LETTERS TO THE EDITOR

Regarding "Stroke after varicose vein foam injection sclerotherapy"

We and many others have read with considerable interest the well-documented report from the St. James Hospital, Dublin group Forlee et al (J Vasc Surg 2006;43:162-4) regarding the patient with hemiparesis after duplex-guided foam sclerotherapy.

There appeared to be nothing in this case, either prior to injection or in retrospect, which might have raised a warning flag. Thousands of patients are treated daily in a similar fashion in phlebology practices worldwide. To our knowledge, there have been no other published reports of cerebrovascular sequelae in the entire history of foam sclerotherapy.[1,2] Therefore, criticism which the article may raise concerning foam sclerotherapy, a method that has shown powerful advantages of efficiency, economy, and utility, should be balanced by a careful review of its positive and negative aspects that have been highlighted in a series of publications in the last few years.[3-10]

Because most authors suggest limiting the volume of foam injected during sclerotherapy, we report here that Morrison et al prospectively studied 49 consecutive patients undergoing duplex-guided foam sclerotherapy. This was reported at the International Union of Phlebology American Chapter meeting in 2003 in San Diego. They used 1% polidocanol obtained from a licensed compounding pharmacy and created foam by the Tessari method in a 4:1 air-to-liquid ratio.[11] To achieve mathematical comparability, the patients were divided into three groups by the volume of foam injected: low volume, 6 to 21 mL; medium volume, 22 to 30 mL; and high volume, 31 to 46 mL. Vital signs and pO_2 were monitored during and for 60 minutes after the procedures.

All patients were followed by telephone interview at 2, 6, and 24 hours after injection, and any adverse events were recorded. No significant changes in vital signs or pO_2 were seen. Adverse events included dry cough (14%), chest discomfort (14%), nausea (4%), dizziness (10%), and visual disturbances (4%). Of these, only dry cough was statistically related to increased volumes of foam. All symptoms cleared within 24 hours. Having subsequently replaced room air with carbon dioxide in the production of foam, adverse events are now only rarely seen.

Because of concern raised by the Food and Drug Administration in the United States regarding embolization after foam sclerotherapy, Morrison et al subsequently studied 21 patients with symptoms of visual disturbances or migraine-like headache after foam sclerotherapy with simultaneous transthoracic echocardiography and foam sclerotherapy. All patients had duplex-guided injections of 1 to 3 mL of 1% foamed polidocanol into peripheral leg veins. Foam particles could be identified in the right heart in all patients within 10 to 30 seconds.

Only cough or Valsalva maneuver in seven of the 21 patients uncovered a PFO. The incidence of PFO is acknowledged to be 20% to 30%.[12] These seven patients with PFO were studied with transcranial Doppler during foam sclerotherapy. A few high-intensity transient signals were identified in the middle cerebral artery in 4 of the 7 patients.

With the collaboration of JJ Guex, FX Breu, P Thibault, and others including Benigni JP, Cabrera A, Caggiati A, Coleridge-Smith P, Creton D, Frullini A, Goldman M, Guggenbichler S, Hamel-Desnos C, Hill D, Parsi K, Rabe E, Ricci S, Schadeck M, Tessari L, Thibault P and Zamboni P who either have contributed heavily to the science of foam sclerotherapy or raised interesting and important comments during an e-mail chat on this subject.

Since the vast majority of patients with PFO have much smaller defects than the 18-mm defect noted in the subject report, we believe it is totally impractical to screen all patients for PFO before foam sclerotherapy.

On transthoracic echocardiographic examination of patients undergoing endovenous laser and radiofrequency ablation of the saphenous vein, many bubbles within the right heart have been detected during laser ablation and a few bubbles during radiofrequency ablation. Apparently, right heart bubbles are not exclusively limited to foam sclerotherapy (Morrison, unpublished data).

A few remarks concerning the article:

1. There is a lack of detail on foam formation, which directly influences the size of the bubbles.
2. Related peri-injection procedures such as elevation of the limb and prolonged immobility are not detailed.
3. The authors correctly point out, but do not emphasize, that the amount of foam used was excessive compared with published reports.

In view of the prolonged reversible ischemic neurological deficit reported by our Irish colleagues, it should be remembered that the biologic test of thousands of foam treatments daily for more than 15 years have proven the safety of foam sclerotherapy.

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doi:10.1016/j.jvs.2006.02.062

Regarding "Stroke after varicose vein foam injection sclerotherapy"

We read with great interest Forlee et al's report of a patient who experienced an ischemic stroke moments after undergoing foam injection sclerotherapy for treatment of varicose veins.[1] The patient was later determined to have a patent foramen ovale. We commend the authors for having the presence of mind to perform a carotid duplex scan immediately to reveal what no doubt were intracarotid bubbles resulting from the foam injection. We note that the patient received a total of 20 mL of polidocanol foam prepared by the double syringe method using room air.

We previously demonstrated, using an in vivo model of arteriolar embolization after polidocanol microfoam sclerosant administration, that two prominent—and potentially controllable—features of foam manufacture contribute to the number and size of bubbles present as well as the resultant duration of blood flow obstruction that is caused by the intravascular gas load.[2] We found that foam made with room air, rather than a gas admixture comprised of carbon dioxide and oxygen, was directly associated with increased bubble number and size and caused the longest obstruction of blood flow. We attribute this to the difference in nitrogen gas content, as nitrogen is far less soluble and diffusible in tissues than are metabolic gases. We also found that bubbles made by the double syringe technique were larger than those created using mechanisms specifically engineered to dispense microfoams having a highly controlled bubble size distribution.

We are relieved that the patient recovered significantly, but we are not surprised by this report of a patient with a patent foramen ovale experiencing a stroke after foam injection sclerotherapy. Although we do not think that more careful attention to patient cardiac anatomy through echocardiographic screening is an effective means of improving patient safety for this treatment, we do believe that our previous findings regarding gas content and foam formation and this case report illustrate the need to change clinical practice regarding what is injected, and not into whom, to assure procedural safety.

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doi:10.1016/j.jvs.2006.02.061

Reply

We would like to thank Dr Morrison and Dr Eckmann and their colleagues for the interest they have shown and the important points they raise in response to our recent case report.[1]

The great saphenous vein was cannulated first in order to minimize the delay between foam production and injection. Foam was produced using the Tessari method, with a 4:1 air-to-liquid ratio. Half the volume of foam was injected with the leg on the level, while compressing the saphenofemoral junction. The leg was then elevated and the rest of the foam was injected and massaged into the targeted veins using ultrasound guidance. Compression stockings were applied with the leg elevated.

With regard to the volume of foam used, we note that in Dr Morrison's study using different volumes of foam, our patient would have been classified in the "low volume" group. Juan Cabrera, the creator of the patented polidocanol foam, writes that volumes of 20 mL to 100 mL of foam can be safely used.[2] There is, however, a lack of consensus regarding the optimal volume, and the European Consensus statement recommends limiting volumes to 8 mL per treatment using the Tessari method.[3]

Given the high prevalence of a patent foramen ovale in the general population, it is surprising that more events have not been reported. This would imply that most are small and hemodynamically insignificant. We agree that screening before foam injection would be impractical and probably unnecessary.

Carbon dioxide is absorbed faster than air in the body and has been shown to produce a foam that degrades quicker.[4] The transient visual symptoms reported in the literature[5] are possibly due to small amounts of air embolism. An argument could thus be made for carbon dioxide to be used as the carrier gas.

We agree with Drs Eckmann and Kobayashi that the quality of foam produced is very important, not only with regard to safety but also efficacy of the procedure. For maximum stability, the size of the bubbles in the microfoam should ideally be $<100\mu$m, spherical, and of uniform size.[6] With lack of uniformity in the size of the bubbles, La Place's Law ($t = p/r$) dictates that the smaller bubbles will empty into the bigger bubbles, resulting in larger bubbles with an increased potential for the air-block effect. Although the Tessari and other methods have been shown to be effective in producing a foam that meets these criteria, it is difficult to accurately regulate or measure bubble size and quality of foam in the clinical setting. This may be a strong argument for the use of the standardized, commercially produced microfoam preparation when treating varicose veins.

Foam sclerotherapy has been shown to be safe and efficacious. Our report describes a rare, but potentially life threatening complication of this treatment.

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