

Letter to the Editor

Tranexamic Acid and Bevacizumab in Hereditary Hemorrhagic Telangiectasia Patients Presenting With Epistaxis

To the Editor:

We congratulate Flanagan et al¹ and wish to make some comments on their article, "Intranasal Tranexamic Acid for the Treatment of Hereditary Hemorrhagic Telangiectasia: A Case Report and Review of Treatment Options" (*Cutis*. 2012;89:69-72). Hereditary hemorrhagic telangiectasia (HHT), also known as Rendu-Osler-Weber syndrome, is an autosomal-dominant disorder characterized by the development of multiple arteriovenous malformations (AVMs). Hereditary hemorrhagic telangiectasia should be clinically diagnosed on the basis of the Curaçao criteria, of which 3 criteria must be fulfilled: (1) multiple mucocutaneous telangiectases; (2) epistaxis; (3) visceral involvement; (4) family history of HHT.² Paradoxical embolism from pulmonary AVM is one of the main causes of morbidity.

Flanagan et al¹ stated that all HHT features are seen in both HHT types 1 and 2. However, the phenotypes may differ according to the mutation type. In most cases (85%), either endoglin (encoded by the *ENG* gene) or activin receptor-like kinase 1 (encoded by the activin A type II-like receptor kinase 1 gene, *ACVRL1*), are involved in HHT types 1 and 2, respectively. According to our own prospective series including 35 patients (19 women and 16 men; mean age, 48.4 years), epistaxis was reported in all cases. The following genetic mutations were identified in 28 patients (80%): *ENG* in 16 (57%), *ACVRL1* in 11 (39%), and *SMAD4* (mothers against decapentaplegic homolog 4) in 1 (4%).³ Hereditary hemorrhagic telangiectasia type 2 patients are most likely to develop pulmonary hypertension and liver involvement, while cerebral and pulmonary AVM are more frequent in HHT type 1 patients.^{4,5} Additionally, pancreatic involvement may be more frequent with *ACVRL1* mutations.³ *SMAD4* mutations (transforming growth factor β signal transduction) also may cause HHT disease in association with juvenile polyposis.⁶

Tranexamic acid, an antifibrinolytic agent that competitively inhibits plasminogen activation, has been used orally or locally in the treatment of

epistaxis in HHT patients, thus reducing the incidence of hemorrhagic episodes.^{7,8} Tranexamic acid also may stimulate the expression of the *ACVRL1* and *ENG* pathway, which is deficient in HHT patients.⁹ Furthermore, bevacizumab, an antiangiogenic vascular endothelial growth factor antagonist, may be useful in the treatment of HHT patients with epistaxis, either via intravenous or local use.^{10,11} Tranexamic acid and bevacizumab combined should be further explored because of their potential synergistic action on angiogenesis. Bevacizumab also may help to decrease cardiac output in patients with liver involvement^{10,12} and prevent pulmonary AVM development.¹³

Sincerely,
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The authors report no conflict of interest.

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