Foam Sclerotherapy of the Saphenous Veins: Randomised Controlled Trial with or without Compression

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Abstract  Objectives: This study aims to compare the efficacy and side effects of foam sclerotherapy of the saphenous veins with or without post-treatment compression using graduated elastic stockings.
Design: This is a prospective open randomised controlled trial conducted in two centres.
Patients and methods: Sixty patients with incompetent great (GSV) or small saphenous veins (SSV) underwent ultrasound-guided foam sclerotherapy. Randomisation was conducted immediately after sclerotherapy to two parallel groups, one (CG) with compression stockings (15–20 mmHg worn during the day, for 3 weeks) and the other (WCG) without compression. Efficacy of sclerotherapy and all of the side effects were assessed, including side effects in the treated region.
On days 14 and 28, clinical and duplex ultrasound (DUS) assessments were performed by independent experts. Patients also completed quality of life (QOL), symptom questionnaires and provided satisfaction scores.
Results: Five men and 55 women ranging in age from 32 to 78 (mean 57 years) years were included: 29 in the WCG and 31 in the CG group. On day 28, abolition of venous reflux and occlusion of the vein was obtained in 100% of the cases in both groups. The length of the occluded vein was the same in both groups (mean 36 cm for the GSV and 30 cm for the SSV) as was the mean diameter of the occluded vein (5 mm). Symptoms and QOL questionnaires showed equivalent improvement in both groups on day 28 compared to pre-treatment assessments. Side effects were few with no statistical difference between the two groups. Patient satisfaction scores were high in both groups for the outcome of sclerotherapy results, and good or very good for compression in 50% of the CG cases.
Conclusion: We found no difference between compression and control groups when comparing efficacy, side effects, satisfaction scores, symptoms and QOL. Further studies are required to establish the role of compression in sclerotherapy and to evaluate other compression strategies.

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Introduction

Compression after sclerotherapy for saphenous truncal incompetence is recommended by experts, but there is little good-quality scientific evidence to support this.¹ The use of compression may improve the results of sclerotherapy by reducing side effects, such as deep vein thrombosis, thrombophlebitis, inflammation, pain, pigmentation and matting. It may also reduce the amount of endoluminal thrombus leading to more rapid occlusion of a treated vein and increasing the efficacy of treatment.² No randomised clinical trial has been published comparing the outcome of the treatment of saphenous varices with and without compression.

The aim of this study was to assess the effect of graduated elastic compression stockings on the outcome of foam sclerotherapy for varices arising from the great and small saphenous trunks in a randomised controlled trial.

Patients and Methods

The study design was a randomised, open, prospective, two-centre study with two parallel arms: one group without compression (WCG) and one group with compression (CG) using stockings (Class 2 French standard 15–20 mmHg), worn during the day for 3 weeks following treatment. Patients considered for inclusion in this study were those presenting for treatment of symptomatic varicose veins. One of the investigation centres was a university hospital (Brest, France), the other was private clinic (Caen, France). In total, 60 patients were included, of both sexes and varying ethnicity, with a minimum age of 18 years, and who suffered from incompetence of the great (GSV) or small (SSV) saphenous vein.

Patients were examined by physicians skilled in the management of venous disease. A history was taken and clinical examination performed allowing assessment of the distribution of varices as well as assignment of the correct clinical, etiologic, anatomic, and pathophysiologic data (CEAP) clinical class. DUS was undertaken with the patient in the standing position to assess the competence of deep and superficial veins and establish the extent of saphenous incompetence. Patients were considered suitable for treatment by foam sclerotherapy when the trunk diameter was a maximum of 8 mm for the GSV and 6 mm for the SSV with venous reflux lasting at least 1 s. CEAP classes, which were included in this study, were C2s–C6, Ep, As2, 4, and Pr with level II examination.³ The exclusion criteria are listed in Table 1.

The objectives were to compare the efficacy and side effects of foam sclerotherapy of the saphenous veins with or without compression stockings. The main outcome measure was ultrasound-assessed obliteration of venous reflux in the treated saphenous trunk 28 days after treatment. Secondary outcome measures included assessment of adverse events such as pain, thrombophlebitis, pigmentation and telangiectatic matting.

Table 1 Exclusion criteria.

- Patient with a history of mental or psychiatric disorder or any factor limiting the ability to participate in an informed manner and compliant with the study.
- Voluntary Consent Form unsigned.
- Patients with isolated sapheno-femoral junction incompetence without saphenous trunk incompetence of the thigh.
- Patients with post-surgical recurrence of varices in the region of the great saphenous vein or small saphenous vein without trunk recurrence in the thigh or calf.
- Patients with chronic liver disease.
- Renal failure (creatinine > 150 μmol/l).
- Pregnant or nursing women.
- Women with a risk of pregnancy during treatment (absence of contraception).
- Physical or geographical impossibility of participation in the study.
- Patients with known progressive malignant disease.
- Patient with uncontrolled hypertension.
- Patient suffering from respiratory or cardiac failure.
- Patient with a history of deep vein thrombosis.
- Patients with known inherited or acquired coagulopathy.
- Patient with alcohol intolerance or having taken a blocking degradation of ethanol (Espéral for example) in the previous month.
- Patient with known allergy to LAUROMACROGOL 400.
- Patients with known patent foramen ovale (PFO).
- Patient presenting in the past with migraine or visual or other neurological disorders after sclerosing foam injection.
- Lycra allergy.
- Inability to apply elastic compression (e.g. osteoarthritis).
The study was approved by the French Ethical Research Committee (Nord Ouest III CPP e.g., Comité de Protection des Personnes, registered on 2 December 2006 under No. N°2006–22). It complies with the Declaration of Helsinki (1964) according to its latest version (Hong Kong, 1989).

Patients who gave informed written consent for their inclusion in the study were investigated further. The sclerosant used was polidocanol (AETOXISCLEROL®, manufactured by Laboratoires Kreussler, Paris, France).

Sclerosant foam was obtained using a sterile disposable syringe kit including sterile air and the TURBOFOAM® machine (Kreussler Pharma, Wiesbaden, Germany). The sclerosant liquid and air mixture was $1 + 4$ (one volume of Aetoxisciérol® + four volumes of air). The characteristics of the foam obtained were standardised and these data have already been assessed and published.4

**Sclerotherapy**

A maximum of three sclerotherapy sessions were permitted to obtain saphenous vein occlusion. The sclerotherapy was guided by ultrasound and performed by direct puncture with needle, with the patient lying recumbent. The volume of foam allowed per session was between 2.5 ml and 8 ml for the GSV and between 2 ml and 5 ml for the SSV.5 The concentration allowed per session was between 2.5 ml and 8 ml for the GSV and 3.6 ml for the SSV (range $0.5-4$). The concentration could be 1–2%, depending on the diameter of the vein.6 No concomitant treatment was performed on other varices.

Randomisation was conducted after sclerotherapy using a randomisation list stratified by centre and type of saphenous vein (small or great) provided by the statistician.

For CG patients, there was an interval of 5–10 min after sclerotherapy before the investigator applied the compression stockings (patient still lying on the treatment couch), to avoid possible dislocation of the foam column.7 Compression hosiery was thigh length for GSV and knee length for SSV.

Follow-up examinations were performed during the 28-day period following treatment.

Patients were reviewed by both clinical and duplex ultrasound (DUS) examinations on days 7, 14 and 28. The aim of the day 7 examination was to investigate the possibility that deep vein thrombosis had arisen following treatment.

Visits and assessments on days 14 and 28 were performed by an independent expert who was not a member of the clinical team at either clinic. Patients on day 0 (inclusion day) and on day 28 completed a quality-of-life (QOL) self-questionnaire, CIVIQ 2 (Chronic Venous Insufficiency Questionnaire), consisting of 20 questions using four criteria: pain, physical, social and psychological effects.8 They also completed further questionnaires about their symptoms (heavy-leg sensation, pain, oedema, paraesthesia and cramps) on days 0, 14 and 28. On days 7, 14 and 28, the practitioner undertook a clinical examination and recorded symptoms arising following treatment. Patients themselves completed a questionnaire evaluating side effects in the region of sclerosis, such as pain, inflammation, ecchymosis, induration, pigmentation and matting. A score was assigned for each criterion, which were summed to produce a total score. On day 28, the investigator and the patients also separately completed a satisfaction score, but only the CG patients provided a satisfaction score for compression.

The criteria for efficacy of sclerotherapy were abolition of saphenous reflux, length of the occlusion and diameter of the occluded vein as assessed by B-mode ultrasound imaging.

Length of occlusion of saphenous vein was the main outcome measure in this study. The main criteria used to assess the severity of side effects were QOL and satisfaction scores and the total score of side effects in the treated region. The secondary criteria were the consumption of analgesics and/or anti-inflammatory drugs, tolerance and compliance with compression treatment and adverse events of sclerotherapy other than those previously described. A comparison was made between the scores obtained from the compression and non-compression groups.

**Statistical methods**

In the absence of prior data, the number of subjects was set at 30 per treatment group, making 60 subjects in total. The sample size of 30 subjects per group was chosen arbitrarily but appears to be sufficient for obtaining a satisfactory and sufficiently accurate assessment of the main parameters.

Statistical calculations were made using SAS software. The efficacy analysis focussed on the two study populations (ITT and PP, i.e., intention to treat and per protocol). With respect to the intra-group analysis (before/after treatment in a group) and inter-group analysis (with compression versus without compression) the paired Student’s $t$-test (or Wilcoxon paired test for non-normally distributed data) was performed on the quantitative variables. Descriptors used to report data are the mean and standard deviation.

Tolerance was assessed in all patients included in the trial and any side effects were reported with a descriptive method.

**Results**

Between January and June 2007, 60 patients (five men and 55 women) ranging in age from 32 to 78 years (median $= 57$ years) were included, 29 in group WCG and 31 in group CG. The groups were homogeneous, except with respect to age, where there was a statistically significant difference, with the CG group being older than the WCG: mean age being 53 SD 14 for WCG and 61 SD 11 for CG ($p = 0.0178$) (Table 2). The right limb was affected in 60% of patients. The GSV was involved in 60% of cases and the SSV in 40%. The average diameter of the veins treated was 5.8 mm for the GSV and 5.1 mm for the SSV.

There was no significant difference between the two groups (Table 2). The mean CEAP clinical class was 2.6 (range 2–6).

**Sclerotherapy**

DUS showed that 100% efficacy of treatment was achieved with abolition of reflux and occlusion of the vein at day 28 in both treatment groups. The protocol for the study permitted a total of three treatment sessions to achieve saphenous occlusion. In fact, only one treatment session was necessary to achieve the intended outcome and employed only moderate volumes of foam. On average 4 ml of foam was used for the GSV and 3.6 ml for the SSV (range 2.5–7.5 ml). In 90% of the patients the concentration used
was 1%; 2% was used in only six of the 60 cases (10%). The average occlusion length was 36 cm for the GSV (CG: 35 and WCG: 37) and 30 cm for the SSV (CG: 26 and WCG: 33). The time taken to complete treatment sessions in the CG and WCG groups was similar. The average diameter of the occluded veins was similar in both treatment groups at 14 and 28 days following treatment. The application of compression had no measurable effect on vein diameter following sclerotherapy (Table 2).

Assessments of QOL investigated four criteria: impact of pain, social impact, physical functioning and psychological dimensions. The overall score decreased compared with the pre-treatment baseline assessments and showed equal improvements in both groups (Table 3).

Assessment of symptoms reported by patients included evaluation of heavy-leg sensation, pain in legs, oedema of the lower limbs, paresthesia and cramp. Symptoms improved after treatment to an equal extent in both treatment groups (Table 3).

The patients reported their opinion of the outcome as satisfaction scores. After 14 days following sclerotherapy, all of the WCG patients found the treatment to be effective or very effective compared with 93% in the CG group (N.S.). After 28 days, 97% of WCG group found the treatment effective or very effective compared to 100% of the CG group (Table 3).

The independent investigators scored the patient’s satisfaction scale of 1–10. The range of satisfaction was 8.2–9, so most patients appeared to be content with the outcome of treatment. However, on day 14 and on day 28, satisfaction was greater in the WCG than in the CG group, with a statistically significant difference between the two groups: p = 0.0046 at day 14 and p = 0.0009 at days 28. Patients in the CG group assessed the compression treatment and reported that 50% were ‘very satisfied’ or ‘satisfied’, 37% were ‘moderately satisfied’ and 13% ‘not at all satisfied’. (Table 3)

### Side effects in the treated region (Table 4)

#### Pain
Comparing the absence of pain at days 14 and 28 between the two groups, no significant difference was apparent. For the mild and moderate levels of pain, there was very little difference between the two groups at day 14. Only one patient reported severe pain at the 14-days assessment (in the CG group), and no patient reported severe pain at day 28.

#### Inflammation
Few patients exhibited signs of inflammation at either day 14 or 28, regardless of the treatment group and there was no difference between groups.

#### Ecchymosis
The difference between the two groups was not statistically significant at either day 14 or 28.

#### Induration
At 28 days following treatment, mild induration was observed in nine patients (four in WCG and five in CG),
moderate induration in three patients (two in WCG and one in CG) and one major induration in CG. The rate of absence of induration was 79% for WCG and 76% for CG (N.S.).

**Pigmentation**
At day 28, the presence of pigmentation was observed in only three patients (one in WCG, and two in CG), no statistically significant difference being observed between the two groups ($p = $ N.S.).

**Matting**
At day 28, six patients in WCG and four patients in CG indicated mild or moderate matting. There was no matting for all other patients and absence of matting rate was 79% for WCG and 86% for CG (N.S.).

The total number of side effects of sclerotherapy was similar in the two treatment groups. Episodes of thrombophlebitis, with extension of sclerosis to saphenous tributaries, were few with no difference between the two groups (three cases in each) (Figs. 1 and 2).

Few patients took analgesics during the study: four at day 14 follow-up in each group, two at day 28 in the WCG group and three in the CG group (N.S.).

Compliance with the compression regime was poor. The mean number of days for wearing elastic compression was 11 for a total of 21 scheduled days. Only 40% of patients wore compression stockings every day. The reasons for not wearing the stockings were: discomfort for 32%, discomfort and painful tightness for 11%, itching for 9%, irritation for 6%, swelling and cold feet for 4% each. Other reasons accounted for 37%.

**Other adverse events** (Table 4)
No deep vein or superficial thrombosis was identified in the DUS. There were two cases of medial gastrocnemius venous thrombosis (in CG). These were minor and asymptomatic and were detected during routine DUS examination performed on day 7. Both patients had had SSV sclerotherapy with POL foam 1% (3 ml for one case and 4 ml for the other). No specific treatment was given.
On day 28, one thrombosis had completely disappeared (thrombus diameter on day 7 = 4 mm) and the other was on a clear downward trend (thrombus diameter on day 7 = 4.5 mm and day 28 = 3 mm). Five patients had five different adverse events, four reported as non-attributable to the treatment. They involved two patients in the WCG group: viral tonsillitis, rhinitis and, in the case of two patients in the CG group, sinusitis and coronary syndrome. The coronary syndrome occurred on day 4. There was good recovery and the cardiologists did not consider that it was related to the study treatment. One patient (WCG) presented with visual disturbance (scotoma) immediately after sclerotherapy but it resolved completely in less than 15 min.

**Discussion**

This randomised study confirms the efficacy and safety of foam sclerotherapy in the treatment of saphenous veins, evaluated here in the short term. On the one hand, for both groups, with or without compression, the saphenous vein occlusion rate was 100%, with rare and benign side effects and significant improvement in QOL. On the other hand, the outcome showed no difference between the two treatment groups. In particular, compression did not demonstrate the expected superiority in the following areas: thrombophlebitis, inflammation, pain, pigmentation and matting. In accordance with the recommendations of the experts, the doses administered were small and this may account for the low incidence of side effects.

Compression did not reduce endoluminal thrombus forming after sclerotherapy since the average diameter of the occluded veins was the same in both groups. An early systematic DUS examination revealed two minimal and asymptomatic gastrocnemius vein thromboses in the CG after SSV sclerotherapy. The prevalence of the muscular thromboses post-sclerotherapy has probably been underestimated in the literature, but their early systematic screening may be a subject for discussion. When they are asymptomatic, they do not appear to require any particular measures.

Only one randomised study in the literature has compared sclerotherapy with or without compression. This

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<th>Neurological complications</th>
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<th>Inflammation</th>
<th>Induration</th>
<th>Pain</th>
<th>Day 28 (moderate)</th>
<th>Pigmentation</th>
<th>Matting</th>
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No link to treatment: Acute coronary syndrome CG 1 Various (viral tonsillitis, rhinitis sinusitis)

**Table 4** Sclerotherapy side effects. Without compression group (WCG) (n)/With compression group (CG) (n). NB it should be noted that a same patient may have several concomitant side effects (for example a patient presenting with thrombophlebitis may describe induration, inflammation and matting and so will appear in several columns).

**Figure 1** Thrombophlebitis on D28 (small saphenous vein tributary).

**Figure 2** Thrombectomy on D28 (thrombophlebitis).
trial involved telangiectases and reticular veins and concluded that the results were better for the compression group (23–32 mmHg for 3 weeks) in the opinion of independent experts undertaking blinded assessments of photographs. The patient satisfaction score, however, showed no difference that would permit a distinction to be made between the two groups.

In the management of reticular veins and telangiectases following sclerotherapy, it has been suggested that 30–40 mmHg compression stockings are worn for a week followed by a 20–30 mmHg compression for 3 weeks. However, there is very limited evidence for the efficacy of this strategy and this does not seem to justify imposing such measures on a large scale. The expected benefit should be at least equal to the constraint, which is particularly high in this protocol, and ought to be genuinely demonstrated.

We decided to use a 15–20 mmHg compression level in our trial because it is the most common compression class used following sclerotherapy in France. This compression probably exerts too low a pressure on the saphenous veins to modify their diameter. It is unlikely that a stronger class of stocking would significantly alter the results of our study, in which we observed a low incidence of side effects following treatment. The use of stronger stockings may also lead to the patients inadvertently performing a Valsalva manoeuvre, which may be a factor leading to systemic side effects after foam injections.

When applying elastic compression stockings, the practitioner needs the patient’s co-operation; even so, it is difficult to avoid Valsalva manoeuvres when applying 15–20 mmHg stockings but quite impossible with 30–40 mmHg stockings. Elastic bandages are sometimes used; nevertheless, a consensus of experts recommends elastic stockings rather than bandages.

Eccentric compression with a newly developed wedge-shaped device (Medi postop® Medi Bayreuth, Germany), combined with thigh length stockings (Struwa 35® Medi Bayreuth, Germany), has been proposed with the aim of preventing the formation of endoluminal thrombus in the saphenous trunk. This system has the ability to apply much higher levels of compression over the treated vein, to the extent that the saphenous diameter is greatly reduced. Clinical trials have yet to be done to confirm that value of this type of compression following sclerotherapy.

The abolition of thrombus from a vein following sclerotherapy may be difficult, or impossible, to achieve. Serial ultrasound imaging of saphenous veins following chemical or thermal ablation shows a transition to fibrosis, healing and disappearance of the vein from a starting point of endoluminal thrombus. This process may take several months or even 1 or 2 years.

Inflammatory and painful reactions and thrombophlebitis occur more frequently in the tributaries than in the saphenous trunks themselves. It has yet to be demonstrated that more rigorous compression will avoid thrombophlebitis.

In our trial, the mean number of days for which elastic compression was worn was 11 out of 21 days for which patients should have worn stockings. Only 40% of patients wore compression stockings every day. Compliance with compression (and its assessment) is a limitation of this treatment. Our experience of poor compliance is consistent with what has been reported previously in venous diseases in general.

It should be noted that use of compression after sclerotherapy has long varied according to the country in which it is practiced. The ‘sclerotherapy cultures’ have differed historically (school of Tournay and compression—sclerotherapy of Fegan and Sigg), and regarding doses and choice of sites of injections, some practices may provoke more local side effects than others. The cultures of the patients are equally diverse, their discipline and perception of body image varying depending on country and region, where climates may also differ. All these factors, added to the variability of the materials and individual practitioners’ habits, have limited the uniformity of practice and render it quite complex to assess the usefulness of compression.

Finally, our study shows that compression stockings do not prevent side effects arising from foam sclerotherapy and do not seem to improve its efficacy in the short term.

Compression treatment may be useful in the management of thrombophlebitis following sclerotherapy, but this was not evaluated in our trial. Achieving effective obliteration of veins while avoiding an excessive dose of sclerosant is probably the most difficult aspect of sclerotherapy, together with the choice of sites of injection. Practitioners should focus on this main target.

Conclusion

The importance of elastic compression in chronic venous disorders has neither been studied nor challenged in this article, which merely studied the impact of compression on sclerotherapy. We found that the additional use of compression stockings following ultrasound-guided foam sclerotherapy made no difference to the outcome measures of effectiveness of obliteration of veins, side effects, satisfaction score, symptoms and QOL. Further controlled studies of compression are required to assess the role of compression in sclerotherapy and to evaluate other compression strategies. Much of current practice in phlebology is based on the opinions of experts rather than level 1 scientific evidence from clinical trials, a failing which should be addressed.

Conflict of interest

The authors declare that they have no conflict of interest.

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References


