

Original Article

Treatment of Varicose Long Saphenous Veins with Sclerosant in Microfoam Form: Long-Term Outcomes*

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ABSTRACT

Objective: To determine whether the injection of sclerosant in microfoam form offers a clear alternative to surgery in large varices of the lower extremities.

Design: Retrospective observational follow-up study (3–6 years).

Patients: Five hundred lower limbs in which pre-treatment duplex ultrasound demonstrated insufficiency of sapheno-femoral junctions (diameters 9–32 mm) and long saphenous veins.

Main outcome measure: Obliteration and subsequent disappearance of treated veins.

Results: After ≥ 3 years follow-up, 81% of treated varicose long saphenous veins were obliterated and 96.5% of superficial branches disappeared. The obliteration of saphenous veins required one injection in 86%, two in 10.5% and three in 3.5% of cases. There were no serious complications such as deep vein thrombosis pulmonary embolism.

Conclusion: The quality and stability of outcomes and ease of repeat treatments when required may make sclerotherapy with microfoam a therapeutic approach of choice for the functional and anatomical elimination of extensive pathological venous areas.

Keywords: Echosclerotherapy; Microfoam; Long saphenous vein

*Note: The microfoam presented in the study was originally patented in 1993 by the authors and is currently being developed by a major technology development company.

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Introduction

In response to the demand for efficacious, minimally aggressive and inexpensive treatments, surgery on leg varices has reduced the size of incisions and has incorporated endoscopy into the treatment of incompetent perforating veins [1,2]. Although sclerotherapy is a technically simple treatment with great therapeutic potential, it is currently only of utility in small or moderate-sized varicose veins [3,4]. The recent use of ultrasonography has given eyes to a traditionally blind technique and represents an important advance [5]. Nevertheless, surgery is still generally regarded as the only approach for incompetent saphenous veins of larger size.

Sclerotherapy is not efficacious in large (>9 mm diameter) veins [4], perhaps because the basic requirements of sclerotherapy are not met when liquids are used. These requirements include knowledge of the intravascular concentration of the sclerosing agent, its homogeneous, extensive and manageable intravenous distribution and controlled duration of contact with the endothelium. In short, the key to successful sclerotherapy lies in control over the action of the sclerosing agent. This is what we have attempted to achieve in our experience of over 6 years using sclerosing agents in microfoam form [6,7]. The present paper briefly describes a novel and efficacious echosclerotherapy technique with microfoam. We report on the long-term outcomes of its application in the treatment of large varicose long saphenous veins.

Materials and Methods

Between July 1993 and July 1996 we treated 500 varicose long saphenous veins with incompetent

sapheno-femoral junctions of diameter ≥ 9 mm (range 9–32 mm) diagnosed by physical examination and echo Doppler explorations. All patients were treated with echo-guided injections of 1–3% Lauromacrogol 400 made into microfoam. Colour photographs of the affected legs were taken before and after treatment. The efficacy of the treatment was confirmed by physical examination and ultrasound imaging at the first treatment session, and then at follow-up sessions after 7 days, 1 month, 3 months, 6 months, and annually. Notes were taken of any adverse effects reported by patients. Documented outcomes were available for all patients in the present study group.

Treatment with sclerosant microfoam was offered to all patients attending the clinic and was not given in a randomised clinical trial. Patients reported in this paper were not subjected to any additional treatment or investigations other than those used as part of our standard treatment regime. The microfoam was prepared from approved ingredients by two registered pharmacists who have contributed to this paper.

Sclerosing Microfoam

Our microfoam is a new form for conventional sclerosing agents that uses physiological gases that are readily metabolised in order to achieve an enormous increase in the active surface area of the sclerosing agent compared with the injection of the agent in liquid form. The active ingredient of the microfoam used on the patients in this study was Lauromacrogol 400, an approved and widely accepted sclerosant. The vehicle was carbon dioxide, a physiological gas of proven safety [8,9]. The large active surface area, which augments in inverse proportion to the size of the bubbles [10,11], combined with the high solubility of the gas, facilitates its metabolism [12,13]. The small dose of microfoam required to inject the largest varicose veins and the low flow rate of its administration are additional safety elements.

A standardised product is currently being developed by Provensis Laboratory (London, UK) in order to make available a consistent, safe, fully authenticated product with pharmacological guarantees. This is important, since the microfoam is injected into the blood stream, with the associated potential dangers.

Instrumental Investigations

As well as a clinical angiological examination, all patients underwent either continuous Doppler investigation with a 9.6 MHz probe plus ultrasonographic study with a 7.5 MHz linear probe (Piomedical ultrasonography apparatus) or colour echo Doppler investigation (Esaote Au-5) with a 10 MHz probe.

We used Doppler with the patient standing to determine reflux at the sapheno-femoral junction and in the saphenous vein in the lower third of the thigh, the

leg and ankle, recording the duration as + (1–2 s), ++ (2–6 s) or +++ (>6 s). We also determined the competence of the ostial valve by the Valsalva procedure.

Ultrasonography was used to measure the diameter of the sapheno-femoral junction and the first portion of the long saphenous vein, and to reveal its morphology and the existence of perforating veins and other branches. Ultrasonography is of particular utility in obese patients, offers a complete picture of the future field of action, and complements the functional data from the Doppler exploration.

Ultrasonography is indispensable to our sclerotherapy procedure. It is used to guide the injection and to indicate the maximum reduction by phlebospasm of the saphenous vein after the injection. It reveals the progression of the microfoam in the proximal and distal filling phases, the level of occupation, the emptying into the common femoral and the filling of perforating veins, etc.

Post-sclerosis ultrasonography shows the endoluminal echogenicity, thickening of the venous wall and the non-compressibility of the vessel. It provides assessment of

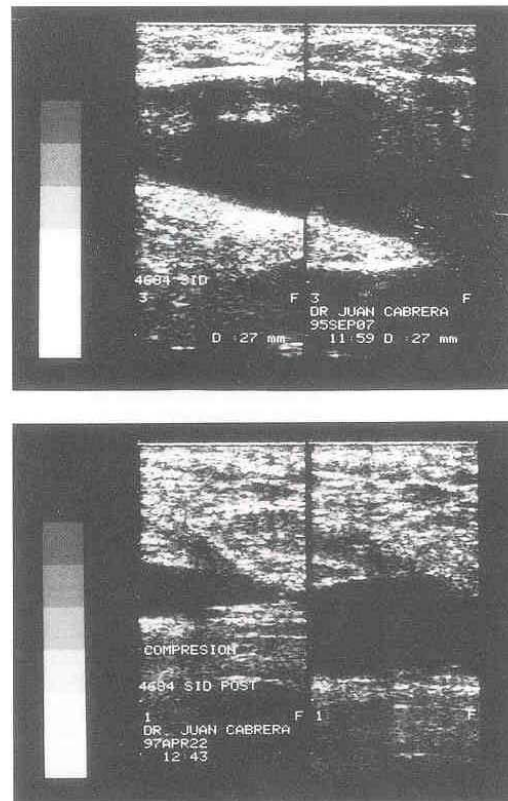


Fig. 1. Ultrasonographic images showing the evolution to fibrosis (from top to bottom).

the evolution to fibrosis at successive follow-up sessions (Fig. 1). Colour echo Doppler is of special value for the early detection of any post-treatment recanalisation.

Procedure

Patients are treated with an injection of 1–3% Lauromacrogol 400 microfoam while in the supine position. The microfoam form produces an enormous increase in volume for the same dose compared with the liquid form. The injection of 15–30 cm³ of microfoam uses a 20G catheter (Abbot) that is sited with ultrasonographic guidance in the long saphenous vein of the middle or lower third of the thigh. From a single injection site the microfoam occupies the saphenous vein from the sapheno-femoral junction and the incompetent leg branches. Apart from the above-mentioned information from ultrasonography, aspiration of the injected microfoam instantly revealed the degree of intravascular occupation (white = complete, pink = partial, red = no occupation).

An extensive and potent vasospasm follows the injection of the microfoam. The varicose vein disappears from view. The patient is able to move about immediately after the injection. The spasm resists the patient standing up and walking, which is an excellent early sign of the efficacy of the therapy. A compressive bandage with stocking is immediately applied and maintained in place until the next revision.

Results

Outcomes of the treatment with microfoam on 500 incompetent long saphenous veins after ≥ 3 years are listed in Tables 1 and 2. The diameter of the sapheno-femoral junctions in the sample ranged between 9 and 32 mm.

This novel technique achieved the obliteration of 81% of the long saphenous veins and 96.5% of superficial branches. Only one injection was required in 86% of the saphenous veins, with 10.5% requiring a second injection and 3.5% a third. Subsequent injections at

Table 1. Results of sclerotherapy with microfoam on 500 saphenous veins

Fibrosed saphenous veins	81%
Permeable saphenous veins with reflux	14%
Permeable saphenous veins without reflux	5%
Disappearance of all superficial branches	96.5%

Table 2. Saphenous veins re-injected of the 500 treated using microfoam

Re-injected once	10.5%
Re-injected twice	3.5%

follow-up sessions were needed for the superficial branches. These outcomes remained stable after ≥ 3 years (Figs. 2, 3).

No patient reported any serious complications such as deep venous thrombosis or pulmonary embolism. Minor complications were very uncommon and consisted of localised segmented inflammatory reactions, which were treated when appropriate with anti-inflammatories.

Discussion

We present the long-term outcomes of the employment of a novel sclerosing microfoam on varicose saphenous veins of a size traditionally indicated for surgery. We demonstrate a very high success rate, with a complete absence of serious adverse effects.

Our echosclerosis protocol is not valid for liquid sclerosants. A given dose of liquid sclerosing agent cannot provide a similar sclerosing action in all cases, since its intravenous concentration varies according to the haemodynamic conditions of the injected vessel and is always unknown. Moreover, contact with the substance is lost after its injection and little can be done to direct it or modify its action. Success in conventional sclerotherapy depends more on the volume and blood flow of the vessel than on the technique applied.

The inability to control liquid agents can sometimes cause undesirable effects on the deep venous systems. When using an adequate dose of liquids around the sapheno-femoral junction or at a leg perforating vein, little can be done to prevent them exerting their action 'a little beyond'. In contrast, the small quantity of sclerosing agent in the minute amounts of microfoam that very progressively enter the high blood flow of the deep venous system would exert no action on its endothelium. This would account for the absence of complications among our microfoam-treated patients.

Liquid sclerosants have some major drawbacks:

- *Progressive dilution in the blood*; as famously expressed by Tournay, 'The important thing is not the concentration of the sclerosant in the syringe but rather its concentration in the vein'.
- *Increasing inactivation* the greater the distance from the injection site, through the fixation of the sclerosant on the lipids of the enormous surface area of the erythrocyte membrane [14].
- *Irregular distribution on the venous endothelium* due to the different density of the liquid sclerosant from that of the blood [15].
- *Absence of control over the duration of sclerosant-endothelium contact*, a critical treatment parameter, especially in large vessels.
- *Inadequate volumes at therapeutic dosage*, which make the intravascular dilution and inactivation effects even more patent.

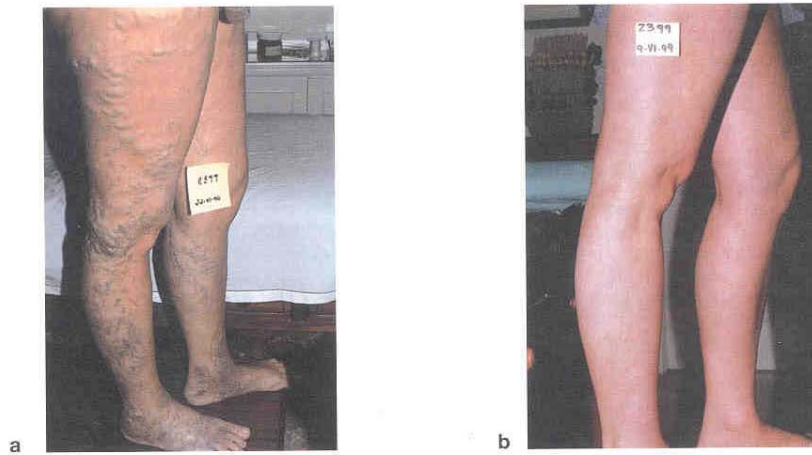


Fig. 2. a Before: extensive varicosity of long saphenous vein branches in both legs. b After: outcome 5 years after sclerotherapy.

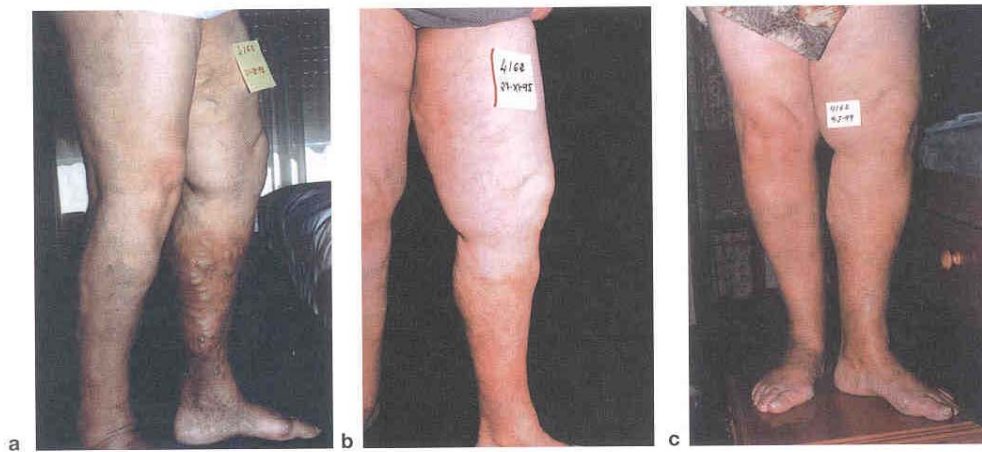


Fig. 3. a Before; advanced skin lesions on the left leg due to varicose long saphenous vein and incompetent perforating veins. b After (short-term outcome): striking improvement 8 months after sclerotherapy. c After (long-term outcome): the improvement is maintained 4 years later.

- *Cannot be manipulated, perceived on Doppler or seen on ultrasonography after injection*, increasing the risk of undesirable sclerosing action.

Our experience has shown that our new pharmaceutical form offers numerous advantages for meeting the requirements of sclerotherapy. The principal benefits of microfoam are:

- *A mechanical action*, displacing the blood at an increasing rate as the diameter of the injected veins is reduced by vasospasm. This ensures: absence of dilution and inactivation of the sclerosing agent, knowledge of the intravascular concentration of the sclerosing agent, uniform and selective endovascular action and control over the duration of sclerosant-endothelium contact.
- *Greater sclerosing ability than the liquid form*. The enormous increase in active surface area achieved by placing the sclerosing agent on microbubbles gives the microfoam a greater sclerosing ability.
- *Manageability or remote control*, since the microfoam has a high degree of internal cohesion that allows it to

be aspirated and reinjected after its initial injection. Information on the level of intravascular occupation by the microfoam and on its dilution is provided by the colour of the aspirated foam visible in the catheter. The 'piston' formed by the microfoam can be directed by the physician. This feature also provides control over the emptying of the microfoam into the deep venous system, which can be done very gradually and in amounts too small to have deleterious effects.

- *Greater volume* at the same dose than the liquid form, which permits a larger segment of vein to be filled and treated.
- *Selectivity of action* due to the complete occupation of the vein, so that the sclerosant only makes contact with the endothelium.
- *Greater fluidity*, which is of particular value in the sclerosis of small vessels using fine needles.
- *Stability of the microbubbles* for the time necessary for the injection and action of the sclerosant on the endothelium.
- *Rapid elimination of the gas*, which is soluble, diffusible and micronised, facilitating the quick elimination of the small total volume injected.
- *Perceptibility on Doppler*, provided by the echogenicity of the microbubbles.
- *Visibility on ultrasound*, permitting knowledge in real time of the level of occupation and allowing the intravascular trajectory of the substance to be tracked.
- *Greater safety*, since the small quantity of sclerosant can be very gradually drained into the high flow deep venous system. Furthermore, our technique of injecting via a 20G catheter placed with ultrasonographic guidance in the long saphenous vein of the middle or lower third of the thigh makes inadvertent intra-arterial injection extremely unlikely.

Conclusions

Through our use of sclerosants in microfoam during the past 6 years we have amplified the indications of sclerotherapy to include large varicose veins traditionally treated surgically, as well as inoperable venous malformations. The quality and stability of our outcomes

using this specific type of microfoam, with its particular and precise chemical and physical characteristics, suggest that sclerotherapy with this microfoam may become a therapeutic approach of choice for the functional and anatomical elimination of an extensive pathological venous area.

References

1. Conrad P. Endoscopic exploration of the subfascial space of the lower leg with perforator vein interruption using laparoscopic equipment: a preliminary report. *Phlebologie* 1994;9:154.
2. Gloviczki P, Cambris RA, Rhee RY, Canton LG, McKusick MA. Surgical technique and preliminary results of endoscopic subfascial division of perforating veins. *J Vasc Surg* 1996;23:517-23.
3. Covo L. Sclérothérapie et maladie variqueuse. A quel stade. *Phlebologie* 1991;1:221-5.
4. Vin FP. Principes de la sclérothérapie des axes saphéniens des membres inférieurs et de leur collatérales à l'exception des veinules et télangiectasies. *Phlebologie* 1994;4:399-406.
5. Knight RM, Vin F, Zygmunt JA. Ultrasonic guidance of injections into the superficial venous system. In: Davy A, Stemmer R, editors. 10^e congrès mondial. UIP. *Phlebologie*. London: John Libbey, 1989.
6. Cabrera J, Cabrera J Jr. Nuevo método de esclerosis en las varices tronculares. *Patol Vasc* 1995;4:55-73.
7. Cabrera J, Cabrera J Jr. Elargissement des limites de la sclérothérapie: nouveaux produits sclérosants. *Phlebologie* 1997;2:181-8.
8. Paul RE, Durant TM, Oppenheimer MJ, Stauffer HM. Intravenous carbon dioxide for intracardiac gas contrast in the roentgen diagnosis of pericardial effusion and thickening. *AJR* 1957;78:224-5.
9. Meltzer RS, Serruys PW, Hugenholz PG, Roelandt J. Intravenous carbon dioxide as an echocardiographic contrast agent. *J Clin Ultrasound* 1981;9:127-31.
10. Bikerman JJ. *Foams*. Berlin Heidelberg New York: Springer, 1973.
11. Sebba F. *Foams and biliquid foams-aprons*. Chichester: Wiley, 1987.
12. Femand M, Marzelle J, Cormier F, Cormier JM. Aorto-artériographie des membres inférieurs au gas carbonique. *Presse Med* 1994;1:19-22.
13. Kerns SR, Hawkins IF Jr. Carbon dioxide digital subtraction angiography: expanding applications and technical evolution. *AJR* 1995;164:735-41.
14. Goldman MP. *Sclerotherapy treatment of varicose and telangiectatic leg veins*. St Louis: Mosby Year Book, 1992.
15. Bilancini S, Lucchi M, Tucci S. Protocolos trombovar et trombovar-iodé. *Phlebologie* 1992; :191-96.

Received for publication 29 September 1999
Accepted in revised form 16 May 2000