DOI: https://doi.org/10.53350/pjmhs221610994

ORIGINAL ARTICLE

Early Adverse Effects of Foam Sclerotherapy for Varicose Veins: An Experience of 50 Sclerotherapy Sessions

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ABSTRACT

Background: Foam injection sclerotherapy for treating varicose veins is a newly emerging and minimally invasive technique. Its safety profile needs to be investigated.

Objective: We documented the adverse effects associated with foam injection sclerotherapy occurring in the first 24 hours and then at 2 and 4 weeks of follow up visits.

Material and Methods: This cross-sectional study was conducted at Department of Surgery in Benazir Bhutto Hospital, affiliated with Rawalpindi Medical University, Rawalpindi from 1st July 2021 till 30th June 2022; on 50 patients of varicose veins. A duplex ultrasound was done in all patients. Varicose veins were classified using the CEAP system. Patients having C1 and/or C2 varicose disease with isolated GSV incompetence on duplex ultrasound were included.

Results: Only minor complications were encountered and no serious complication was seen. The minor side effects included nausea, hyperpigmentation, matting, headache, vomiting, pruritus around injection site, vomiting and shortness of breath. Serious complications like anaphylactic shock, stroke, TIA, deep venous thrombosis, superficial venous thrombosis, tissue necrosis and skin necrosis were not encountered in any patient.

Conclusion: Injection sclerotherapy with sodium tetra decyl sulphate in the foam form for the treatment of varicose veins is a safe modality; since only minor complications were encountered and no serious complication was seen.

Keywords: Varicose veins; Foam sclerotherapy; Duplex ultrasound; Complications; Side effects

INTRODUCTION

Varicose veins as a disease entity have been recognized since antiquity and their treatment was described by even Hippocrates and Galen[1]. Varicose veins are not just a cosmetic problem instead they gives rise to many complications related to chronic venous insufficiency and venous hypertension. Surgical modalities for varicose veins have been under evolution for last 2000 years. Currently the trend is shifting from open procedures to minimally invasive ones i.e. endovenous ablation or sclerotherapy.

Sclerotherapy involves obliteration of varicose veins by targeted injection of liquid or foam sclerosant agent. The sclerosant agent damages the endothelium of the vessel wall and the varicose vein gets converted into a string of connective tissue in which re-chanelling is impossible. The functional results are equivalent to removal of the vein.

Sclerotherapy as a treatment modality for varicose veins has been describes in literature for many years[2]. Sodium tetradecyl sulphate was approved by FDA in 2004 for the treatment of varicose veins. After different trials in the beginning of 21st century European guidelines for sclerotherapy were published in 2014[3]. These guidelines have recently been updated in light of futher trials and are published in 2021[4].

Sclerotherapy can be used for all forms of varicose veins; including incompetent saphenous veins, incompetent perforators, varicose tributaries, reticular varicosities, telangiectasias (spider veins), varicose veins around a skin ulcer, and recurrent varicose veins after previous surgeries.

Due to authentic data liquid sclerotherapy is the treatment of choice for reticular veins and spider veins which fall in the category of C1 varicose veins according to CEAP classification[5]. Foam sclerotherapy is also considered as a successful option for C2 class varicose veins.

Sclerotherapy with liquid or foam is a cost-effective and successful treatment option since it can be repeated as required and has few side effects. However, the recurrence rates and re-channeling rates are higher than with thermal and surgical methods[6].

Sodium tetra decyl sulfate is a synthetic, surface active substance. It is a long chain fatty acid salt of an alkali metal with properties of soap. It mainly acts on the endothelium of the veins. The sclerosant agent can be converted into foam by different techniques like Tessari method[7] or the double syringe system (DSS). Foam sclerotherapy has been found to be more effective than liquid sclerotherapy[8].

The popularity of injection sclerotherapy for treating varicose veins has waxed and waned over the last century. For its use to become more widespread; the safety profile of foam sclerotherapy needs to be investigated. We documented the adverse effects associated with foam injection sclerotherapy occurring in the first 24 hours and then at 2 and 4 weeks of follow up visits.

MATERIAL AND METHODS

We conducted this cross-sectional study at the department of Surgery in Benazir Bhutto Hospital, affiliated with Rawalpindi Medical University, Rawalpindi. The study was carried out from 1st July 2021 till 30th June 2022. Data of 50 patients of varicose veins was collected.

After taking a detailed medical history and clinical examination we got a Doppler ultrasound done in all patients. We classified the varicose veins using the CEAP system of classification as shown in Table 1. We used this method to treat small uncomplicated varicose veins with isolated GSV incompetence on duplex ultrasound. Patients having C1 and/or C2 varicose disease according to CEAP classification were included, if they gave an informed consent.

The following patients were excluded from the study;

- Known allergy to the sclerosant
- Acute venous thromboembolism
- Local infection in the region of sclerotherapy or severe generalized infection
- Known symptomatic right-to-left shunt (patent foramen ovale)
- Pregnancy
- Lactation
- Severe peripheral arterial occlusive disease
- Long term immobility or bed ridden patients
- Varicose veins associated with edema, skin changes active or healed ulcers (C 3-6)

The sclerosing agent used was Sodium tetra decyl sulphate. The concentration used was 1%. It was converted into a foam by Tessari method. In this method we used two syringes connected

by a three way stopcock. In the first syringe 1 ml of sclerosing agent is drawn and in the second syringe 4 ml of air is drawn. They were pushed back and forth about 20 times till a foam is produced.

Patients were treated in an operating room with duplex ultrasound. We gave 0.5 ml as a test dose initially and then observed the patient for next half hour for any untoward reaction. Under ultrasound guidance foam was injected using a cannula of 24 G or 22 G. Vein was punctured at most accessible site. The tip of the cannula was placed at the center of the vein lumen under ultrasound guidance. A volume of 0.5 ml was injected into spider and reticular (C1) veins and a volume of 1.0 to 2.0 ml was injected into varicose tributaries (C2). Adjacent injection sites were kept at least 6 cm apart. A maximum volume of 10 ml was used in one sitting.

Immediately after injection they should not move leg for 15 minutes. Patients should not carry out valsalva maneuver. We retained patients for 24 hours after the injection sclerotherapy and discharged them after 24 hours. They were advised to wear compression stockings for 4 weeks in the postoperative period and to maintain their normal activity. They were called in OPD for follow up after 02 and 04 weeks.

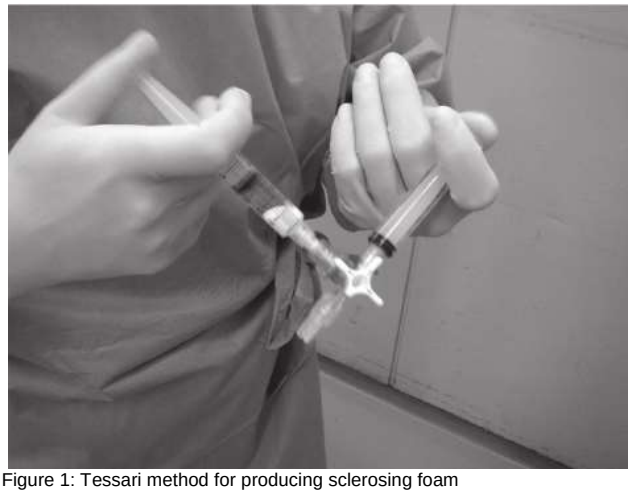

Figure 1: Tessari method for producing sclerosing foam

Table 1: CEAP (Clinical-Etiology-Anatomy-Pathophysiology) classification of varicose veins[9]

C 0	No visible or palpable sign of venous disease
C 1	Reticular veins or telangiectasias
C 2	Varicose veins; distinguished from reticular veins by a diameter of 3 mm or more
C 3	Edema
C 4 • C 4a • C 4b	Changes in skin or subcutaneous tissue secondary to CVD • Pigmentation or eczema • Lipodermatosclerosis or atrophie blanche
C 5	Healed venous ulcer
C 6	Active venous ulcer
S:	Symptomatic
A:	Asymptomatic

RESULTS

The study included 50 patients who underwent foam sclerotherapy with foam of Sodium tetra decyl sulphate prepared by Tessari method for varicose veins of the legs. The age of the patients ranged from 18 to 55 years with a mean age of 39.8±9.03 years. It included 21 (42%) male patients and 29 (58%) female patients. All patients had primary early uncomplicated varicose veins of C1 and/or C2 CEAP class varicosities. Thirty two (64%) patients had C2, 14 (28%) patients had both C1 and C2 varicosities and 4 (8%) had C1 varicose veins. The number of varicose veins injection at one session ranged from 3 to 9 veins with a mean number of varicose veins of 6.6±1.42. Total volume of sclerosant used in one patient ranged from 4 to 10 ml with a mean volume of 7.84±1.37 ml per patient per session.

The adverse effects were noted in immediate post-procedure period up to 24 hours and then on OPD visits at 2 and 4 weeks. Minor complications were encountered but no serious complication was encountered. The commonest side effect observed was nausea in 4 (8%) patients followed by hyperpigmentation in 3 (6%) and matting in 3 (6%) patients. Two (4%) patients developed hematoma and blistering at injection site. Other adverse effects included headache and migraine in 1 patient (2%), vomiting in 1 (2%) and pruritus around injection site in 1 (2%) patient. One patient (2%) developed shortness of breath with wheeze on auscultation; this patient was a diagnosed asthmatic in the past.

Serious complications like anaphylactic shock, stroke, TIA, deep venous thrombosis, superficial venous thrombosis, tissue necrosis and skin necrosis were not encountered in any patient.

Table 2: Adverse effects

Adverse effect	Frequency
Nausea	4 (8%)
Vomiting	1 (2%)
Metallic taste in mouth	0
Redness of conjunctiva	0
Pruritus	1 (2%)
Cough, dry	0
Shortness of breath and/or tightness in chest	1 (2%)
Headache and migraine	1 (2%)
Blurring of vision/ visual disturbances	0
Injection site blistering/ hematoma/ ulcer/ necrosis	2 (4%)
Deep vein thrombosis	0
Superficial vein thrombosis	0
Pulmonary embolism	0
Matting	3 (4%)
Hyperpigmentation	3 (6%)
Damage to motor nerve	0
Extensive tissue necrosis	0
Skin necrosis	0
Embolia cutis medicamentosa	0
Stroke and TIA	0
Anaphylaxis	0
Death	0

DISCUSSION

The popularity of injection sclerotherapy for treating varicose veins has waxed and waned over the last century. Recently the newer sclerosants have shown acceptable safety profile and since then their use has expanded[9]. In the beginning it was used as an adjunct to saphenectomy for treating residual varicosities, reticular veins or telangiectias. Now it is also used for treating great saphenous vein and its main tributaries.

Sodium tetradecyl sulphate is an amphiphilic substance and becomes biologically active when it is in micelle form. It is the preferred sclerotherapy agent as it has low incidence of allergic reactions, staining and is quite forgiving if extravasated. Other agents like sodium morrhuate, ethanolamine oleate and hypertonic saline have fallen out of favor. The introduction of Tessari technique is also beneficial because making of foam reduces the amount of sclerosant and hence the side effects are reduced. In the foam the sclerosant is in micellar form which makes it biologically active. The foam also pushes blood out of the vein which reduces the dilutional effect of blood and increases the contact of the sclerosant with the endothelium.

Review of published literature shows sclerotherapy to be a safe and effective form of treatment for varicose veins[10]. In 1978 Tretbar[11] reported injecting spider angiomata with a sclerosant agent in 144 patients and noted epidermal necrosis and a 30% incidence of hyperpigmentation with this. Then in dermatologic literature, Shields and Jansen in 1982[12] described injection sclerotherapy of telangiectasias with STS in 105 patients. With 1% solution no systemic reactions were reported and one episode of necrosis and some pigmentary changes were reported.

In a meta analysis of 684 studies sclerotherapy with foam sclerosant was found to be as effective as laser therapy but less effective than surgery. Moreover major adverse effects were rare[13]. Foam sclerotherpy was regarded as a highly safe procedure by Cavezzi et al[14]. They reported that anaphylaxis is extremely rare, but thrombotic and embolic phenomenon account for most of the adverse effects.

Guex et al[15] reported outcome of 12,173 sessions of sclerotherapy, 5,434 with liquid, 6,395 with foam, and 344 using both. Ultrasound guidance was used in 33.9% sessions. Most common side effect was visual disturbance in 20 cases which resolved shortly in all patients. The only serious complication was femoral vein thrombosis that occurred in one patient.

Our study showed this procedure to a safe option since only minor complications were encountered and no serious complication was seen. The common minor side effects included nausea, hyperpigmentation, matting, headache, vomiting, pruritus around injection site, vomiting and shortness of breath. Serious complications like anaphylactic shock, stroke, TIA, deep venous thrombosis, superficial venous thrombosis, tissue necrosis and skin necrosis were not encountered in any patient.

In literature different complications have been reported. The most serious yet very rare complication is anaphylactic shock. It is to be treated as an emergency, by administration of corticosteroids, anti-histamines and epinephrine[16]. If the injection is inadvertently given intra-arterial, it may result in extensive tissue necrosis[17]. This complication can be minimized by doing the procedure under ultrasound guidance. Moreover, if severe pain occurs during the injection, it must be stopped immediately. In case of intra-arterial injection local anticoagulation should be given along with systemic corticosteroids. Use of high concentration sclerosant or perivascular injection may result in skin necrosis, which results in wounds with protracted healing. Some patients can experience a transient migraine-like headache, which is seen more frequently with foam sclerotherapy than with liquid sclerotherapy[18]. No reports of permanent visual impairment has been documented in literature. Transient visual impairment probably is migraine with aura[19] rather than an ischemic cerebrovascular accident. It is postulated that patent foramen ovale with right-to-left shunt may be responsible for vision disorders. Confirmed TIAs and strokes have been reported after foam sclerotherapy and are the result of paradoxical thromboembolism[20]. However all such patients recover completely and no significant after effects have been reported. Deep venous thrombosis is usually distal and proximal DVT and lung embolism are rare[21]. Frequency of DVT as reported by Dermondy is 0.6%[22]. Mean frequency of 4.7% is reported for superficial vein thrombosis[23]. The occurrence of nerve damage after sclerotherapy is very rare. Incidence of skin pigmentation has been reposted between 0.3 to 30%, but in majority it is transients and disappears over a period of months[24]. Literature reveals a higher frequency of hyperpigmentation with foam than with liquid sclerotherapy. Sometimes spider veins appear in the region of injected vein, this is called matting. This occurs due to insufficient treatment of underlying reflux. Using higher concentration or volumes of sclerosant agent can also result in matting. Other minor adverse effects reported in literature include wheals or blistering at injection site, erythema, nausea, tightness in chest, metallic taste, and clot or hematoma formation[25].

In order to avoid these side effects adequate imaging and good technique is required. Moreover, following the recommendations in terms of using correct sclerosant concentration, adequate dose per injection and correct choice of vein been injected is important[26-27]. Finally strict compliance with postoperative instructions can also help minimize the complication rate.

CONCLUSION

Injection sclerotherapy with sodium tetra decyl sulphate in the foam form for the treatment of varicose veins is a safe modality; since only minor complications were encountered and no serious complication was seen. In order to avoid the side effects adequate imaging, good technique and strict adherence to recommended guidelines is required.

REFERENCES

1. Royle J, Somjen GM. Varicose veins: Hippocrates to Jerry Moore. *ANZ J Surg*. 2007;77(12):1120-7.
2. Ricardo de Ávila Oliveira, Rachel Riera, Vladimir Vasconcelos, Jose Cc Baptista-Silva. Injection sclerotherapy for varicose veins. *Cochrane Database Syst Rev*. 2021;12(12):CD001732.
3. Rabe E, Breu FX, Cavezzi A, Coleridge Smith P, Frullini A, Gillet JL, Guex JJ, et al. European guidelines for sclerotherapy in chronic venous disorders. *Phlebology* 2014; 29:338–354.
4. Rabe E, Breu FX, Flessenkämper I, Gerlach H, Guggenbichler S, Kahle B, et al. Sclerotherapy in the treatment of varicose veins : S2k guideline of the Deutsche Gesellschaft für Phlebologie (DGP) in cooperation with the following societies: DDG, DGA, DGG, BVP. Hautarzt. 2021 Dec;72(Suppl 2):23-36.
5. Rabe E, Schliephake D, Otto J, Breu FX, Pannier F. Sclerotherapy of telangiectasias and reticular veins: a double-blind, randomized, comparative clinical trial of polidocanol, sodium tetradecyl sulphate and isotonic saline (EASI study). *Phlebology*2010;25:124–31.
6. Venermo M, Saarinen J, Eskelinen E, Vähäaho S, Saarinen E, Railo M, et al. Finnish Venous Study Collaborators. Randomized clinical trial comparing surgery, endovenous laser ablation and ultrasound guided foam sclerotherapy for the treatment of great saphenous varicose veins. *Br J Surg* 2016;103:1438–44.
7. Tessari L, Cavezzi A, Frullini A. Preliminary experience with a new sclerosing foam in the treatment of varicose veins. *Dermatol Surg* 2001;27:58–60
8. T. Ukritmanoroat Comparison of efficacy and safety between foam sclerotherapy and conventional sclerotherapy: a controlled clinical trial. *J Med Assoc Thai*,2011;94:35-40.
9. Fedor Lurie, Marc Passman, Mark Meisner, Michael Dalsing, Elna Masuda, Harold Welch, et al. The 2020 update of the CEAP classification system and reporting standards. *Journal of Vascular Surgery* 2020;8:342-35.
10. Coleridge Smith P. Foam and liquid sclerotherapy for varicose veins. Phlebology. 2009;24 Suppl 1:62-72.
11. Tretbar LL. Spider angiomata: treatment with sclerosant injections. J Kansas Med Soc. 1978;79:198.
12. Shields IL, Jansen GT. Therapy of superficial telangiectasias of the lower extremities. J Dermatol Surg Oncol 1982;8:857.
13. 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.
14. Cavezzi A, Parsi K. Complications of foam sclerotherapy. Phlebology. 2012 Mar;27 Suppl 1:46-51
15. Guex JJ, Allaert FA, Gillet JL, Chleir F. Immediate and midterm complications of sclerotherapy: report of a prospective multicenter registry of 12,173 sclerotherapy sessions. *Dermatol Surg* 2005;31(2):123-8.
16. FeiedCF, JacksonJJ,BrenTS,BondOB, FernandoCE, Young VC, Hashemiyoon RB. Allergic reactions to Polidocanol for vein sclerosis. *J Dermatol Surg Oncol* 1994;20:466–68.
17. Hannaford PKP. Intra-arterial injection of sclerosants: report of three cases treated with systemic steroids. *Phlebology* 2016;31:241–50.
18. Hill DA. Neurological and chest symptoms following sclerotherapy: a single centre experience. *Phlebology* 2014;29:619–27.
19. Zouitina TM, Hyra M, Seryer D, Chillon J-M, Bugnicourt J-M. Prolonged acute migraine with aura and reversible brain MRI abnormalities after liquid sclerotherapy. *J Headache Pain* 2014;15:1–4.
20. HahnM, Shulz T, Juenger M Late s.troke after foam sclerotherapy. *Vasa* 2010;39:108–10.
21. Fabi SG, Peterson JD, Goldman MP, Guiha I. An investigation of coagulation cascade Activation and induction of Fibrinolysis using foam Sclerotherapy of reticular veins. *Dermatol Surg* 2012;38:367–72.
22. Dermody M, Schul MW, O'Donnell TF. Thromboembolic complications of endovenous thermal ablation and foam sclerotherapy in the treatment of great saphenous vein insufficiency. Phlebology 2015;30:357–64.
23. GuexJJ, Allaert FA, Gillet JL. Immediate and midterm complications of sclerotherapy: report of a prospective multicenter registry of 12,173 sclerotherapy sessions. *Dermatol Surg* 2005;31:123–8.
24. Reich-Schupke S,Weyer K, Altmeyer P, Stücker M. Treatment of varicose tributaries with sclerotherapy with polidocanol 0.5%foam. *Vasa* 2010;39:169–174
25. Gibson K, Gunderson K. Liquid and foam sclerotherapy for spider and varicose veins. Surgical Clinics. 2018 Apr 1;98(2):415-29.
26. Karmacharya RM, Shrestha B, Singh A, Chandi N, Bhandari N. Short Term Outcome of Adjunct Foam Sclerotherapy for Varicose Veins in Patients Subjected to RFA at Dhulikhel Hospital, Nepal. International Journal of Vascular Medicine. 2019 Oct 7;2019.
27. Reina L. How to manage complications after sclerotherapy. Phlebolymphology. 2017 Jan 1;24(3):130-43.