Available online at www.sciencedirect.com

ScienceDirect

Journal of Current Ophthalmology 31 (2019) 214–217

http://www.journals.elsevier.com/journal-of-current-ophthalmology

Original research

Sclerotherapy for eyelid and anterior orbital venous-lymphatic malformation

Mohammad Etezad Razavi [a], Mohammad Taher Rajabi [b], Narges Hassanpoor [b,*], S. Saeed Mohammadi [b]

[a] *Mashhad Eye Research Center, Khatam Alanbia Eye Hospital, Mashhad University of Medical Sciences, Mashhad, Iran*
[b] *Eye Research Center, Farabi Eye Hospital, Tehran University of Medical Sciences, Tehran, Iran*

Received 4 September 2018; revised 26 December 2018; accepted 4 January 2019
Available online 30 January 2019

Abstract

Purpose: To assess the efficacy of sclerotherapy with sodium tetradecyl sulfate (STS; Fibrovein 1%) in superficial periocular venous and lymphatic malformations.

Methods: Eleven patients with low-flow venous and lymphatic malformations with extension predominantly to the eyelids, conjunctiva, and anterior orbit were selected. Sclerotherapy with STS was undertaken as an office-based procedure without any radiological guidance. Injections were repeated every 4 weeks until desired response occurred. Therapeutic effect was assessed objectively by change in the size of the lesions in serial photography.

Results: The lesions completely resolved in 4 cases with small eyelid and fornix lesions. In other 7 cases there was partial resolution to less than half of primary size. We did not have any significant complications.

Conclusion: Sclerotherapy with STS is an easy and effective modality for treatment of venous-lymphatic malformations and can be undertaken as an office-based procedure in lesions which are limited to eyelids and anterior orbit.

Keywords: Fibrovein; Cosmetic; In office procedure; Sclerotherapy; Venous-lymphatic malformation

Introduction

Venous-lymphatic malformations are benign vascular malformations which can cause cosmetic and functional side effects like extraocular muscle dysfunction, strabismus, infection, amblyopia, and even visual dysfunction. Occasionally, intra-lesional hemorrhage leads to sudden change in size which affects adjacent structures. Although surgical ablation of the lesion was the treatment of choice, it was very challenging and complicated because of vascular and infiltrative nature of the lesion. Furthermore, recurrence rate was high in patients who underwent surgical excision.[1–3] Although percutaneous intra-lesional sclerotherapy is a well-known therapy in superficial vascular lesions throughout the body and various sclerosing agents like sodium tetradecyl sulfate (STS), bleomycin, doxycycline, ethanol, and OK-432 (Picibanil) are used for this reason, there are few studies about percutaneous intra-lesional sclerotherapy efficacy and its complications in orbital region.[1,4–7]

STS, a synthetic surfactant, is one of the few US Food and Drug Administration (FDA) approved sclerosing agents.[8] Intravenous injection of this agent causes intimal inflammation and thrombus formation which usually occludes the injected vein. Subsequent formation of fibrous tissue results in partial or complete venous obliteration that may or may not be permanent. STS has shown its safety, reliability, and effectiveness with few side effects in the treatment of varicose veins since 1946.[9]

Authors declare that they have no financial interest or relationships in the subject matter or materials discussed in this manuscript.

* Corresponding author. Eye Research Center, Farabi Eye Hospital, Qazvin Square, Tehran, 1336616351, Iran.
E-mail address: nargeshassanpoor@gmail.com (N. Hassanpoor).

Peer review under responsibility of the Iranian Society of Ophthalmology.

https://doi.org/10.1016/j.joco.2019.01.002

In this study, we report 11 cases of venous-lymphatic malformations in superficial periocular are treated with percutaneous intra-lesional sclerotherapy as an "in office procedure".

Methods

This retrospective case series was conducted based on principles of the Declaration of Helsinki, and its protocol was supervised and approved by the Ethical Committee of Mashhad University of Medical Sciences. All patients whose photographs are shown here signed the informed consent for publication of their pictures in this study. Written informed consent was obtained following complete explanation of procedure to the patients. Then thorough ophthalmologic examination was done. The lesions were diagnosed clinically as venous-lymphatic malformation (all vascular lesions including lymphangiomas and cavernous hemangiomas were included), and patients did not mention any history of previous treatment. Face photography was done for all patients in order to evaluate the change in lesion size after injection of the sclerosant agent. All lesions were low-flow malformations (less than 10% increase in size with 1 min of Valsalva maneuver) with extent predominantly to the eyelids, conjunctiva, and anterior orbit. Because selected cases were almost prominent, superficial anterior venous-lymphatic disorders injections were done without guidance of ultrasonography. Lidocaine 2.5% ointment was applied to the skin 15 min prior to injection in the office. Then 0.1 ml STS 1% (Fibrovein 1%, STD Pharmaceutical Products, England) was injected into the lesion using 25 gauge needle after assurance of needle placement out of arterial lumen (with manual aspiration before injection) in order to check any allergic reactions. After that, intralesional injection at suitable sites was performed with variable volume based on the size and distribution of lesions (0.1–0.3 ml in each site) with maximum total volume of 2 ml in one session. The amount of volume calibrated by amount of mild distension of lesion (not over inflate) and then semi-pressure patch applied over the eyelids after injection. All injections were performed by an expert oculoplastic surgeon (M.E.R.). Patients were visited 1 h after procedure for proptosis caused by intra-lesional hemorrhage or severe edema. Intraocular pressure was checked in all patients before and after the injection.

First postoperative visit was 1 day after procedure for assessment of potential complications. All cases were followed 4 weeks after injection, and if needed, repeated injections were done for them every 4 weeks. This protocol continued until no significant clinical lesion remained or based on patients' desire. After final treatment all patients had visits with 6 months intervals for 24 months. Outcome measure of the study was clinical decrease in size of the lesion; therefore, the resolution of lesions was documented based on comparison of photographic pictures by an expert oculoplastic surgeon (M.E.R.).

Results

Eleven patients including 8 female and 3 male with eyelid, conjunctiva, and anterior orbital venous-lymphatic malformation were included in the study. Mean age of patients was 25 years (ranged, 14–38 years old). Six cases had eyelid vascular malformation (No 1, 2, 4, 5, 7, and 10), and 3 cases had conjunctival fornix and caruncle vascular lesion (No 6, 9, and 11). Two of our cases (No 3 and 8) were large and had intra-orbital extension which was documented by orbital CT scan. In other superficial cases, diagnosis made only by clinical appearance, and no imaging was done.

Partial resolution of the vascular malformation was revealed in 7 cases (66.6%) with various extents (Fig. 1 and Table 1.) In 4 cases (36.3%) (No 5, 6, 9, 11), complete resolution of lesions developed.

Two of our cases were large with intra-orbital extension of lesion. Case No 8 had dystopia and inferior displacement of the globe due to deep orbital venous-lymphatic malformation, causing 6 mm of proptosis. Partial improvement (to 3 mm) of proptosis occurred after 3 injections with maximum dose of 6 mL (case No 8 - Fig. 1e). Another patient with intra-orbital extension was case No 3 with eyelid and anterior orbital varix. After two times of injection, a firm fibrous mass developed in her left eye which was excised by surgery.

Bruising and hematoma (case No 3), mild pain during the injections, and in one case (case No 1) superficial tiny skin necrosis and infection (which resolved with medication: Fig. 1a and b) were the only side effects of our injections. There was not any other significant complication after sclerosant injections in our case series. Also, there was not any recurrence in the mentioned follow-up period.

Discussion

Nowadays, less invasive therapeutic procedures are trending. Percutaneous sclerotherapy is suggested as an alternative to surgery in treatment of superficial periocular venous-lymphatic disorders. Although efficacy of sclerotherapy has been established in other parts of the body, few studies have been done to show its efficacy in orbital region.[1,10] STS is an anionic surfactant solution in benzyl alcohol 2% that can cause endothelial cell necrosis and thrombus formation of abnormal vessels. As it is the most potent sclerosant agent, we can use the least volume in order to treat venous-lymphatic lesions. The importance of this character is that orbit is a crowded region filled with very important structures. There is always a potential risk of compartment syndrome after any injection in orbital region especially with high volume injections.[1,11] Also, because the volume to be injected is limited per session, repeated sessions are usually needed (2–4 on average). To prevent a possible allergic reaction, it is recommended that a small test dose of STS should be given at the beginning of each session.

Barnacle et al. have done the largest single center study of sclerotherapy in orbital region on 29 patients. In that study, all patients presented with proptosis and/or pseudo-ptosis, and 79% of patients had a decrease in visual acuity at presentation. All treatment procedures in Barnacle et al. study have been done by an interventional radiologist under ultrasound guide (to find best needle placement site) and cystography by digital subtraction angiography to exclude communication between

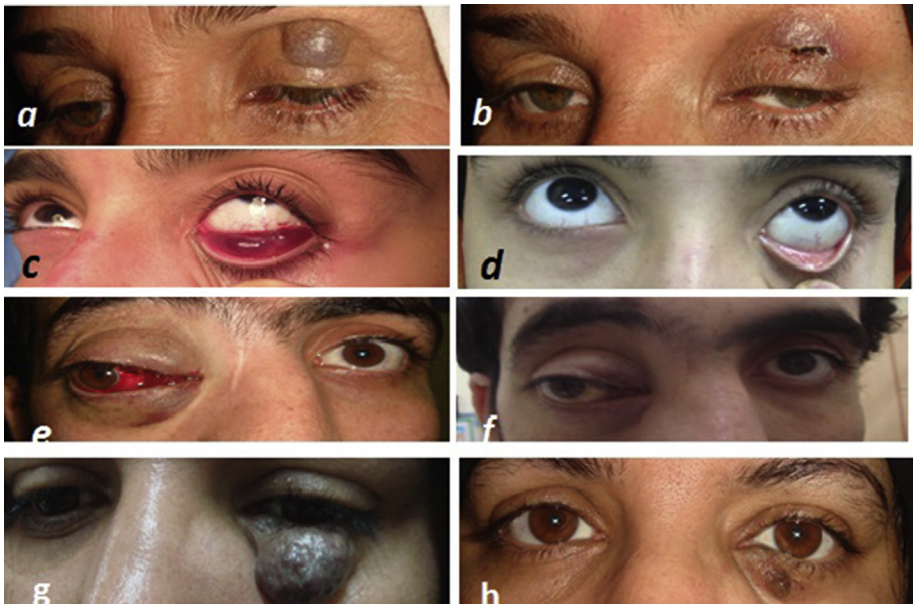

Fig. 1. Before (a) and one month after (b) sclerosant injection into left upper lid lesion of our first patient. As it is visible, superficial tiny skin necrosis and infection which resolved with medication has occurred in this case after injection. Before (c) and 2 months after (d) sclerosant injection into a left lower fornix conjunctival lesion. Patient No 6. Before (e) and 1 months after second injection (f) for a huge anterior orbital venous-lymphatic infiltrating lesion which had a very good response (decreased proptosis of globe with two times of injection). Case No 10 Pre-injection photo (g) and 3 months after third injection (g).

lesional cysts and cavernous sinus. They have shown sclerotherapy with STS under ultrasound (US) guide by an experienced interventional radiologist in deep orbital lymphatic malformations is safe and very effective with minimum side effects.[1]

In 2017, Patel et al. presented three cases of orbital lymphangioma that were treated with sclerotherapy. One of their patients was a 6-month-old boy who was refractory to sclerotherapy with STS and doxycycline but showed response to OK-432. The other two cases reported in their case series were responsive to STS as sclerosant agent.[10]

Chiramel and colleagues selected ten patients with orbital venous-lymphatic lesions and reported resolution of lesion in all patients by injecting STS in the digital subtraction angiography suite.[12] Hill et al. did a procedure that needs an expert interventional radiologist and consists of percutaneous drainage of the cystic component of malformations and then dual-drug chemoablation with sodium tetradecyl sulfate and ethanol for macrocysts (>1 cm) and doxycycline chemoablation alone for microcysts (<1 cm). In addition, for drained macrocysts, a catheter was left in place for 3 days to prevent inflammatory edema and re-endothelialization of the cyst.[6]

Table 1
Patient demographics, pre- and post-sclerotherapy data.

Case no	Age (y)/Sex	Location of lesion	Size of lesion pre-injection (mm)	Size of lesion post-injection (mm)	Number of injections	Total volume of injection (ml)	Orbital imaging
1	36/F	Left upper lid	20*18	12*11	1	0.8	No
2	22/M	Right lower lid and inferior fornix	17*12	Resolution of lid lesion and 3*4 fornix lesion	2	1.7	No
3	17/F	Left lateral upper lid and anterior orbit	30*25	20*15 After minimizing the lesion surgical removal	2	3.4	Yes, extension of vascular lesion laterally to mid globe position
4	24/M	Left upper lid	25*22	10*8	1	1	No
5	28/F	Right upper lid	23*17	resolution	1	0.8	No
6	16/F	Left lower fornix	20*8	resolution	1	1	No
7	19/F	Right upper lid and sub brow	25*20	20*15	2	2.8	No
8	28/M	Right supranal anterior orbit and fornix	Diffuse anterior and deep midorbital lesion	Reduced size of orbital vascular lesion/resolving fornix lesion	3	6	Yes, diffuse anterior and midorbital vascular lesion
9	38/F	Right caruncular lesion	15*15	resolution	1	0.7	No
10	34/F	Left lower lid	30*35	8*10	3	4.5	No
11	14/F	Left lower fornix	20*10	resolution	1	0.8	No

F: Female; M: Male.

In the current study, selected patients had superficial low-flow venous and lymphatic malformations with extension to the eyelids, conjunctiva, and anterior orbit. As almost all parts of the lesions were visible, there was no need to perform ultrasound imaging. Therefore, STS was injected into the lesions by an ophthalmologist without any ultrasound and digital subtraction angiography guidance. Despite the fact that we did not do the treatment under ultrasound or digital subtraction angiography guide due to the superficial nature of the lesions, like previous investigations, sclerotherapy with STS in these patients was effective and safe. This office-based procedure showed different degrees of resolution of the vascular malformations in all cases (Table 1). Two of our patients had large lesions with intra-orbital extension which caused proptosis (documented by orbital CT scan) (Fig. 1 e). Both of them were treated successfully with percutaneous STS injections by an ophthalmologist in his clinic.

The most common side effects are pain at the site of injection, red itchy skin (hives), temporary discoloration of the skin (mostly hyperpigmentation), and superficial thrombophlebitis. Microthrombectomy has been shown in limbal region to be able to decrease post-sclerotherapy hyperpigmentation.[13] Other possible side effects are tissue necrosis due to drug extravasation,[14] neuropathy,[15] and thrombophlebitis.[16] The most serious and devastating side effect in sclerotherapy with STS is a severe form of allergic reaction (anaphylactic shock). It is extremely rare but should be diagnosed and treated immediately, otherwise it may be fatal.[17] Fortunately, we did not have any problem in this regard, but our clinic was equipped with emergency setting table and CPR set. Rarely, disastrous vascular embolic events could happen following STS injections, and these serious complications should be discussed with the patient prior to performing the procedure.[18] To avoid this side effect, we used a small gauge needle after assurance of needle placement out of arterial lumen (with manual aspiration before injection). There were few reported side effects and health problems associated with the procedure and sclerosant material. Minor skin necrosis and superficial infection in limbal region was found in one of the patients (case No 1) after superficial intralesional STS injection which was treated with simple dressing with topical antimicrobial agents and resolved without any significant scar (Fig. 1 a and b). In this study, bruising and hematoma, mild pain during the injections, and in one case superficial tiny skin necrosis and infection (which resolved with medication) were the only side effects. There was not any other significant complication after sclerosant injections in our case series.

There are a few drawbacks of this study. A small number of cases, which could affect the evaluation for efficacy and complication of the procedure, is the first limitation. Another limitation is not assessing the patients' satisfaction based on a standardized questionnaire.

As a conclusion, in-office sclerotherapy with STS seems to be a safe and effective treatment in superficial orbital region, conjunctiva, and eyelids. This study is a small case series study, and further studies with higher sample size are needed to show this approach efficacy and safety in superficial venous-lymphatic lesions of orbit and eyelid. Considering low success rate, high complication, and recurrence rate of surgical treatment of venous-lymphatic malformations, sclerotherapy can be the first line treatment of them in anterior orbit and eyelid region.

References

1. Barnacle AM, Theodorou M, Maling SJ, Abou-Rayyah Y. Sclerotherapy treatment of orbital lymphatic malformations: a large single-centre experience. *Br J Ophthalmol*. 2016;100(2):204–208.
2. Tunç M, Sadri E, Char DH. Orbital lymphangioma: an analysis of 26 patients. *Br J Ophthalmol*. 1999;83(1):76–80.
3. Kennerdell JS, Maroon JC, Garrity JA, Abla AA. Surgical management of orbital lymphangioma with the carbon dioxide laser. *Am J Ophthalmol*. 1986;102(3):308–314.
4. Suzuki Y, Obana A, Gohto Y, Miki T, Otuka H, Inoue Y. Management of orbital lymphangioma using intralesional injection of OK-432. *Br J Ophthalmol*. 2000;84(6):614–617.
5. Svendsen PA, Wikholm G, Rodriguez M, et al. Direct puncture and sclerotherapy with sotradecol ((r)) . Orbital lymphatic malformations. *Intervent Neuroradiol*. 2001;7(3):193–199.
6. Hill 3rd RH, Shiels WE, Foster JA, et al. Percutaneous drainage and ablation as first line therapy for macrocystic and microcystic orbital lymphatic malformations. *Ophthalmic Plast Reconstr Surg*. 2012;28(2):119–125.
7. Poonyathalang A, Preechawat P, Jiarakongmun P, Pongpech S. Sclerosing therapy for orbital lymphangioma using sodium tetradecyl sulfate. *Jpn J Ophthalmol*. 2008;52(4):298–304.
8. Park HS, Do YS, Park KB, et al. Clinical outcome and predictors of treatment response in foam sodium tetradecyl sulfate sclerotherapy of venous malformations. *Eur Radiol*. 2016;26(5):1301–1310.
9. Jenkinson HA, Wilmas KM, Silapunt S. Sodium tetradecyl sulfate: a review of clinical uses. *Dermatol Surg*. 2017;43(11):1313–1320.
10. Patel KC, Kalantzis G, El-Hindy N, Chang BY. Sclerotherapy for orbital lymphangioma - case series and literature review. *In Vivo*. 2017;31(2):263–266.
11. Rosenblatt M. Endovascular management of venous malformations. *Phlebology*. 2007;22(6):264–275.
12. Chiramel GK, Keshava SN, Moses V, Mammen S, David S, Sen S. Percutaneous sclerotherapy of congenital slow-flow vascular malformations of the orbit. *Cardiovasc Interv Radiol*. 2015;38(2):270–279.
13. Scultetus AH, Villavicencio JL, Kao TC, et al. Microthrombectomy reduces postsclerotherapy pigmentation: multicenter randomized trial. *J Vasc Surg*. 2003;38(5):896–903.
14. Dietzek CL. *Sclerotherapy: Introduction to Solutions and Techniques*. Los Angeles, CA: Sage Publications Sage CA; 2007.
15. Stuart S, Barnacle AM, Smith G, Pitt M, Roebuck DJ. Neuropathy after sodium tetradecyl sulfate sclerotherapy of venous malformations in children. *Radiology*. 2015;274(3):897–905.
16. Cavezzi A, Parsi K. Complications of foam sclerotherapy. *Phlebology*. 2012;27(1_suppl):46–51.
17. Crippen C. Anaphylactic reaction to sodium tetradecyl sulfate after sclerotherapy: a case report. *Phlebologie*. 2011;64(2):47–48.
18. Dehghani A, Rezaei L, Ghanbari H, Nasrollahi K, Tavakoli M. Ophthalmic artery occlusion following facial sclerosing therapy. *J Ophthalmic Vis Res*. 2018;13(3):351–354.