

Case Report

The Use of Subconjunctival Erythropoietin Injection to Treat Avascular Bleb after Trabeculectomy: A Case Report

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Abstract

Purpose: To report a patient with avascular bleb after trabeculectomy who showed promising results after subconjunctival erythropoietin injection.

Case Report: A 45-year-old woman with the diagnosis of primary open-angle glaucoma and history of trabeculectomy three years prior was admitted to our center. The corrected distance visual acuity (CDVA) was 20/20 in both eyes. Her ocular examination revealed an avascular and cystic bleb in the right eye. Seidel test was negative while bleb sweating was observed after fluorescein staining of the bleb area. Intraocular pressure (IOP) was 5 mmHg in the right eye. Erythropoietin (2000 unit in 0.1 ml) was injected subconjunctivally around the bleb area in the temporal quadrant. Six weeks after the injection, the bleb area just superior to the conjunctiva showed an increased fibrosis formation while the IOP remained the same as before injection.

Conclusion: Erythropoietin might play a role in preventing the progression of a cystic avascular or hypovascular bleb to a leaking bleb.

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Introduction

Late-Onset bleb leakage, as a result of a thin, cystic and avascular bleb remains one of the major complications after trabeculectomy combined with Mitomycin-C injection. Various methods have been proposed for the management of bleb leakage¹. However, there are no prophylactic methods to prevent the progression of a thin avascular or hypovascular bleb to a leaking bleb. Recently, erythropoietin has been widely used in ophthalmic pathologies including management of recent-onset traumatic, methanol-induced, and non-arteritic ischemic optic neuropathy². We used the subconjunctival injection of erythropoietin in a thin avascular bleb after trabeculectomy. We hypothesized that erythropoietin might increase the bleb vascularity which can prevent future leakage.

Case Report

A 45-year-old woman was referred to our clinic for the routine follow-up with the diagnosis of primary open-angle glaucoma and history of trabeculectomy three years prior. The corrected distance visual acuity (CDVA) was 20/20 in both eyes using a Snellen chart. The ocular examination revealed the presence of an avascular and cystic bleb in the right eye (Figure 1, A and B). Seidel test using fluorescein stripe and blue light was negative for the possible leakage while bleb sweating was observed after fluorescein staining of the bleb area. Intraocular pressure measured by Goldmann applanation tonometry was 5 mmHg in the right eye. Anterior segment examination revealed no pathology except a mild cataract. Macular examination and optical coherence tomography showed no sign of hypotony maculopathy. Other ocular examinations of the right eye and all examinations of the left eye were normal.

To treat the patient initially one drop of povidone Iodine 5 % was instilled in the right eye. Then after using topical tetracaine, erythropoietin was injected subconjunctivally with a dosage of 2000 units in 0.1 mL (PDpoetin®, 10,000 IU/0.5 mL, Pooyesh Darou Biopharmaceutical Co., Tehran, Iran) around the bleb area in the temporal quadrant while the patient was sitting behind a slit lamp. Topical chloramphenicol was instilled after the procedure and was continued every 6 hours for 1 week. The patient was visited daily for one week and then weekly. No leakage was found after injection and on the post injection visits up to six weeks. No cellular reaction in the anterior chamber, sign of episcleritis or scleritis was observed. Figure 1 (C and D) shows the bleb area 6 weeks after the injection. The bleb area just superior to the conjunctiva showed an increase in the fibrosis formation and a mild increase in bleb vascularity. The patient's IOP remained the same as before injection. The present study protocol was approved by our local ethics committee and adhered to the tenets of the declaration of Helsinki. Informed consent was received from the patient before starting the treatment.

Discussion

Our case showed promising results for the use of subconjunctival erythropoietin injection as a preventive measure in avascular thin blebs after trabeculectomy. Both neuroprotective and angiogenic effects have been proposed for erythropoietin in different pathologies³. The neuroprotective effect occurs through the inhibition of apoptosis while the angiogenic effects require the presence of erythropoietin receptors on the capillary endothelial cells. Recently, various studies have reported the expression of erythropoietin receptors on capillary endothelial cells of many tissues

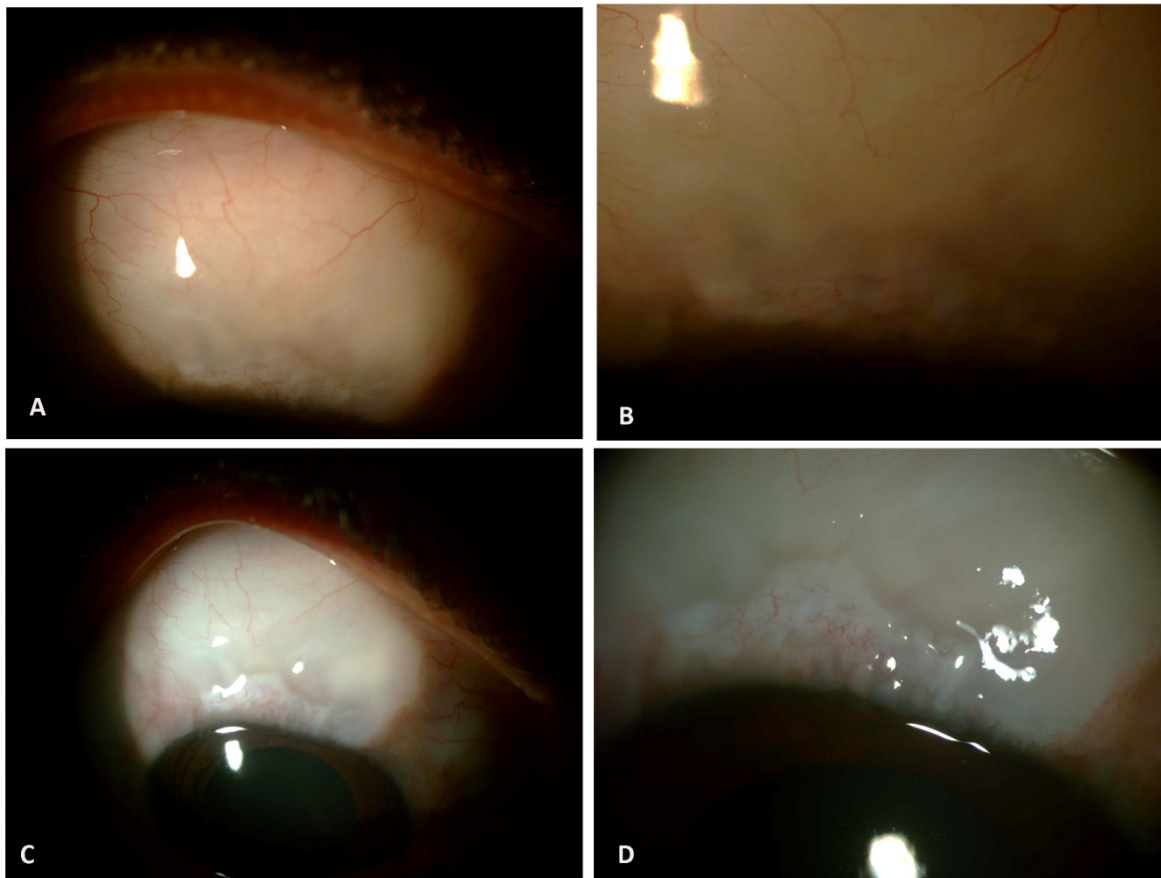


Figure 1: A thin bleb with areas of necrosis and avascularity can be seen in part A, and with higher magnification in part B. Parts C and D show the same patient six weeks after injection of 2000 units of erythropoietin subconjunctivally in the temporal region of the bleb. The fibrosis formation is observed in the bleb just superior to the conjunctiva. Increased vascularization is also evident in this area of the bleb

including the conjunctival stroma ². These receptors may stimulate angiogenesis as effective as a vascular endothelial growth factor ². Besides the erythropoietin's role in the angiogenesis, collagen deposition which leads to fibrosis formation can also be induced by erythropoietin ⁴. Although the angiogenic effects have been observed in the present study, our result is more in favor of collagen deposition induced by erythropoietin as the possible mechanism of action. Repeated doses of erythropoietin might result in further angiogenesis. There is a concern that

fibrosis formation can lead to bleb failure after erythropoietin injection. However, the prevention of a bleb leak at the expense of bleb failure can reduce the chance of possible future endophthalmitis and also the need for extra surgeries.

Regarding the safety issues in the present case, similar route for erythropoietin injection has been used by Resende et al., ⁵ investigating neuroprotective effect of erythropoietin in animal models of glaucoma. The authors reported the subconjunctival route as a safe method of injection with no complications

like scleritis or episcleritis, scleral melt, conjunctivitis, uveitis and endophthalmitis. Furthermore, the erythropoietin dosage used in the present study has been safely used in intravitreal injection of erythropoietin with no sign of retinal toxicity ⁶. However, the safety of subconjunctival injection of erythropoietin cannot be inferred solely based on the results of the present study and needs larger studies to be confirmed.

To the best of our knowledge, subconjunctival erythropoietin has not been used to treat the thin blebs with reduced vascularity. Our study is limited by its case report nature. We recommend case series with longer follow

up periods to further investigate the effect of erythropoietin on avascular or hypovascular blebs.

Conclusion

Erythropoietin might play a role in preventing the progression of a cystic avascular or hypovascular bleb to a leaking bleb.

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References

1. Leung DY, Tham CC. Management of bleb complications after trabeculectomy. *Semin Ophthalmol.* 2013;28(3):144-56.
2. Abri Aghdam K, Soltan Sanjari M, Ghasemi Falavarjani K. Erythropoietin in ophthalmology: A literature review. *J Curr Ophthalmol.* 2016;28(1):5-11.
3. Hernández CC, Burgos CF, Gajardo AH, Silva-Grecchi T, Gavilan J, Toledo JR, et al. Neuroprotective effects of erythropoietin on neurodegenerative and ischemic brain diseases: the role of erythropoietin receptor. *Neural Regen Res.* 2017;12(9):1381-9.
4. Hamed S, Ullmann Y, Masoud M, Hellou E, Khamaysi Z, Teot L. Topical erythropoietin promotes wound repair in diabetic rats. *J Invest Dermatol.* 2010;130(1):287-94.
5. Resende AP, Rosolen SG, Nunes T, São Braz B, Delgado E. Functional and Structural Effects of Erythropoietin Subconjunctival Administration in Glaucomatous Animals. *Biomed Hub.* 2018;3(2):1-11.
6. Acar U, Kucuk B, Sevinc MK, Aykas S, Erdurmus M, Sobaci G. Intravitreal erythropoietin injection in late-stage optic neuropathy: a safety study on human. *Int Ophthalmol.* 2018;38(3):1021-5.

Footnotes and Financial Disclosures

Conflict of interest:

The authors have no conflict of interest with the subject matter of the present manuscript.