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Efficacy of a Topical Sesame/Rose Geranium Oil Compound in Patients with Hereditary Hemorrhagic Telangiectasia Associated Epistaxis

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Objectives/Hypothesis: Topical Sesame/Rose geranium oil compound is an effective therapy for hereditary hemorrhagic telangiectasia (HHT) associated epistaxis.

Study Design: Cohort Study.

Methods: Twenty patients with HHT confirmed by the Curaçao criteria were treated with a sesame/rose geranium oil topical compound between January 2010 and June 2011. A treatment evaluation survey was conducted at least 3 months after treatment initiation. Changes in epistaxis severity scores (ESS), patient satisfaction, and any adverse effects were assessed.

Results: A total of 20 patients completed the study. The average (SD) age was 54.4 (14.6), and 14 (70%) were female. The median time on rose geranium oil was 183 days (IQR: 114–311). At the conclusion of the study, 18 (90%) were still using rose geranium oil. The majority (75%) of patients subjectively felt improvement with the treatment. The improvement was felt to be gradual in 25% and immediate in 50% of patients. Mean (SD) overall satisfaction using a 10-point Likert scale was 7.8 (3.1), with 50% of the patients reporting a satisfaction rating of 10. Mean (SD) epistaxis severity score (ESS) prior to treatment was 5.3 (1.7). After treatment with sesame/rose geranium oil, mean (SD) ESS was found to be 3.5 (1.8). Treatment with sesame/rose geranium oil was associated with a statistically significant improvement in ESS by 1.81 ($P < 0.0001$). There were no adverse side-effects from the treatment.

Conclusion: A sesame/rose geranium oil compound can significantly reduce the epistaxis severity scores of patients with hereditary hemorrhagic telangiectasia-related epistaxis.

Key Words: Hereditary hemorrhagic telangiectasia, epistaxis, sesame oil, rose geranium oil, Osler-Weber, treatment.

Level of Evidence: 4.

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INTRODUCTION

Hereditary hemorrhagic telangiectasia (HHT) or Osler-Weber-Rendu syndrome is an inherited autosomal dominant disease with a prevalence of 1/5,000[1] and is characterized by the presence of recurrent epistaxis; mucosal telangiectasias involving the oral and nasal cavity; visceral arteriovenous malformations (AVMs) including pulmonary, cerebral, and hepatic; and a family history involving first-degree relatives. The presence of three or more of these Curaçao criteria are used to establish the diagnosis of HHT.[2]

The most common symptom of HHT is recurrent epistaxis, which in some cases can lead to blood transfusions and require multiple surgical procedures. Many different surgical procedures have been utilized to control HHT-related epistaxis, including heat or laser cauterization, septodermoplasty, and Young's procedure.[3–5] Additionally, topical therapies have also been used such as oral estrogen, tamoxifen, topical estrogen, aminocaproic acid; and more recently, topical and injected bevacizumab, which has shown promising results for severe, recurrent epistaxis.[6–10] The improvements in epistaxis resulting from these treatments have historically been temporary, with the symptoms often returning over time necessitating repeat interventions.

Physicians at the Johns Hopkins HHT Center of Excellence have been treating HHT-related epistaxis for the past 4 years with a topical sesame oil/rose geranium oil (RGO) therapy that was formulated from a compound used at the Mayo Clinic, Rochester, MN. The purpose of this study is to determine the efficacy of this treatment, as well as to ascertain overall patient satisfaction with the medication and characterize any associated side-effects or complications.

MATERIALS AND METHODS

This is a cohort study of HHT patients treated by the senior author (D.D.R.) for HHT-related epistaxis between January 2010 and June 2011 at the Johns Hopkins Department of Otolaryngology. Patients were included in this study if they presented with at least three of the Curaçao criteria for HHT,[2] and were treated with RGO topical therapy for at least 3 months. The RGO therapy was compounded at the Johns Hopkins Hospital outpatient pharmacy and was developed from a formulation used at the Mayo Clinic in Rochester, MN. For this,

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TABLE I.
Individual Pre- and Post-treatment ESS and Satisfaction in Patients Treated with RGO.

Age	Sex	ESS Score		Change in ESS Score	Level of Satisfaction (1–10)
		Initial	Final		
50	F	6.98	0.5	−6.48	10
63	F	4.53	4.7	0.17	3
20	F	5.31	3.91	−1.4	9
56	M	4.02	2.49	−1.53	8
57	F	6.31	4.63	−1.68	10
44	M	5.98	2.74	−3.24	8
71	F	7.51	5.94	−1.57	7
57	M	8.22	8.22	0	2
64	F	4.66	3.7	−0.96	10
49	F	3.73	3.56	−0.17	1
32	M	3.56	3.02	−0.54	2
37	F	4.52	2.56	−1.96	10
65	F	5.9	4.14	−1.76	10
66	F	6.48	4.7	−1.78	5
77	F	8.22	3.99	−4.23	10
64	F	5.59	4.45	−1.14	10
58	F	3.56	1.6	−1.96	10
31	M	3.17	2.03	−1.14	10
58	M	4.16	1.07	−3.09	9
59	F	2.74	1.07	−1.67	7

0.05 mL of an essential rose geranium oil compound (Fagron, St. Paul, MN) was mixed with 29.95 mL of sesame oil (Letco Medical, Decatur, AL) for a total of 30 mL of topical compound. Three to four drops of this compound was administrated twice daily to each nostril using an eye dropper, with the patient in the Mygind position.[11] All of the patients were asked to refrain from using other topical therapies while on RGO. Patients were excluded if they were younger than 18 years old, had a follow-up of less than 3 months, or underwent any additional treatments for their epistaxis during the study period. Recently, a validated instrument, the Epistaxis Severity Score (ESS), has been developed to assess epistaxis severity in HHT patients.[12] Each patient's ESS was calculated prior to the onset of treatment. A posttreatment survey was administered to each patient at their follow-up visit, or over the phone, at a time greater than 3 months after commencing the RGO in order to determine their posttreatment ESS. Questions on the survey also included whether the RGO was well tolerated; whether the patient subjectively felt that there was improvement, and if so, was it immediate or gradual; any side-effects due to the treatment; and how frequently and often the patient was using the therapy. Additionally, patient satisfaction was determined using a 10-point Likert scale. ESS and survey results were placed in the patient's medical records at time of follow-up. Following the Johns Hopkins Institutional Review Board approval of this study, a review was conducted of the ESS, and clinical information and survey results were collected for each of the patients who met the aforementioned study inclusion criteria.

A descriptive analysis was performed with calculation of means and standard deviations (SD) for continuous variables and proportions for categorical variables. Bivariate analyses were performed using the Student t test for continuous variables, and the Fisher exact test for categorical variables. ESS prior to treatment was compared to those after treatment using a paired t test. A P value <0.05 was considered statistically significant. Analyses were performed using STATA/IC 12.0 (College Station, TX) .

RESULTS

Between January 2010 and June 2011, 24 patients were treated with RGO while 20 patients had follow-up greater than 3 months and completed the study survey (Table I). The average patient (SD) age was 54.4 (14.6), and 14 (70%) were female. The median time on rose geranium oil was 183 days at time of follow-up (IQR: 114–311). On chart review, none of the patients admitted to having a surgical procedure within 3 months prior to starting RGO. At the conclusion of the study, 18 (90%) were still using rose geranium oil. The majority (75%) of patients subjectively felt improvement with the treatment. Eighty-five percent of patients reported that they tolerated RGO well; and of the three who did not, two were still using RGO. The improvement was felt to be gradual in 25% and immediate in 50% of study patients. Mean (SD) overall satisfaction using a 10-point Likert scale was 7.8 (3.1), with 50% of the patients reporting a satisfaction rating of 10. Mean (SD) epistaxis severity score (ESS) prior to treatment was 5.3 (1.7). Figure 1 demonstrates that after treatment with RGO, mean (SD) ESS was found to be 3.5 (1.8). Treatment with RGO was associated with a statistically significant improvement in ESS by 1.81 (P <0.0001). In subjects with an initial ESS of less than 5, treatment with RGO was associated with a statistically significant improvement in ESS by 1.29 ($P = 0.002$). Among subjects with an initial ESS of greater than 5, treatment with RGO resulted in a much greater, but similarly statistically significant improvement in ESS by 2.33 ($P = 0.003$). There were no adverse side-effects from the treatment, although one patient complained of a bad taste associated with the RGO.

DISCUSSION

Laser and/or heat cauterization have been the traditional surgical approaches to treating HHT- related

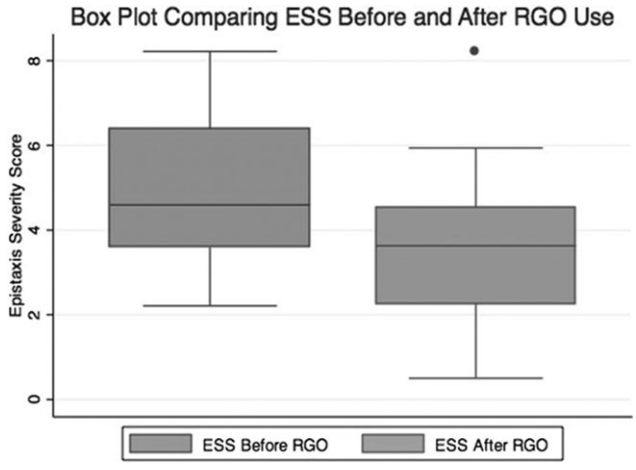

Fig. 1. Mean (SD) epistaxis severity score (ESS) prior to treatment was 5.3 (1.7). After treatment with RGO, mean (SD) ESS was found to be 3.5 (1.8).

epistaxis. Other surgical procedures for control of epistaxis have included embolization,[13] arterial ligation,[14] and nasal closure.[15] While studies may show temporary improvement in the control of epistaxis, these improvements are rarely durable and repeat procedures are usually required.[4,16–17] Septodermoplasty (SDP) is a procedure in which mucosa is removed from the nasal septum in a submucosal/supraperichondrial plane and replaced by a skin graft. Prior studies have shown that this technique reduces the need for subsequent laser treatments.[3] Nasal closure or the Young's procedure has been demonstrated to improve quality of life (QOL) in HHT patients with epistaxis.[15]

Medical therapy for HHT-related epistaxis has included estrogen therapy, progesterone, and topical estrogen.[10,18] Other case reports have demonstrated a positive response with systemic aminocaproic acid[8] and intranasal tranexamic acid.[19] A randomized placebo controlled trial using the anti-estrogen agent Tamoxifin showed a reduction in the severity and frequency of epistaxis.[7]

Previous studies looking at surgical and medical therapies are limited as they lack a standardized tool for measuring improvement in epistaxis severity, and few use other validated measurements of success such as quality-of-life (QOL) instruments. Recently, a validated questionnaire, the Epistaxis Severity Score (ESS), was developed as a standardized measure of epistaxis severity.[12] Karnezis and Davidson used this tool to calculate improvement in epistaxis severity in patients undergoing topical and injected Bevacizumab.[6,20] These studies have demonstrated that this is a promising therapy, yielding significant improvement in HHT-related epistaxis, even in patients with severe nosebleeds. To the best of our knowledge, no other studies have used the ESS to measure HHT treatment outcomes.

This study used the ESS to determine that patients with HHT treated with an RGO topical therapy had improvement in their ESS, with no significant side effects. Patient satisfaction with the RGO therapy was very high, and a majority of patients (90%) continued to use RGO at the completion of this study.

Nasal drying and crusting is extremely common in HHT patients, and this likely contributes to the frequency and severity of their epistaxis. Nasal gels and saline sprays, as well as topical ointments, are frequently recommended to ameliorate these effects and promote nasal humidification. RGO is a viscous liquid that likely creates a durable moisturizing layer. This aids in reducing crusting and preventing superficial telangiectasias from damage, which leads to episodes of epistaxis. Further study is needed to elucidate the exact mechanism. The advantage of RGO is that it is a minimally invasive, well-tolerated therapy that can yield significant sustained improvement in epistaxis severity without the morbidity of surgical procedures that oftentimes fail to provide durable patient benefits. Another potential advantage is that RGO could be used as an adjuvant therapy to other treatments such as Bevacizumab injections. Although this study shows potential promise for future therapy for epistaxis among patients with HHT, it is understood that the small sample size and lack of long-term follow-up may limit generalizability. This study, however, highlights the need for multi-institutional, prospective placebo-controlled trials using the ESS and quality-of-life instruments. These would be extremely valuable in comparing RGO therapy with other traditional approaches, as well as newly developed therapies such as Bevacizumab.

CONCLUSION

RGO topical therapy is a safe and effective therapy for the treatment of HHT-related epistaxis. Further studies using validated tools, such as the ESS and QOL instruments, are required to determine RGO's effectiveness as compared to traditional and newly emerging therapies.

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