Relevant factors affecting the outcome of ultrasound guided foam sclerotherapy of the great saphenous vein

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Abstract

Ultrasound guided foam sclerotherapy (UGFS) constitutes a valid ablative treatment for superficial vein diseases for the great saphenous vein (GSV), but no standardized protocol for its execution has yet been defined. Different variable factors involved in this procedure influence the final outcome and clinical results. The aim of our study was to analyze the respective influence on efficacy and side effects of three variable factors (foam volume, foam concentration, and contact time between the foam and the endothelium) for UGFS procedures for GSV insufficiency in order to select the best protocol for treatment. A retrospective analysis was made of UGFS procedures (190 patients, 201 legs) performed for GSV insufficiency in our institute from January 2007 to January 2010. All great saphenous veins included in our study exhibited a trans-ostial reflux and caliber range was 7-11 mm. In all cases, foam was prepared according to the Tessari method, using polidocanol (POL) and a gas mixture of CO_2 (70%) and filtered room air (30%), in a proportion of 1:4. A single injection procedure in the GSV was performed under Doppler ultrasound guidance at mid to lower third of the thigh. Legs were randomly assigned to one of three different treatment protocols: - Group A (71 legs): POL 3%, mean foam volume 4.5 cc, intermittent groin pressure 5 min, supine bed rest 10 min; - Group B (61 legs): POL 2%, mean foam volume 9 cc, intermittent groin pressure 5 min, supine bed rest 10 min; - Group C (69 legs): POL 2%, mean foam volume 9 cc, continuous groin pressure 5 min followed by intermittent groin pressure 5 min, continuous leg compression 5 min, supine bed rest 10 min. Efficacy of treatment and occurrence of side effects were evaluated in each group at two weeks and again at two years after the procedure and the cumulative results compared. Analysis of outcomes did not show any significant difference between the complete obliteration rate (P=0.825) or occurrence of local inflammatory reactions (P=0.883) between legs in Group A and in Group B. However, a significantly better outcome was observed between the complete obliteration rates and the local inflammatory reaction for legs in Group C compared to both legs in Group A (P=0.020 and P=0.015, respectively) and legs in Group B (P=0.013 and P=0.018, respectively). The type of procedure did not seem to have any effect on the extent of recanalization (over or less than 50% of the original lumen). No major adverse events such as deep vein thrombosis, significant allergic reactions, or serious neurological events occurred in any patient in any group. Further studies are still necessary to identify the best concentration ratios, volumes and length of contact time between foam and endothelium according to class size of specific veins to promote possible standardization of the procedure. However, measures to increase the contact time between foam and endothelium were shown to improve late results. In addition, the same efficacy and side effects are observed with lower POL concentration if foam volumes are increased.

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Introduction

Ultrasound guided foam sclerotherapy (UGFS) of the great saphenous vein (GSV), has become a widely accepted treatment for GSV disease with trans-ostial reflux. Efficacy and safety of this treatment have been well documented in the literature.[1-21] Properties of foam include echogenicity, homogeneous filling of the vein lumen, a prolonged contact with the endothelium and the need for a low dose of sclerosant. The efficiency of the foam for GSV ablation is now well documented for the short to medium term. However, a significant rate of recanalization of the vein's lumen at five years[5,20,22,23] could compromise this procedure, although it can easily be repeated if the patient agrees. The published results concerning this procedure, however, are often discordant and not easily comparable. This mainly depends on the different criteria used in performing this treatment. The main flaw of UGFS seems to arise from the lack of homogeneous protocols for the procedure.[20,23] In particular, there is as yet no consensus as to optimal foam characteristics such as, foam volume:sclerosant concentration ratios or the correct contact time between the foam and the endothelium according to specific vein size ranges. Our results regarding efficacy and side effects after using different foam concentrations, volumes and contact times with the endothelium were evaluated to identify the best protocol for a specific GSV class size.

Materials and Methods

We carried out a prospective analysis of UGFS procedures performed for GSV insufficiency at our center from January 2007 to January 2010. We examined the outcomes of 190 patients (201 legs) that had been randomly treated according to one of three different protocols. Results of both the efficacy of the procedure and the occurrence of side effects were analyzed at two weeks and at 2-years after treatment and compared. All treatments were made by a single injection in the GSV at mid to lower third of the thigh under Doppler ultrasound (DUS) guidance in a recumbent position. Treatment protocol 1: mean foam volume 4.5 cc (range 4-5 cc); polidocanol (POL) 3%; gentle, intermittent compression immediately on evidence of arrival of foam by DUS probe at saphenous/femoral junction (SFJ) for 5 min. Treatment protocol 2: mean foam volume 9 cc (range 8.3-10 cc); POL 2%; gentle intermittent compression immediately on evidence of arrival of foam by DUS probe at SFJ for 5 min. Treatment protocol 3: mean foam volume 9 cc (range 7.5-10.2 cc); POL 2%; continuous compression below the knee by sphygmo cuff inflated at 50 mmHg just before the injection and maintained for 5 min thereafter; gentle compression immediately on evidence of arrival of foam by DUS probe at the SFJ, maintained continuously for first 5 min and intermittently (after release of distal sphygmo compression) for an additional 5 min. It should be noted that in all cases the compression maneuvers at the SFJ (pre-marked on the skin) with the DUS probe were tailored so as to occlude the last segment of the GSV while maintaining full patency of the femoral vein (Tables 1 and 2).

Patients were divided into three groups (A, B or C) according to the treatment protocol (1, 2 or 3) to which they had been randomly assigned. Four patients in group A, 3 patients in group B and 4 patients in group C had similar bilateral GSV disease and received the same treatment protocol for both sides. Inclusion criteria were: i) presence of a GSV trans-ostial reflux by DUS examination. GSV caliber range 7-11 mm (at 5 cm below SFJ in standing position); ii) availability for follow up for at least two years (Clinical, Etiological, Anatomic, Pathophysiological classification: Class II-IV). Exclusion criteria were: i) recurrent GSV disease after any sort of ablative procedure; ii) presence of localized dilatations of more than 50% of the original caliber at 5 cm from SFJ; iii) presence of associated small saphenous vein disease.

Procedures and materials

Foam was prepared according to the Tessari method with 2 silicone-coated 10 cc syringes (Pentaferte SpA, Campli, TE, Italy), and one 3-way stopcock (15 strokes) mixing a 2% or 3% standard POL solution (Kreussler Pharma Inc., Tampa, FL, USA) with a gas mixture made up of 70% sterile medical CO2 and 30% filtered room air in a proportion of 1:4 liquid and gas. The correct proportion of room air was added to CO2 in the same syringe by direct aspiration of the room air through a membrane disc filter with a Luer slip attack to the syringe (Whatman 0.0002 mm air filter - FP 30/02 - Puradisc 25; Whotman Int'l. Ltd., Meadstone, UK). A single injection technique was performed in the GSV at mid to lower third of the thigh under DUS guidance through a straight 20G-1.5" needle (Chemo srl., Kevilmare Holding GmbH, Vienna, Austria) with the patient in a supine position and the bed tilted at a 10-15° Trendelemburg position.All patients rested supine for 10-12 min after injection and a 35-mmHg single leg stocking (Mediven-Struva 35; Medi Italia, Bologna, Italy) was positioned up to the groin with the aid of the Medi butler introducer before standing. All patients were discharged after a 30-min observation period during which they walked up and down in a room contiguos to the treatment room. Patients were instructed to engage in normal activities of daily life and to wear the stocking continuously for the following ten days. All patients were checked at two weeks and at two years. Response to treatment was assessed through DUS. A positive response was considered to be the absence of any color or sound signals during hand compression maneuvers together with no lumen compressibility by DUS probe from 2-4 cm below the SFJ to at least the knee. A patent proximal stump up to 4 cm below the SFJ was accepted and considered physiological (drainage of inguinal collaterals). Recanalizations, either partial or total, were considered as treatment failure. However, clinical evidence showed that partial recanalizations, if homogeneous and of moderate extent (generally less than 50% the original lumen), were often associated with a very short reflux time (usually <1 s) while still obtaining a good cosmetic result and safeguarding patient well-being.

Side effects

Side effects were either local or general. Local side effects were: i) significant venous and/or perivenous inflammatory reactions with pain and need for additional therapeutic measures; ii) residual skin pigmentation; iii) matting. Transient localized skin reactions were excluded. General side effects were: i) deep vein thrombosis; ii) neurological disturbances; iii) allergic reactions. While both femoral and popliteal veins were routinely examined by DUS at every checkup, no routine assessment of the calf veins was made nor was this ever considered necessary. Results were evaluated using Pearson's χ^2 test.

Results

All procedures were completed uneventfully by a single injection. The GSV was usually centered at mid to lower third of the thigh at the first attempt. Occasionally a second or third attempt was necessary and in these cases fresh foam was used. The presence of an assistant helped ensure the injection point was centered by the DUS probe while the fresh foam was being prepared, to correctly inflate the sphygmo cuff on the leg, and also to tilt the electric bed (Trendelemburg tilting) at the start of injection. Results are summarized in Table 3. A complete obliteration of the GSV was achieved after two weeks in 66 legs (93%) in Group A, in 57 legs (93.4%) in Group B, and in 65 legs (94.2%) of Group C. Failures (early recanalizations) occurred in 5 legs (7%) in Group A, in 4 legs (6.6%) in Group B, and in 4 legs (5.8%) in Group C. At two years, a complete GSV obliteration was still present in 49 legs (69%) in Group A, in 41 legs (67.2%) in Group B, and in 58 legs (84%) in group C, while a partial or total recanalization had occurred in 22 legs (31%) in Group A, in 20 legs (32.8%) in Group B, and 11 legs (16%) in Group C. In addition, partial recanalization of less than 50% the original caliber (measured at 5 cm below the SFJ) was observed in 8 legs (11.3%) in Group A, in 9 legs (14.8%) in Group B, and in 6 legs (8.7%) in Group C. In these cases, no reflux or minimal diastolic reflux (<1 s) was present at ultrasound examination while these patients remained generally asymptomatic. Soon after the injection, a diffusion of the foam into the GSV below the knee and also into leg collaterals was reported in 69 legs (97%) in Group A, in 61 legs (100%) in Group B and only in 19 legs (27.6%) in Group C. This caused often a transient inflammatory reaction of the smallest collaterals (see above). Statistical analysis of closure rates at two years showed no difference between Groups A and B (P=0.825), but a significantly better outcome in Group C versus either Group A (P=0.020) or Group B (P=0.013). Most patients tolerated the full procedure well with-

Table 1. Patients' characteristics.

	Group A	Group B	Group C
No. patients (no. legs)	67 (71)	58 (61)	65 (69)
Female/male (ratio)	46/21 (2.19)	45/13 (3.46)	48/17 (2.82)
Age in yrs, range (mean)	30-81 (56.2)	32-80 (57.7)	34-80 (57.6)
GSV calib,* in mm, range, (mean)	7-11 (8.1)	7-11 (7.9)	7-11 (8.2)

yrs, years; GSV, great saphenous vein; calib, caliber. *Measured at 5 cm below saphenous/femoral junction in a standing position.

Table 2. The 3 treatment protocols used in the study.

	Protocol 1	Protocol 2	Protocol 3
Mean foam volume (cc)	4.5	9	9
POL (%)	3	2	2
SFJ intermittent comp. (min)	5	5	-
SFJ cont. intermittent comp. (min)	-	-	5+5
Leg comp. (min)	-	-	5

POL, polidocanol; SFJ, saphenous/femoral junction; comp., compression; cont. intermittent comp., continuous followed by intermittent compression.

out any major events. No evidence of deep vein thrombosis or allergic reactions was reported. A very few patients in all three groups exhibited transitory hypotension, sweating or tremors at the start of the procedure (or just before); this was clearly related to emotional distress and these cases were not considered as side effects. Transitory visual disturbances (blurred vision, flashes of light) lasting a few minutes were reported by one patient in each group 30-60 min after injection with no further sequelae. In one patient (Group B), the visual disturbance was accompanied by frontal headache. One patient (Group A), exhibited paresthesia and transitory motor palsy of her right arm soon after injection; she made a full recovery spontaneously within 10 min. Finally, one patient (Group C) experienced sudden cervical pain, moderate dizziness and face flushing 10 min after injection on standing up; intravenous betamethasone was promptly administered and the patient fully recovered within 15 min. Localized minimal skin inflammatory reactions that cleared up spontaneously in a few days occurred quiet frequently in all groups and were not considered as side effects. In 18 legs (25.4%) in Group A, in 15 legs (24.6%) in group B, and in 8 legs (11.6%) in group C, venous inflammatory reactions with extension to contiguous tissues occurred from a few days to a few weeks after treatment. These involved segments of the GSV or, most frequently, superficial leg/thigh collaterals. Treatment was often needed; this included clotted blood evacuation, site compression, and, occasionally, administration of low molecular weight heparin. It is worthy of note that none of the patients in Group C exhibited a significant inflammatory reaction in the leg. All patients eventually recovered well; local tissue induration only reoccurred in a few cases. Faint skin pigmentations were fairly common in all groups: most of them vanished spontaneously during the observation period. Persistent skin pigmentations were always related to the closeness of the vein to the skin and/or to the extent of previous inflammatory reactions. These were most often localized around the medial knee and upper leg levels. Persistent skin pigmentations occurred in 19 legs (26.8%) in Group A, in 17 legs (27.9%) in Group B, and in only 9 legs (13%) in Group C. This implies a significantly better result in Group C than in either Group A (P=0.015) or Group B (P=0.018). Matting also sometimes occurred and was often concomitant with excessive local inflammatory reactions. This was subsequently alleviated by local low concentration POL sclerotherapy with the aid of a trans-illuminating device and/or by local intense pulsed light applications. Visible spots of matting, however, reoccurred in 9 legs (12.7%) in Group A, in 6 legs (9.8%) in Group B, and in 4 legs (5.8%) in Group C.

Table 3. Efficacy at 2-week and at 2-year checkup.

Checkup	2 weeks			2 years		
	Group A	Group B	Group C	Group A	Group B	Group C
Total no. legs	71 N (%)	61 N (%)	69 N (%)	71 N (%)	61 N (%)	69 N (%)
Complete obliteration	66 (93)	57 (93.4)	65 (94.2)	49 (69)	41 (67.2)	58 (84)
Recanalization <50%	-	-	-	8 (11.3)	9 (14.8)	6 (8.7)
Recanalization >50%	14 (19.7)	11 (18)	5 (7.3)	5 (7)	4 (4.61)	4 (5.81)

Table 4. Local and general side effects 0-2 years post-procedure. Total 201 legs.

	Group A	Group B	Group C
Total no. legs	71	61	69
Side effects			
Local			
Inflammatory reactions	18 (25.4)	15 (24.6)	8 (11.6)
Pigmentation	19 (26.8)	17 (27.9)	9 (13.5)
Matting	9 (12.7)	6 (9.8)	4 (5.8)
General			
Neurological	2 (2.8)	1 (1.6)	2 (2.9)
Deep vein thrombosis	0	0	0
Allergic reactions	0	0	0

Discussion

Foam is a physical dispersion of a gas (*e.g.* air) into a surfactant. The polyhedral bubbles constituting the foam display an outer layer of surfactant encasing the gas inside. Complex laws regulate the behavior of the bubbles that are highly unstable. They slowly coalesce into bigger-sized bubbles and eventually the liquid portion separates from the gas (drainage). The speed of degradation depends mainly on: i) the quality of foam (gas/fluid proportion and size of bubbles; ii) the properties of the surfactant; iii) the physical characteristics of the environment.[24,25] POL (atossisclerol/lauromacrogol 400) is a surfactant that acts by irreversibly denaturing the endothelial membrane. This ultimately results in endothelial cell death and inflammatory reaction, thrombus formation, and activation of fibroblasts. Experiments have shown that hemolysis also occurs in whole blood samples at POL concentrations greater than 0.45%;[26] however, erythrocyte lysis, platelet lysis and platelet-derived microparticle formation have not been a significant concern in reports of any clinical trials of sclerosant therapy.[16] After injection, the foam displaces the blood and homogeneously fills the vein's lumen. The spontaneous degradation of the foam is responsible for its contraction in volume and progressive loss of activity.[24] In an empty tubular system, however, foam of good consistency can persist for several minutes;[27] the same occurs in the vein's lumen if, by appropriate manual compression, the blood flow is stopped. Complete and homogeneous damage of the endothelium by the injected foam is chiefly dependent on three major variable factors: i) the volume of foam; ii) the concentration of the sclerosant; and iii) the length of the contact time between the foam and the endothelium, in relation to the total surface area to be treated (vein caliber and length). Specific individual sensitivity to the sclerosant also constitutes an additional variable factor that will certainly need further investigation. *In vivo*, the plug of the foam displaces the fluid content of the vessel, thus allowing the sclerosant to gain proper contact with the inner wall of the vessel. However, this only occurs if the volume of the foam is appropriate for the caliber and length of the vein; in fact, poor volumes of foam are the main cause of an incomplete and inhomogeneous filling.[25] Spastic vein reaction evoked by high sclerosant concentrations (disappearance of lumen) tends to instantly displace the foam, thus preventing its correct action. This does not happen if bigger volumes of foam are injected. Another important factor is the concentration of the sclerosant in the foam. This determines the aggressiveness of the foam's action and its penetration. An accurate selection of the scle-

rosant concentration in relation to the vessel caliber and thickness of the vessel wall is required to achieve a proper efficacy while avoiding serious overreactions.[21] Chemical kinetics studies the complex laws that regulate the molecular aspect of all biochemical reactions which are determined by specific collisions between particles of reactants: the number of such collisions determines the progress and completion of the reaction.[28] Factors influencing the biochemical reactions mainly include: concentration of reactants, surface characteristics, temperature, and time.[28] Sclerotherapy is a biochemical reaction between two reactants: surfactant and lipoproteins of the cellular membrane. Proper contact time between the foam and the venous inner wall is, therefore, essential for optimal UGFS efficacy. The disappointing results in the past with liquid sclerotherapy were probably caused not only by the excessive dilution of the sclerosant inside the vein and by its partial inactivation by the blood, but also by its rapid wash out. Our experience with same volume/same concentration foams (*i.e.* Protocols 2 and 3) in veins of similar calibers has proved a better efficacy in terms of occlusion rate when foam drainage was significantly slowed by appropriate compressive maneuvers, thus providing a prolonged contact. A successful venous chemical ablation implies a proper sequential activation of the following processes: complete and homogeneous endothelial necrosis, damage of sub-endothelial layers and fibroblastic activation, homogeneous thrombus formation, progressive fibrinolytic and thrombolytic activity, concomitant proliferation of fibroblasts and synthesis of new collagen. The correct evolution of this sclerosing process is in part critically determined by the specific extent of the damage to the vessel wall. Characteristics and type of local reflux can also have an influence. It has been demonstrated that obliteration of the GSV can be achieved also with low POL concentrations and appropriate foam volumes,[26] but no studies have as yet identified the most appropriate techniques and foam concentrations to achieve the best results.[20] It seems essential to establish the proper ratios between sclerosant concentrations, foam volumes and lengths of contact time in relation to specific ranges of vein caliber/length (total surface areas). In terms of complete occlusion rate at two years, better outcomes were reported for legs in Group C compared to legs in Group A (P=0.020) and in Group B (P=0.013), while no significant difference was found between legs in Group A and in Group B (P=0.825). These results imply the effectiveness of a prolonged contact time for the foam regardless of its concentration. In contrast, no difference was reported in the extent or speed of recanalization in any of the groups. In fact, recanalization, when it occurs, is probably influenced by local factors such as persistence of significant collaterals or points of re-entry of the original reflux. However, patient wellbeing is maintained when recanalization stabilizes at a substantial degree of lumen narrowing. Neurological disorders were rare. The pathological mechanisms resulting in cerebrovascular events and transient ischemic attacks are likely to be different to those leading to migraine and visual disturbances.[29] In general, occurrence of neurological disorders is frequently associated with right to left shunting conditions (patent foramen ovale).[29,30] However, no direct relationship has ever been documented with foam volume and concentration.[17,23,31-34] Also, although less frequently, occurrence of neurological disorders has been described with liquid sclerotherapy. Recently, there has been growing evidence to support the hypothesis that, at least for some neurological disorders, chemical mediators (endothelin) act as pathophysiologically causative agents.[32,35] The cumulative incidence of neurological disorders in all our patients was consistent with published data and no significant difference was found between the three groups. Local inflammatory reactions with residual skin pigmentation and matting are reported as a common occurrence after UGFS.[1,9,10,31] One view of four randomized controlled trials including a total of 517 patients documented skin pigmentation at a median rate of 32% after the procedure at 1-year follow up.[13] Excessive inflammatory reaction eventually leads to massive transparietal migration of macrophages and deposition of hemosideryn in sub-dermal layers. Legs in Group C exhibited a significantly lower incidence of skin pigmentations than legs in Group A (P=0.015) and in Group B (P=0.018). Also, general inflammatory reactions were significantly less common in Group C than in Group A (P=0.044), and lower than in Group B (P=0.072). These data clearly show the benefits of both the lower POL concentration and the protection of the superficial below the knee collaterals of the GSV by leg compression so to avoid undesirable excessive inflammation in certain areas. It is also worth noting that leg compression during the procedure provides a prophylactic protection from deep vein thrombosis by increasing the deep vein blood flow in the calf.

Conclusions

More investigations are undoubtedly necessary to identify the most accurate foam volumes, foam concentrations and contact time ratios for specific vein class sizes to ensure the best results of ultrasound guided foam sclerotherapy for superficial vein diseases of the great saphenous vein. The aim for the future must be to achieve a proper standardization of procedures.

References

1. Rabe E, Otto J, Schliephake D, Pannier F. Efficacy and safety of great saphenous vein sclerotherapy using standardized polidocanol foam. Eur J Vasc Endovasc Surg 2008;35:238-45.
2. Breu FX, Guggenbichler S, Wollmann JC. Second European Consensus meeting on foam sclerotherapy. Tegernsee. VASA 2008; 37:90-5.
3. Alos J, Lopez JA, Estadella B, Serraprat M. Efficacy and safety of sclerotherapy using polidocanol foam. A controlled clinical trial. Eur J Vasc Endovasc Surg 2006;94: 925-36.
4. Cabrera J, Cabrera J jr, Garcia-Olmedo A. Treatment of varicose long saphenous veins with microfoam form: long term outcomes. Phlebology 2000;15:19-23.
5. Grondin L. Foam echosclerotherapy of incompetent saphenous veins. Phlebolymphology 2003;42:S24.
6. Coleridge-Smith P, Wright D, Tristram S. Foam sclerotherapy of saphenous trunk varices. Phlebology 2002;17:75. [Abstract].
7. Cavezzi A.,Frullini A,Ricci S,Tessari L.Treatment of varicose veins by foam sclerotherapy;two clinical series.Phlebology 2002;17:13-18.
8. Van den Bos R, Arends L, Kockaert M, et al. Endovenous therapies of lower extremities varicosities: a meta analysis. J Vasc Surg 2009;49:230-9.
9. Frullini A, Cavezzi A. Sclerosing foam in the treatment of varicose veins and teleangectases: history and analysis of safety and complications. Dermatol Surg 2002;28:11-5.
10. Barrett JM, Allen B, Ockelford A, Goldman MP. Microfoam ultrasound guided sclerotherapy of varico veins in 100 legs. Dermatol Surg 2004;30:6-12.
11. Wright D, Gobin JP, Bradbury AW, et al. Varisolve polidocanol microfoam compared with surgery or sclerotherapy in the management of varicose veins in the presence of trunk vein incompetence. European randomized controlled trial. Phlebology 2006;21:180-90.
12. Hamel-Desnos C, Desnos P, Wallman JC, et al. Evaluation of the efficacy of polidocanol in the form of foam compared with liquid form in sclerotherapy of the greater saphenous vein: initial results. Dermatol Surg 2003;29:1170-5.
13. NIHCE Engl. Ultrasound guided foam sclerotherapy for varicose veins, overview and

guidance IPG 440; august 2009, updated February 2012. Available from: http://publications.nice.org.uk/ultrasound-guided-foam-sclerotherapy-for-varicose-veins-ipg440
14. Coleridge Smith P. Chronic venous disease treated by ultrasound guided foam sclerotherapy. Eur J Vasc Endovasc Surg 2006;32:577-83.
15. Hamel-Desnos C, Guias B, Jousse S, et al. Foam echosclerotherapy by puncture direct injection: technique and quantities. J Mal Vasc 2006;31:180-9.
16. Eckmann DM. Polidocanol for endovenous microfoam sclerosant therapy. Expert Opin Investig Drugs 2009;18:1919-27.
17. Rathbun S, Norris A, Stoner J. Efficacy and safety of endovenous foam sclerotherapy: meta-analysis for treatment of venous disorders. Phlebology 2012;27:105-17.
18. Coleridge-Smith P. Sclerotherapy and foam sclerotherapy for varicose veins. Phlebology 2009;24:260-9.
19. Bradbury AW, Bate G, Pang K, et al. Ultrasound - guided foam sclerotherapy is safe and clinically effective treatment for superficial venous reflux. J Vasc Surg. 2010;52:939-45.
20. Myers KA, Robert S. Evaluation of published reports of foam sclerotherapy: what do we know conclusively? Phlebology 2009;24:275-80.
21. Myers KA, Jolley D, Clough A, Kirvan J. Outcome of ultrasound guided sclerotherapy for varicose veins: medium term results assessed by ultrasound survellance. Eur J Vasc Endovasc Surg 2007;33:116-21.
22. Chapman-Smith P, Browne A. Prospective five-year study of UGFS. Phlebology 2009;24:183-8.
23. Morrison N. Foam sclerotherapy. How to improve results and reduce side effects. Phlebology 2008;37:211-20.
24. Wollmann JC. Sclerosant foams stabilities, physical properties and biological behavior. Phlebologie 2010;39:208-17.
25. Mengual O, Meunier G, Cayre I, et al. Characterization of instability of concentrated dispersion by a new optical analizer. Colloids Surf Physicochem Eng Aspects 1999;152:111-13.
26. Parsi K, Exner T, Low J, et al. In vitro effects of detergent sclerosants in cloth formation and fibrinolysis. Eur J Vasc Endovasc Surg 2011;41:267-77.
27. Wong KC. Rheology of sclerosant foam in vitro. Sydney: University of Sidney; 2009. SID 310334209. Available from: http://www.aeromech.usyd.edu.au/rheologyofsclerosantfoam
28. House JE. Fundamental concepts of kinetics and reaction mechanisms. In: House JE, ed. Principles of chemical kinetics, 2nd ed. Burlingtom, MA: Academic Press; 2007. pp 1-30.
29. Sarvananthal T, Shepherd AC, Willemberg T, Davies AH. Neurological complications of sclerotherapy for varicose veins. J Vasc Surg 2012;55:243-51.
30. Raymond-Martinbeau P. Transient adverse events positively associated with patent foramen ovale after ultrasound guided foam sclerotherapy. Phlebology 2009;24:114-9.
31. Jillet JL, Guex JJ, Hamel Desnos C, et al. Side effects and complications of foam sclerotherapy of GSV and SSV. Phlebology 2009;24:131-8.
32. Gillet JL, Donnet A, Laurecker M, et al. Pathophysiology of visual disturbances occurring after foam sclerotherapy. Phlebology 2010;25:261-6.
33. Bush RG, Derrick M, Manjonej D. Major neurological events following foam sclerotherapy. Phlebology 2008;23:189-92.
34. Hartman K, Harms L, Simon M. Reversible neurological deficits after foam sclerotherapy. Eur J Vasc Endovasc Surg 2009;38:648-9. 35.
35. Frullini A, Felici E, Burchielli S, Di Stefano R. High production of endothelin after foam sclerotherapy: a new pathogenetic hypotesis for neurological and visual disturbances after foam sclerotherapy. Phlebology 2011;26:203-8.