

Topical timolol for the treatment of epistaxis in hereditary hemorrhagic telangiectasia^{☆,☆☆}

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Epistaxis is the most common problem affecting patients with hereditary hemorrhagic telangiectasia (HHT). Approximately 90% of patients with HHT experience epistaxis that can range in severity from a social nuisance to life-threatening hemorrhages. Until recently, the treatment of significant epistaxis in these patients consisted of surgery. Surgical options have included laser photocoagulation, septal dermoplasty, and modified Young's procedure [1]. Recently, the vascular endothelial growth factor (VEGF) inhibitor bevacizumab has shown promise as a medical treatment for HHT-related epistaxis [2].

Propranolol is a nonselective β -blocker that has been shown to be useful for the treatment of infantile hemangiomas [3]. Timolol is also a nonselective β -blocker and is commonly used in the treatment of glaucoma. It has been used topically for the treatment of superficial hemangiomas [4]. Because of its potential mechanism of action, it is possible that timolol could also be useful for the treatment of epistaxis related to HHT. This report describes a case of epistaxis in a patient with HHT that was improved with the use of topical timolol drops.

A 48-year-old man with a known diagnosis of HHT presented with frequent epistaxis. His past treatment had included nasal cauterization with silver nitrate as a child and topical bevacizumab. His epistaxis had improved after topical bevacizumab on several occasions. The effect would last for several months with retreatment needed when the nosebleeds became more frequent. Six months after his last treatment, he was experiencing 3 to 4 nosebleeds a day. Some would last for more than 30 minutes. It was

decided to try topical timolol at that time. He began using timolol 0.5% ophthalmic solution and placed 1 drop in each nostril 3 times a day. Within 3 to 4 days, he noticed a significant reduction in the frequency and severity of his epistaxis. A month after the initiation of treatment, his nosebleeds had decreased to an average of 1 to 2 per week, and they lasted less than 5 minutes when they occurred. There was no change in blood pressure or heart rate during the treatment.

1. Discussion

Topical timolol has been used to treat superficial hemangiomas in infants. The mechanism of action of β -blockers in the treatment of hemangiomas is currently unknown but may be related to vasoconstriction, endothelial cell apoptosis, and decreased VEGF expression [5]. Vascular endothelial growth factor levels have been shown to be elevated in patients with HHT and may play a role in the development of nasal telangiectasia [6]. Therefore, it was theorized that timolol could be a viable option in the treatment of epistaxis in patients with HHT. The patient described in this report had both a rapid and persistent response to treatment as is seen in infants with hemangiomas that are treated with β -blockers. The initial response may be secondary to the vasoconstrictive properties of timolol. The longer term effect may be due to endothelial cell apoptosis as well as decreased VEGF expression. The potential advantage of topical timolol compared with bevacizumab includes greater availability of the medication without the need for compounding, ease of application, and decreased cost. Although this is a single case report, the results are encouraging, and further study will allow a greater understanding of the potential use of topical β -blockers in this patient population.

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