Office-based sclerotherapy for recurrent epistaxis due to hereditary hemorrhagic telangiectasia: a pilot study

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Background: **The aim of this pilot study is to evaluate office-based sclerotherapy using sodium tetradecyl sulfate (STS) for epistaxis due to hereditary hemorrhagic telangiectasias (HHT). Patients with HHT suffer from unpredictable, recurrent, severe nasal bleeding necessitating emergency care, nasal packing, blood transfusions, and invasive procedures.**

Methods: **In this retrospective study 7 patients with a history of treatment for recurrent epistaxis due to HHT were treated in an office-based setting with intralesional injection of STS. Treatment results were evaluated using a questionnaire. All patients had undergone multiple prior procedures attempting to control epistaxis.**

Results: **Patients had an average of 5 sclerotherapy treatments for HHT. Patients were treated using topical and/or local anesthesia with no reports of discomfort. Bleeding requiring intervention did not occur during the procedures. After the procedure all patients (100%) reported significantly less frequent and less severe nasal bleeding. A total of 83% reported that their need for nasal packing was reduced. All patients were willing to undergo the same treatment again. No complications such as perforation, crusting, or foul smell were reported.**

Conclusion: **This is the first clinical experience demonstrating that office-based sclerotherapy with STS is a safe, tolerable, and useful alternative for the treatment of epistaxis due to HHT.** © 2011 ARS-AAOA, LLC.

Key Words:
epistaxis; hereditary hemorrhagic telangiectasia; sclerotherapy; sodium tetradecyl sulfate; Osler-Weber-Rendu syndrome

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Hereditary hemorrhagic telangiectasia (HHT) is a familial disorder characterized by the development of vascular malformations throughout the body. Inheritance is autosomally dominant with variable penetrance and expression, affecting genes that produce elastic fibers of blood vessels. This disease affects 1:5000 people with equal tendencies in males and females and it affects all ethnicities.[1] Affected individuals exhibit vascular malformations primarily affecting the nose, gastrointestinal (GI) tract, brain, liver, and lung. Lesions demonstrate markedly dilated, convoluted venules with abnormal smooth muscles, often directly connected to abnormally dilated arterioles.[2]

Recurrent epistaxis is often the presenting symptom in patients with hereditary hemorrhagic telangiectasia, and occurs in 90% of individuals with the disorder.[3] In the nasal epithelium, exposure of the thin-walled telangiectasias to dryness and nasal crusting causes frequent damage to these vessels. The lack of effective elastic fibers prevents constriction, and difficult to control hemorrhage ensues.[2] The frequency and severity of bleeding varies between patients and throughout the life of an individual with HHT, with 50% of patients being symptomatic by age 10 years and 80% to 90% symptomatic by their third decade. The severity is usually worse with advancing age and can vary from minor daily bleeding to major life-threatening bleeding leading to hospitalizations and frequent transfusions.[4]

A step-wise approach to treatment depending on the severity and frequency of bleeding is recommended.[5,6] Often the "less is more" approach is effective, and the patient

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is able to control the bleeding with pressure and or simple packing. Mild recurrent bleeding is reduced by careful and diligent moisturization of the nasal passages. Many patients require iron supplementation to treat anemia. Recurrent or severe epistaxis necessitates referral to the otolaryngologist for treatment.

Common treatments utilized by otolaryngologists are laser coagulation (CO_2, argon, neodymium-doped yttrium aluminum garnet [Nd-YAG], flashlamp-pulsed dye, and potassium titanyl phosphate [KTP]) and septodermoplasty. A reduction in bleeding and improved quality of life is described.[7,8] There are limitations of these procedures, however, including short-term and long-term complications and the need for frequent retreatment. Laser coagulation performed in the operating room can be associated with acute bleeding, necessitating transfusions, packing, or even electrocautery, which can lead to excessive tissue damage. Patients undergoing repeated procedures are at risk for septal perforation, which often leads to worsening of epistaxis as well as crusting and foul odor. Often only 1 nasal cavity can be treated in each setting to prevent tissue damage that puts the patient at risk for perforation. Ultimately many patients undergoing laser treatments will continue to have bleeding necessitating subsequent septodermoplasty.[6] Septodermoplasty is associated with the additional morbidity of the donor site, and nasal issues of crusting, foul odor, and reduced breathing ability.[8] Failures can be seen due to inadequate graft coverage or regrowth of telangiectasias through the grafts, which leads to the need for additional procedures.[9] The limitations of these commonly performed procedures leads to the search for alternative options for treatment.

Sclerotherapy is an established treatment modality for vascular malformations in the skin, GI tract, and genitourinary tract, and has been used for lesions in various sites in the head and neck. Our experience with sclerotherapy using foamed sodium tetradecyl sulfate (STS) for large vascular lesions in the larynx and pharynx led to consideration for its use for epistaxis in patients with HHT. Initial treatments performed under general anesthesia were associated with minimal bleeding; therefore, an office-based setting using topical and or local anesthesia was subsequently implemented for the procedure. The aim of this study was to analyze the tolerability and effectiveness of this procedure in a series of patients with recurrent epistaxis due to HHT.

Patients and methods

Institutional Review Board approval was granted at the University of Minnesota for this retrospective study. The study objective was to assess the treatment outcomes from patients undergoing sclerotherapy for HHT as analyzed by a self-administered questionnaire. All patients with a diagnosis of epistaxis due to HHT treated at the University of Minnesota Otolaryngology clinic with office-based sclerotherapy with STS were identified through review of electronic medical records and were invited to participate in this study. Patients received by mail a package containing a letter with an introduction for the study, a consent form with a thorough description of the study, and a questionnaire (Fig. 1) assessing the patient's perspectives on the outcome of the procedure. Patients who returned both the signed consent form and the questionnaire completed were included in the study. Patients' demographic information and previous treatment data were collected from medical records.

Treatment technique

Topical anesthetic is applied to the nasal mucosa. Local anesthetic can be used if the patient prefers. Endoscopic visualization of the lesions is performed. The interventional radiologist prepares the STS solution for injection by foaming with air at a 4:1 ratio. A 25-gauge needle is inserted into the lesion in a submucosal fashion, penetrating approximately 1-2 mm. Using minimal pressure, small quantities of the STS are injected into the lesion. Individual injection amounts vary between lesions, patients, and treatment sessions. No more than a total of 3 mL of solution is used in 1 session. Injection ceases when the mixture exudes from the lesion or blanching of the lesion is seen. The needle is kept in place for several seconds and then withdrawn. Multiple lesions are treated bilaterally, each with a separate injection. Minimal bleeding is usually encountered, and stops within seconds using pressure or no treatment.

Results

A total of 8 patients were identified and sent the study package. One patient declined to participate and 7 patients responded and voluntarily participated in the survey. The average age of the patients was 58 years, and the average elapsed time since sclerotherapy treatment for HHT was 4.2 months. Three days was the minimum time since treatment. Patients had an average of 5 sclerotherapy treatments for HHT, range 1-7 treatments. The mean follow-up period between sclerotherapy sessions was 3.1 months, with the longest total follow-up period being 3.7 months. Several different treatment modalities had been attempted before sclerotherapy in these patients, with the most common modalities being: cauterization (reported by 71% of the patients), laser therapy (29% of the patients), embolization (43% of the patients), and septodermoplasty (14% of the patients). Additionally, 14% of the patients have had nasal septum perforation, and 43% of the patients had needed blood transfusion due to epistaxis in the past.

The average pain reported during the procedure was 3.9 on a visual analog scale. One patient reported pain that was greater than 4.9, which was 7.7. Bleeding requiring intervention did not occur during the procedures. After the procedure all patients (100%) reported significantly less frequent and less severe nasal bleeding as compared to nasal bleeding before the procedure. A total of 83% of patients reported that their need for nasal packing had reduced significantly after the treatment as compared to before the treatment. Three patients had had previous blood transfusions prior to the treatment and they all reported that their

1. Please indicate on the following scale the level of pain you experienced during the procedure. Place a vertical mark on the line below to indicate how bad you feel your pain was during the procedure.

No pain |_____| *Worst possible pain*

2. Did the frequency of bleeding differ before and after the procedure? Compare the 1-2 month time period before the procedure to the 1-2 month period after the procedure. Please circle the best answer.

Much worse Somewhat worse No different Somewhat better Much better

3. Did the severity of bleeding (amount of blood) differ before and after the procedure? Compare the 1-2 month time period before the procedure to the 1-2 month period after the procedure. Please circle the best answer.

Much worse Somewhat worse No different Somewhat better Much better

4. Did your need for nasal packing differ before and after the treatment? Please circle the most appropriate answer. Nasal packing after the treatment became:

More frequent Same Less frequent

5. Did your need for ER visits for nose bleeding change before and after the sclerotherapy treatment? Please circle the best answer. ER visits for me have become:

More frequent Same Less frequent

6. Did having sclerotherapy treatment affect your need for blood transfusions? Please circle the best answer. Blood transfusions for me have become:

More frequent Same Less frequent

7. Since you have had sclerotherapy treatment for your nose bleeds, has nasal crusting changed? Please circle the best answer. Nasal crusting has become:

More severe Same Less severe I never had nasal crusting

8. Since having sclerotherapy treatment for nose bleeds, have you had a change in foul odor in your nose? Please circle the most appropriate answer. Foul odor in my nose has been:

Better Same Worse I never had foul odor

9. How likely are you to consider undergoing sclerotherapy treatment in the future if you have recurrent nose bleeds?

Never again Not likely Not sure Probably Very likely

FIGURE 1. Patient questionnaire.

need for blood transfusion became less frequent after sclerotherapy. One patient reported temporary nasal crusting after the treatment. No complications such as perforation, crusting, or foul smell were reported. The patients with a preexisting septal perforation, and previous septodermoplasty also reported a reduction in bleeding. All patients (100%) reported that they were willing to undergo the same treatment again in the future.

Discussion

In this select group of patients with recurrent epistaxis due to HHT, sclerotherapy with foamed STS resulted in improvement in nasal symptoms in all patients. All patients reported less severe and less frequent bleeding and most reported a reduction in the need for nasal packing. Besides the beneficial effects of treatment, it was well tolerated, with minimal reports of discomfort, and there were no adverse effects. The procedure could be conveniently performed in the office, saving its cost, and reducing risk associated with general anesthesia. All patients in this series reported willingness to undergo the procedure again if their bleeding recurs in the future.

Current treatments for recurrent epistaxis are aimed at reducing the frequency and severity of bleeding and preventing significant tissue damage that can lead to perforation, crusting and foul odor. Table 1 lists many treatments that have been reported in the literature.[9–45] Many of these are case reports or series demonstrating a positive result in a select group of patients. More extensive reports are available for laser treatments and septodermoplasty and most treatment algorithms that have been promoted rely

TABLE 1. Treatments for epistaxis due to hereditary hemorrhagic telangiectasia

Local
Topical agents
Fibrin glue[10,11]
Hormones[12–14]
Antifibrinolytics[15]
Antiangiogenic agents[16,17]
Cautery
Bipolar[18]
Laser therapy
CO_2[19]
KTP[9,19,20]
Argon[13,14,21–23]
ND:Yag[7,19,24,25]
Flashlamp pulsed-dye[26,27]
Lesion removal methods
Harmonic scalpel[28]
Microdebrider[29]
Septodermoplasty[9,30]
Nasal obturator[31]
Nasal closure[32–36]
Regional
Embolization
Percutaneous[37]
Endovascular[38–40]
External beam radiation[41]
Systemic
Hormones[42,43]
Antifibrinolytics[44]
Antioxidants[45]

KTP = potassium titanyl phosphate; ND:Yag = neodymium-doped yttrium aluminum garnet.

on these modalities as the primary treatments.[6] As previously mentioned, laser coagulation can be beneficial for reduction in bleeding; however, drawbacks include tissue damage, acute bleeding, frequent repeat procedures, and the need for general anesthesia. Septodermoplasty has been beneficial in respect to bleeding and quality of life; however, foul odor, crusting, and frequent recurrence of bleeding was noted.[8,9]

Sclerotherapy with other agents for HHT related epistaxis has been described in case reports and small case series. Etoxisclerol was used for 2 patients who failed cautery, ligation, dermoplasty, and embolization. Control of epistaxis persisted during the 2-year follow-up.[46] A follow-up study treating an additional 6 patients with HHT also showed efficacy.[47] In another study in which 13 patients were treated with Ethibloc, all patients demonstrated decrease in hemorrhage, 90% of them after only 1 treatment. Fifty percent maintained improvement for 4 years of follow-up.[48] A case report of a patient who had failed multiple surgical procedures and embolizations and had subsequently developed a septal perforation, reports successful use of Bleomycin injections. The patient received palliation from bleeding for 2 years of follow-up without requiring adjuvant therapy.[49]

STS is an anionic surfactant commonly used in treatment of varicose veins and other vascular lesions. It is a detergent-based chemical that acts on the lipid molecules in the vein wall which causes destruction of the internal lining of the vein leading to sclerosis. Immediate pathologic effects demonstrate damage of the vascular endothelium within 2 minutes, with increasing edema, vascular damage, and thrombus formation at 15 and 30 minutes.[50] STS has been used to treat cutaneous vascular malformations throughout the body, esophageal varices, spermatoceles, hydroceles, and epididymal cysts. In the head and neck lymphovascular malformations,[51,52] facial telangiectasia,[53] and craniofacial venous malformations[54] have been treated with STS and similar agents. Foam sclerotherapy is a popular variation of the method. The advantage is air bubbles allow the agent to have a more direct contact with the lesion's endothelium, giving a greater effect than liquid alone, which is diluted in blood.[55] Subsequently, a lesser amount of active drug is necessary to treat the lesion successfully.

The most common complications related to sclerotherapy are tissue necrosis and cellulitis due to extravasation of the agent into tissues around the lesion. In a large series treating lymphovascular malformations in the head and neck, cellulitis was a complication in 3 of 31 patients treated with STS in combination with doxycycline and ethanol.[52] Additional adverse reactions and complications of sclerotherapy with STS have been reported. For varicose vein treatment they include: headache, nausea, and vomiting, allergic reactions, anaphylaxis, and pulmonary embolism. For varicose veins in the extremities it is recommended that 0.5 mL to 2 mL of STS be used for each injection, with a maximal single treatment not exceeding 10 ml. Our series used no more than a total of 3 mL of the agent, foamed with air at a 4:1 ratio.

A feared complication of any nasal injection is visual loss. This has occurred during sclerotherapy for HHT using fibrin glue, and is reported as a complication during injections in the head and neck area using a variety of substances.[56] The complication arises when a substance is injected under high pressure, forcing it retrograde through collateral circulation and anastomoses between the external and internal carotid artery back into the internal carotid artery where it can embolize to the ophthalmic artery.

The nature of small-volume, low-pressure, and precisely placed injections minimizes the risk of embolization.

Interventional radiologists frequently use STS to treat vascular lesions. The agent requires mixing, careful handling, and consistent injection technique. The

Otolaryngologist is occupied with endoscopic visualization of the lesion and careful needle placement. The team approach is important and helpful to successfully implement this treatment into the office-based setting.

The authors recognize that this is a pilot study with the inherent weaknesses of the lack of concurrent control subjects, the retrospective and limited nature of the study, the small sample size, and the possibility of response bias.

Conclusion

The outcomes demonstrated in this series warrant further investigation of STS foam sclerotherapy as a treatment for recurrent epistaxis in patients with HHT. Clinical trials comparing the various treatments for epistaxis due to HHT would be beneficial and including office-based sclerotherapy with STS would be worthwhile.

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