than foam sclerotherapy when treating saphenous veins. One study showed that it is equivalent to surgical stripping, with 77-78% success rates respectively at three years, determined by duplex ultrasound examination.¹⁰

Varisolve®, a polidocanol endovenous microfoam product with a controlled density, consistent bubble size, and proprietary gas mix, is currently under investigation. A European Phase III clinical trial showed that 90% of patients treated had no reflux in the GSV after 3 months and fewer than 10% of patients had recurrence after 1 year. Preparatory phase III studies focusing on patient-reported outcomes and photographic endpoints are underway in the United States, as of September 2010.¹²

**Complications and Side Effects of Sclerosant Foam**
Three major complications from foam sclerotherapy have been published in the world literature,\textsuperscript{13,14} despite millions of injections worldwide. These same complications and side effects can happen after both liquid and foam sclerotherapy, but they are more frequent after using foam. Transient side effects from foam sclerotherapy are much more common. A metallic taste, dry cough and chest tightness are frequently reported, but pass spontaneously. Transient visual disturbances are the most frequent side effect of importance, and occur in approximately 1-2\% of patients, and may be dose-related. These visual disturbances often occur in patients who have a previous history of migraine headaches, but may occur in anyone. The clinical presentation is similar to the aura of a migraine headache. Such side-effects are likely the result of foam particles entering the optic vasculature, or by circulating endothelin which is released during the sclerosing process.\textsuperscript{15}

The most common local complications are telangiectatic matting and hyperpigmentation <20\%, while the rate of superficial thrombophlebitis is <5\%. Serious adverse events such as anaphylaxis and DVT are very rare.\textsuperscript{16}

**Safety and Use of other Gases**

How can we keep foam from entering the deep venous system? Many maneuvers have been described from elevating the leg, to keeping the patient motionless in Trendelenberg with pressure on the SFJ. It has been shown, however, foam will go wherever it wants and it is futile to try and keep foam from reaching the central venous circulation, even when small volumes (3 ml) are injected.\textsuperscript{17} It is important to note, in the presence of a right-to-left shunt, it can proceed into the arterial circulation.

Even though we know that sclerosant foam is very safe, we should always strive to decrease any known risk when using it. Using room air to produce foam has been shown to have the highest incidence of side effects. When room air was substituted with a physiologic gas, such as CO\textsubscript{2} or a combination of physiologic gases, such as CO\textsubscript{2}-O\textsubscript{2}, the incidences of side-effects were much lower. Morrison\textsuperscript{18} has shown that when using the gas mixture of 70\% CO\textsubscript{2} and 30\% O\textsubscript{2} patients were 40 times less likely to experience the side effects of dry cough, metallic taste, and chest tightness. Additionally, patients were 7 times less likely to experience the side effects of nausea, visual disturbances, and dizziness, as compared to patients treated with air-based foam.

In the US, I do not know of any 70/30 pre-mixtures of medical grade CO\textsubscript{2}/O\textsubscript{2} commercially available in tanks, and such a mixture would require separate tanks of each of the gases, with a measuring system for creating the mixture within your office. Most medical gas supply companies can make up the tank, but sometimes they are reluctant to do so if you tell them it is for injection directly into humans. It has also been found that the two gases do not maintain
the mixed state when housed together in tanks for periods of time. The gases separate resulting in uneven, unreliable mixtures of the gas; or all of one gas and none of another. There is also some question as to the sanitary nature of the re-fillable tanks, and some have been found to carry a number of fungi and molds which would compromise the safety of the sclerotherapy procedure. There is, however, a new medical device called the CO₂MMANDER™ which was designed to deliver medical grade CO₂ gas, or a mixture of CO₂/O₂ from cartridges, in a safe and portable fashion. (Figure 1) The device is registered with the FDA and has a Declaration of Conformity for the European market. It uses USP and CE certified medical-grade cartridges, which are disposable. Containing a 77/23 mixture of CO₂/O₂, the mixed gas cartridges provide what seems to be an optimum mixture for nitrogen-free foam, with greater foam stability. Additionally, the disposable cartridges keep the gas in the proper mixed state when using the CO₂/O₂ gas mixture. The entire system can fit in a drawer.

Stability of Sclerosant Foam with other Gases

We know that foam created with CO₂/O₂ produces fewer side effects and complications than air-based foam. Foam made with CO₂/O₂, however, tends to deteriorate more quickly in the syringe prior to injection, thus making it more difficult to work with and creating a barrier to its widespread acceptance. This is even more so with CO₂ based foam.

The most commonly used system to produce foam today is the double-syringe system (DSS) technique whereby two syringes are connected by a two-way connector or with a three-way stopcock. With the sclerosing solution in one syringe, and air/gas in the another syringe, the sclerosant is drawn back and forth with pump-like movements through the connector/stopcock. The narrower the passage between the two syringes, the greater the turbulence and the smaller the bubbles’ size. Foam with smaller bubbles has a greater half-life than foam with larger bubbles.³

A 5-micron filter is traditionally used as a safety precaution in filtering any glass fragments from medication ampules, or any crystalline particles from various medical solutions. When a 5-micron filter is used with the DSS technique, the stability of the foam produced will almost double. This was shown by Shirazi ¹⁹ using room air, and Hill ²⁰ using CO₂. The filter can be used with a two-way connector (Figure 2), or a three-way stopcock (Figure 3). This greater stability will make it much easier to work with CO₂, or CO₂/O₂ based foam and optimize your results with foam ECA.

Conclusions
Sclerosant foams have better clinical outcomes than their liquid counterparts. Although safe and effective in providing good results at low cost and with few major complications, foam sclerotherapy does have risks. The gas mixtures used in foam production definitely influence the rate of post treatment side effects.

References


20. Hill D. Effect of a 5 micron filter on CO₂ sclerosant foam stability. XVI World Congress of the UIP. Monaco, 31 August - 4 September 2009
Figure 1. In addition to dispensing medical grade CO\textsubscript{2}, the CO\textsubscript{2}MMANDER\textsuperscript{®} also accommodates a medical-grade CO\textsubscript{2}/O\textsubscript{2} cartridge.

Figure 2. Double-syringe system with a two-way connector and 5-micron filter.
Figure 3. Double-syringe system with a three-way stopcock and 5-micron filter.