Ultrasound-Guided Foam Sclerotherapy

With more studies on the horizon, foam therapy is finding its role in treating venous medical conditions.

BY JOSE I. ALMEIDA, MD, FACS, RVT

Ultrasound-guided foam sclerotherapy (UGFS) has significantly increased in popularity and acceptance in the international vascular community for treating venous disease. Foam is of value in treating saphenous trunks, varicosed tributaries, perforating veins, and venous malformations. The term *sclerotherapy* is problematic, however, in that it conjures up images of spider vein treatment—a purely cosmetic concern—when in fact, sclerotherapy has a role in treating the full gamut of venous disease.

Going forward, the term *chemical ablation* may be more appropriate nomenclature because it is difficult to change the cultural milieu of third-party payers—chemical ablation may better reflect the fact that a true medical condition is being addressed. In fact, UGFS is truly ready for prime time and deserves dedicated Current Procedural Terminology reimbursement codes reflecting the increased relative value units from traditional sclerotherapy.

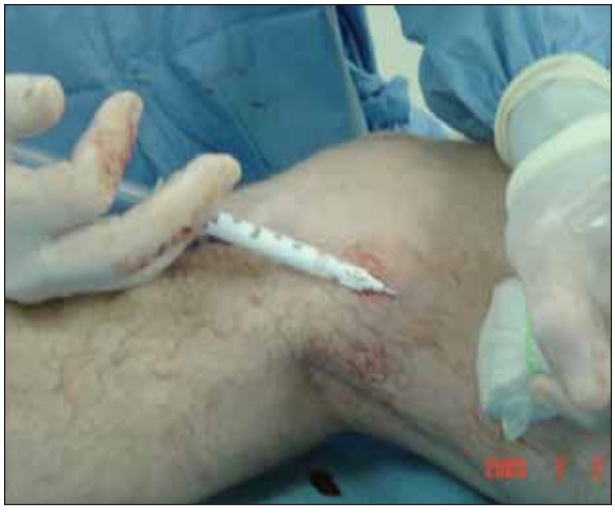

Figure 1. Ultrasound-guided foam sclerotherapy.

MECHANISM OF ACTION

Sclerotherapy refers to the introduction of a drug into the vein lumen for the specific purpose of producing endoluminal fibrosis and subsequent vein closure. Schneider and Fischer[1] showed that endothelial damage is concentration-dependent and occurs immediately after injection, with resulting rapid thrombus formation leading to vascular sclerosis. In 1944, Egmont James Orbach first proposed the use of foam by simply shaking a liquid sclerosant with air. However, interest faded because it could only be used for small veins, owing to large bubbles and a high air-liquid ratio.[2] The renaissance of foam sclerotherapy is credited largely to the work of Cabrera et al in the 1990s.[3]

Liquid sclerosants are diluted by blood, thus reducing the delivered concentration to the vein wall. Foam, on the other hand, displaces the blood and allows direct contact with the endothelium. It follows that the efficacy of a given concentration of a sclerosant can be enhanced with a foamed preparation. The air contained in the foam is echogenic and renders it visible during injection under ultrasound control (Figure 1).

Variables such as type and concentration of the sclerosing agent, gas, gas-liquid ratio, bubble size, and time between preparation and use determine the efficacy of the agent. The foam is composed of tiny bubbles of gas covered by a tensioactive liquid. Small bubbles make the foam highly interactive, whereas large bubbles produce ineffective foam. It is accepted that microfoam with bubble diameters < 250 µm are commonly used and are the ideal effective choice (macrofoams have bubbles > 500 µm, and minifoams have bubbles ranging from 250–500 µm). Foam is most commonly produced by the Tessari method,[4] with two disposable syringes and a three-way stopcock using a liquid-to-gas (air) ratio of 1:4.

EFFICACY

Cabrera et al[3] published a clinical series of 500 legs treated with foam sclerotherapy and reported that after 3 years, 81% of treated great saphenous trunks remained occluded, and 97% of superficial varices had disappeared. This required one session of sclerotherapy in 86% of patients, two sessions in 11%, and three sessions in 3% of patients. No deep vein thrombosis or pulmonary embolism were encountered in this series.

The relative efficacy of foam versus liquid sclerotherapy has been investigated in a detailed study.[5] Patients with truncal saphenous incompetence were injected with 3% polidocanol liquid or foam into the great saphenous vein (GSV) under ultrasound guidance on only one occasion. Obliteration of saphenous incompetence was obtained in 35% of liquid-treated patients and 85% of foam-treated patients after 3 weeks. At 2 years, 53% of foam-treated and 12% of liquid-treated patients had successful obliteration of the GSV.[6] This randomized controlled trial clearly showed the superiority of foam over its liquid counterpart.

A number of publications have discussed the outcome of foam sclerotherapy in patients with venous ulceration and severe venous disease. In one study,[7] 109 limbs with CEAP (clinical picture, etiology, anatomic distribution, and pathophysiology) classification C4 to C6 disease were compared to 76 limbs with CEAP C1 to C3 disease. In approximately 75% of patients in both groups, the saphenous trunk remained obliterated at 6 months. The investigators concluded that foam sclerotherapy was equally applicable in complicated and uncomplicated venous disease.

Two large meta-analyses have shown that endovenous laser ablation had the best results concerning the long-term effectiveness parameters for "saphenous vein occlusion at the end of follow-up" and "recanalization, recurrence, or development of new veins" compared to radiofrequency ablation and UGFS. Foam sclerotherapy of varicose veins is associated with a higher recurrence rate in patients with saphenofemoral incompetence compared to the rates after endovenous laser ablation or radiofrequency treatment.[8,9] However, in cases in which the pathology results from tortuous internal incompetent veins, neovascularity after previous procedures, and recurrent varicose veins in general, there is nothing better than UGFS for tackling these lesions.

SAFETY

It has been recommended that a 10-mL limit be placed with regard to total foam volume injected because of possible paradoxical embolization via patent foramen ovale.[10] Only three permanent adverse events from paradoxical embolization of foam have been published;[11,12] however, transient events are more common.

Transient visual disturbance occurs in approximately 2% of patients and is probably dose related. This may happen after both liquid and foam sclerotherapy but is more frequent after using foam. It often occurs in patients who have a previous history of migraine but may occur in anyone. Scotomata are probably the result of foam particles entering the optic vasculature. It is suggested that affected patients lie supine for up to 30 minutes after injection of foam to try and mitigate this complication.

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Some patients may develop tightness in the chest or coughing after foam injection. This is probably a direct effect of the foam on the lungs and can also occur after injections of liquid sclerosant. This resolves in about 30 minutes. Lying supine for 30 minutes after treatment may be useful then, as well. The incidence of visual disturbance and chest symptoms has been reported to be reduced by using CO_2 foams.[13]

ON THE HORIZON

CO_2 has been used as a contrast agent in radiology,[14] echocardiography, and angiography,[15-17] with good efficacy and safety since 1957. CO_2 is 50 times more diffusible than nitrogen through the capillary vein wall. The formula $TP = r^2\, d/2D\, Sf$ (in which TP is the time of persistence of the bubbles, r is the radius of the microbubble, d is the density of the gas inside the microbubble, D is the diffusibility of the gas through the microbubble membrane, and Sf is the saturation factor of the gas in the blood)[18] summarizes the most important gas-related factors that may interfere with the time of persistence of foam bubbles. The use of CO_2 alone leads to a less-robust foam, which can be overcome by the mix of this gas with another physiologically acceptable gas (such as oxygen) that has a lower diffusibility. This gas mixture, in variable percentages, can also reduce microbubble size when compared with air-based foam microbubbles, both under experimental conditions[4] and in the blood stream.[19]

A proprietary polidocanol endovenous microfoam product with a unique controlled density and consis-

> ". . . a safe, FDA-approved foamed sclerosant will be a welcome addition to the vein surgeon's armamentarium."

tent bubble size is under development. A European phase III clinical trial showed that 90% of patients treated with polidocanol endovenous microfoam had no reflux in the GSV at 3 months and 90% closure at 1 year. A phase II safety study in the United States has been completed, and the US Food and Drug Administration (FDA) has reviewed the study data and confirmed that screening patients for right-to-left cardiac shunts is no longer required because the presence of circulatory bubbles did not result in any cerebral insult by diffusion-weighted magnetic resonance imaging. Preparatory phase III studies focusing on patient-reported outcomes and photographic endpoints are underway in the United States, and approval is expected in 2013.

CONCLUSION

UGFS is quite different from sclerotherapy of spider telangiectasias and requires significantly more work by the treating physician. It is reserved for CEAP C2 to C6 venous disease, which represents true medical conditions. UGFS requires a thorough preoperative duplex-ultrasound-guided workup of venous incompetence with complete mapping of truncal reflux and all escape and re-entry points. In addition, the procedure must be performed with real-time duplex ultrasound control to accurately identify the targets, control the foam volume, and ensure clearance of foam from the deep system before terminating the procedure. This treatment should be reimbursed by third-party payers based on its own dedicated Current Procedural Terminology code. UGFS is the only viable method for treating tortuous internal leg veins, and a safe, FDA-approved foamed sclerosant will be a welcome addition to the vein surgeon's armamentarium. ■

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