



COMPARISON OF SUBCONJUNCTIVAL BEVACIZUMAB AND CONJUNCTIVAL AUTOGRAFT IN MANAGEMENT OF RECURRENT PTERYGIUM

Ophthalmology

Dr Sharmistha Behera

Asso. Professor, Department of Ophthalmology, VSSIMSAR, Burla

Dr Kshyanaprava Priyadarshini*

3rd year PG Resident, Department of Ophthalmology, VSSIMSAR, Burla *Corresponding Author

Dr Sasmita Sahu

Asst. Professor, Department of Ophthalmology, VSSIMSAR, Burla

Dr Jayashree Dora

Professor & HOD, Department of Ophthalmology, VSSIMSAR, Burla

ABSTRACT

AIM: To evaluate the efficacy of subconjunctival bevacizumab injection versus conjunctival autograft in management of recurrent pterygium.
METHODS : 64 eyes of 64 patients affected with recurrent pterygium underwent surgical excision with bare sclera in the study group followed by subconjunctival bevacizumab while the control group was followed by conjunctival autograft. 32 eyes received subconjunctival bevacizumab injections, at the dosage of 1.25mg/0.5 ml. Recurrence rate was evaluated among the two groups.

RESULTS: Mean age of patients in the study group was 39.62yrs while it was 41.5yrs in the control group. Post operative complications & recurrence were more in the control group. 12.5 % of patients had recurrence within 6months in the study group whereas there was 37.5 % recurrence in the control group.

CONCLUSION: This study showed that subconjunctival injection of bevacizumab has better results in treatment of patients with recurrent pterygium without local or systemic adverse effects. At the present time we still await widespread standardization on the modality of administration, timing, and dosage of bevacizumab.

KEYWORDS

INTRODUCTION :

Pterygium is a common ocular surface disorder with a wing shaped fibrovascular overgrowth of bulbar conjunctiva onto the cornea and it is often triangular in shape and consists of a head, i.e., the part which rests on the cornea, a neck, and a body.^[1] Risk factors include exposure to ultraviolet and sunlight, wind, dust, trauma, and inflammation.

Treatment modalities are grouped as :

Adjunctive medical methods	Surgical methods
Mitomycin C	Bare sclera technique
5-fluorouracil	Conjunctival flaps
Daunorubicin	Conjunctival autograft
Thiotepa drops	Amniotic membrane grafts
Cyclosporine drops	Excision with lamellar keratoplasty

Since pterygia are composed of proliferating fibrovascular tissue, it is clear that neovascularization is involved in its development and progression. It has been shown that there is angiogenesis during the formation of pterygia.^[2] Many studies have shown VEGF to be increased in the pathogenesis of pterygia. In order to reduce the rate of recurrence, various modalities have been proposed. The success of pterygium surgery is dependent on the degree of postoperative wound healing and the amount of scar tissue formation. Recurrence occurs as fibroblasts proliferate and migrate towards the cornea.^[3] Various studies have shown that recurrence is high from 30% to 88% after simple excision in pterygium and in excision with bare sclera it may be 32%. VEGF has been detected in increased amounts in pterygium epithelium, compared with normal conjunctiva by studies employing immunohistochemistry.^[4] The most common cause of recurrent pterygium is surgical trauma, and the histopathological components include neovascularization and fibroblast proliferation. Bevacizumab is a recombinant human monoclonal antibody against VEGF, which is approved by FDA treating neoplasms. Many randomized controlled trials (RCTs) were performed to assess the safety and efficacy of bevacizumab in management of pterygium, showing conflicting conclusions.^[5]

This study aims to evaluate the efficacy of subconjunctival bevacizumab injection versus conjunctival autograft in management of recurrent pterygium.

METHODS :

64 eyes of 64 patients with recurrent pterygium were enrolled in this study. A prospective comparative study conducted over a period of 18 months from Sept 2017 to Feb 2019, the patients were randomized into two groups of 32 patients each. Each patient underwent a complete ocular examination including visual acuity, slit lamp biomicroscopy

, intraocular pressure (IOP) measurement & fundoscopy.

Group A - received intraoperative 1.25 mg/0.05 ml subconjunctival bevacizumab after pterygium surgery with bare sclera technique. Group B - underwent pterygium surgery with bare sclera technique followed by repair with conjunctival autograft.

All patients with recurrent pterygium age > 25 years, patients willing to participate in the study, patients willing to follow-up were included in the study. Patients with hypertrophied or atrophic pterygia, acute or inflamed pterygia, pseudo-ptyerygium, conjunctival intra epithelial neoplasia, history of glaucoma, Diabetes mellitus, hypertension, pregnancy, ocular surface disorders, autoimmune diseases were excluded from the study. Patients were followed up at day 1, 1 week, 3 months. Symptoms such as pain, lacrimation and photophobia, grittiness, and redness were noted at each visit. Best-corrected visual acuity, refraction, clinical photographs, and slit lamp examination for any complications such as ischemia, necrosis, infection, graft dehiscence at surgical site were observed. Main outcome measures were recurrence of pterygium & postoperative complications.

Surgical procedure : Peribulbar anesthesia using 2% xylocaine + 0.5% bupivacaine was injected. Then 0.2–0.3 ml injection of 2% xylocaine was given at the site of the pterygium to raise it up to its attachment to the cornea. Using Crescent blade, the pterygium was shaved off the cornea. The pterygium attached with the conjunctiva was separated from the scleral surface with conjunctival scissor and excised leaving about 3–4 mm area of the bare sclera

- In Group A patients, intraoperative subconjunctival bevacizumab 1.25 mg/0.05 ml injection given after the surgery
- In Group B patients, a free conjunctival autograft was then taken from the superior limbal region shifted to the recipient area and stitched limbus to limbus with 6-0 vicryl suture.

RESULTS :

The study & the control group comprised 32 eyes of 32 patients with recurrent pterygium each. This included 12 males & 20 females with a mean age of 39.62yrs in the study group whereas 16 females & 16 males were included in the control group with a mean age of 41.5 yrs.

Table 1: Patient characteristics for groups A and B

	GROUP A	GROUP B
No. of patients	32	32
Mean age	39.62 (32-48)	41.5 (34-52)
Male	12	16
Female	20	16

No significant differences were noted regarding sex and age between the two groups were noted.

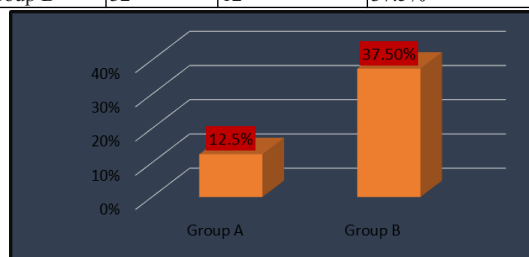
Table 2: Postoperative complications during follow-up period

Postoperative complications	Group A	Group B
Subconjunctival haemorrhage	8	8
Displacement of graft	—	4
Vascularization of graft	—	4

Postoperatively subconjunctival hemorrhage was observed in 8 patients each in both the study & the control group. Displacement & vascularization of the graft was noted in the patients in the control group as compared to bare sclera in the study group.

Table 3: Recurrence rate in study groups after 3 months of follow-up

Treatment group	Number of eyes	No. of patients with recurrence	Recurrence rate
Group A	32	4	12.5%
Group B	32	12	37.5%



12.5 % of patients had recurrence within 6months in the study group whereas there was 37.5 % recurrence in the control group.

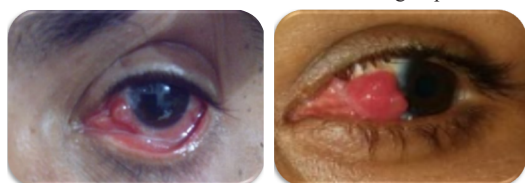
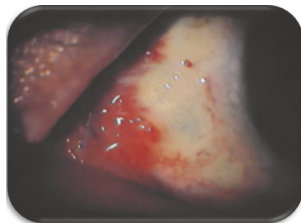


Fig 1 & 2 : Preop images of patients with recurrent pterygium included in the study



Results of application of subconjunctival bevacizumab injections after pterygium surgery with bare sclera technique:



Results after pterygium surgery with conjunctival autograft(CAG)

DISCUSSION:

Inflammation and fibrovascular proliferation are important factors in the pathogenesis of the pterygium which is a degenerative process. The extent and severity of the fibrovascular growth of pterygium seem to comprise a reliable morphologic index for predicting recurrence after surgery.^[6] Anti-VEGF agents such as bevacizumab and ranibizumab have been evaluated as an adjunctive therapy for pterygium along with surgical excision or as a nonsurgical therapy.^[7]

Bevacizumab has been used at various doses at various times by different routes of administration. Nonetheless, the results remain limited and controversial, and there is no clear randomized controlled trial that has studied the efficacy of subconjunctival bevacizumab in

patients with impending recurrent pterygium^[8-10].

A single dose of 1.25 mg of intravitreal bevacizumab has been reported to provide complete intravitreal VEGF blockade for a minimum of 4 weeks, with an intravitreal bevacizumab half-life of approximately 3 days^[8]. The bare sclera technique has been chosen for this study because it is easy to perform and usually associated with higher recurrence rates, thus proving that surgery alone cannot be sufficient to prevent recurrence. The application of subconjunctival bevacizumab in addition to surgical excision seemed to be well tolerated in previous studies. Even in our study, no complications after subconjunctival bevacizumab injections have been reported. Minor side effects of bevacizumab subconjunctival injections, like conjunctival hemorrhage, have been reported but, due to small number of subjects in previous studies, definitive conclusions on safety and long-term effects are still debated. Razaheinejad et al. reported that a single intraoperative subconjunctival bevacizumab injection (1.25 mg/0.1 ml) had no effect on recurrence rate^[11]. Singh et al. used a single low-dose (1.25 mg/0.5 ml) preoperative subconjunctival injection of bevacizumab with no significant effects on recurrence rate after 3 months, even if there was a significant improvement in grade, color intensity, and size of the pterygium.^[12] The recurrence rate in the control group was 37.5 % which was comparable to a study was Simona et al where it was 35% unlike in the study by Allan et al where it was 14%. The complication rates in the control group was comparable to a study by Sinha et al.

A study by El Shafie *et al.*, described that the preoperative subconjunctival bevacizumab (1.25mg/0.05ml) reduces the recurrence rate of pterygium surgery^[13]. Fallah et al. evaluated the efficacy of intralesional bevacizumab injection (2.5mg/0.1ml) in recurrent pterygium, reducing the size of pterygia.^[14] The application of subconjunctival bevacizumab in addition to surgical excision seemed to be well tolerated in previous studies. However, since bevacizumab effects may be transient, a second injection is required in order to inhibit the acute fibrovascular phase that occurs in the immediate postoperative time and may be responsible of the recurrence onset.

CONCLUSION :

This study showed that subconjunctival injection of bevacizumab has better results in treatment of patients with recurrent pterygium without local or systemic adverse effects. At the present time there is still no widespread standardization on the modality of administration, timing, and dose of bevacizumab. The mechanism of pterygium recurrence is still not fully clear, but VEGF and neovascularization play a crucial role in its development. The surgeon must take into consideration many factors in order to lower the risk of recurrence as much as possible. Further investigations are needed to comprehend the real efficacy and limits of an adjunctive therapy with subconjunctival bevacizumab injections. In fact, there is still little experience in the application of bevacizumab as adjunctive treatment to surgical pterygium removal; thus, its recommendation as a first-line therapy is still controversial.

REFERENCES :

- Wright KW. Conjunctival degenerations. In: Cooke DB, Klass FM, editors. Text Book of Ophthalmology. Vol. 1. USA: RR Donnelley; 1997. p. 681-2
- Aspiti M, Tsanou E, Gorezis S, et al. Angiogenesis in pterygium: study of microvessel density, vascular endothelial growth factor, and thrombospondin-1. Eye (London, England) 2007;21(8):1095–1101. doi: 10.1038/sj.eye.6702495.
- Prabhasawat P, Tesavibul N, Leelapatranura K, Phonjan T. Efficacy of subconjunctival 5-fluorouracil and triamcinolone injection in impending recurrent pterygium. Ophthalmology. 2006;113(7):1102–1109. doi: 10.1016/j.ophtha.2006.02.026
- Lee DH, Cho HJ, Kim JT, Choi JS, Joo CK. Expression of vascular endothelial growth factor and inducible nitric oxide synthase in pterygia. Cornea 2001;20:738–42.
- Razaheinejad M. R., Hosseini H., Ahmadi F., Rahat F., Eghbal H. Preliminary results of subconjunctival bevacizumab in primary pterygium excision. Ophthalmic Research. 2010;43(3):134–138. doi: 10.1159/000252980.
- Tan DTH, Chee SP, Dear KBG, Lim AS. Effect of pterygium morphology on pterygium recurrence in a controlled trial comparing conjunctival autografting with bare sclera excision. Arch Ophthalmol. 1997;115(10):1235–1240
- Ozgunhan EB, Alper A, Kara N, Yuksek K, Dermican A, Demirok A. Topical application of bevacizumab as an adjunct to recurrent pterygium surgery. Cornea. 2013;32(6):835–8
- Beer PM, Wong SJ, Hammad AM, Falk NS, O'Malley MR, Khan S. Vitreous levels of unbound bevacizumab and unbound vascular endothelial growth factor in two patients. Retina. 2006;26(8):871–6.
- Mansour AM. Treatment of inflamed pterygia or residual pterygial bed. Br J Ophthalmol. 2009;93(7):864–5.
- Enkvetchakul O, Thanathane O, Rangsin R, Lekhanont K, Suwan-Apichon O. A randomized controlled trial of intralesional bevacizumab injection on primary pterygium: preliminary results. Cornea. 2011;30(11):1213–8.
- Razaheinejad M. R., Hosseini H., Ahmadi F., Rahat F., Eghbal H. Preliminary results of subconjunctival bevacizumab in primary pterygium excision. Ophthalmic Research. 2010;43(3):134–138. doi: 10.1159/000252980.
- Singh P, Sarkar L., Sethi H. S., Gupta V. S. A randomized controlled prospective study to

- assess the role of subconjunctival bevacizumab in primary pterygium surgery in Indian patients. *Indian Journal of Ophthalmology*. 2015;63(10):779–784. doi: 10.4103/0301-4738.171508.
13. El Shafie AM, Mohamed AS, Sayed MF. The outcome of preoperative subconjunctival bevacizumab injection in pterigium surgery. *J Egypt Ophthalmol Soc* 2014;107:113-6.
 14. Fallah Tafti M. R., Khosravifard K., Mohammadpour M., Hashemian M. N., Kiarudi M. Y. Efficacy of intralesional bevacizumab injection in decreasing pterygium size. *Cornea*. 2011;30(2):127–129. doi: 10.1097/ICO.0b013e3181e16d67.