

Efficacy and safety of subconjunctival bevacizumab injection in the management of pterygium

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Abstract

Purpose: To assess the efficacy and safety of sub-conjunctival bevacizumab in the management of grade II and III pterygium.

Materials and Methods: Cases of pterygium with no other ocular abnormality and with no systemic disorders were subjected to anterior segment photography and graded. Ten cases of grade III pterygium and eleven cases of grade II pterygium were administered subconjunctival intralesional injection of 2.5mg/0.1ml of bevacizumab. Anterior segment photographs were taken on day 7, day 28 and day 90 along with complete ocular examination and general physical examination. The pterygium vascularity, size and thickness were assessed keeping note of any adverse effects ophthalmic or otherwise. An evaluation of the symptoms before injection and at day 90 was also done.

Results: There was statistically significant improvement in the grade, color, intensity, size of pterygium, and symptoms of patients. There was a decrease in symptoms of redness, itching, watering, and irritation.

Of the 10 cases with Grade III on enrollment, 08 (80%) had shown a decrease in vascularity with half of them graded as II and the remaining half as grade I.

Of the 11 cases of Grade II pterygium at baseline, 05 (45%) cases changed to grade I by day 90.

Conclusion: This study revealed that the sub-conjunctival injection of bevacizumab was found to be useful in reduction of symptoms of patients with grade III & II pterygium with no local or systemic adverse effects.

Keywords: Bevacizumab, Pterygium, Subconjunctival, Treatment.

Introduction

Pterygium is a fibrovascular growth of subconjunctival tissue which grows into the cornea. There are many hypothesis for the aetio-pathogenesis of this condition. Various regions in the world there is varied prevalence rates ranging from 0.7% to 31%. The condition is more common in warm, dry climates. It has been shown that pterygium cells express cytokines and growth factors on exposure to ultraviolet radiation.¹

Of importance are the studies that suggest an immunologic dysfunction which plays a role in the pathogenesis of pterygium, and many studies have shown increased levels of fibroblast growth factor (FGF) and vascular endothelial growth factor (VEGF) in development of pterygium. In angiogenesis and promotion of endothelial cell proliferation and migration. Vascular endothelial growth factors are directly or indirectly involved in the pathogenesis of pterygium. It has been shown by immunohistochemistry studies that increased levels of VEGF are found in pterygium than in normal conjunctiva. An increase in stimulators as well as decrease in antiangiogenic factors have been found to be important in formation and progression of pterygia.²⁻⁴ Since bevacizumab, a known anti-VEGF agent has already been used for the management of vascular endothelial growth factor induced pathologies in the retina, it has been used in pterygium management as well.⁵⁻⁷

Recurrent pterygium has been treated with topical bevacizumab.^{8,9} Delay in recurrence and regression of limbal conjunctival neovascularization have been reported with use of subconjunctival bevacizumab.

Sub-conjunctival injection of bevacizumab has been used as an adjunct in pterygium surgery¹⁰ and for the recurrent pterygium treatment.^{11,12} But the subconjunctival bevacizumab injection has not been studied widely for the management of primary pterygium.

Hence this study was carried out to evaluate the subconjunctival bevcizumab efficacy and safety for the management of grade II and III pterygium.

Materials and Methods

Cases of pterygium reporting to the eye OPD were evaluated.

The baseline characteristics of pterygium were noted. Grading of pterygium was done according to Tan an coworkers grading scheme.¹³ Slit lamp examination was undertaken and grading was done according to visibility of underlying episcleral blood vessels which has been validated previously as a marker of severity of pterygium. They were divided into grade 1,2 and 3.

Grade I (“atrophic”) episcleral vessels clearly visible under the body of the pterygium.

Grade II (“intermediate”) episcleral vessels partially visible under the body of the pterygium.

Grade III (“fleshy”) episcleral vessels totally obscured under the body of the pterygium.

Pterygium with Grade II and III were taken up for study.

A complete eye evaluation was performed for each patient. This included visual acuity, applanation tonometry and slit lamp examination. Two digital corneal photographs were obtained using an anterior segment digital camera.

According to the system used by Tan et al the size of pterygium was measured from limbus to apex of the pterygium. Using caruncle as landmark its length was measured in centimeters on a slit lamp microscope and the width was measured in centimeters at the apex as well as at the base of pterygium.

Grading of color intensity on scale of 0-4 was done according to Teng et al.¹⁰

(0 = unremarkable, 1 = trace, 2 = mild, 3 = moderate, 4 = diffuse).

Exclusion Criteria

- (a) Women of childbearing potential, pregnant women and lactating women.
- (b) History of myocardial infarction or stroke.
- (c) Case of bleeding diathesis.
- (d) Presence of any other ocular disease.
- (e) Prior ocular trauma
- (f) Patient on any other medication for pterygium treatment
- (g) Patient refusing treatment or follow up
- (h) Patient allergic to bevacizumab

Eligible patients as per the inclusion and exclusion criteria as enumerated above were subjected to subconjunctival injection of bevacizumab. 0.05 cc of bevacizumab (1.25 mg) in area of pterygium body using an insulin syringe with 30 gauge needle.

Patients were then evaluated on day 7, 28 and 90. On each follow up best corrected visual acuity, anterior segment photography for evaluation of grade of pterygium and applanation tonometry were done. Any

adverse events were noted. Complications like corneal epithelial defect, sub-conjunctival hemorrhage or infection, were taken into account.

Results

The age of the patients was between 18 and 65 years with a mean age of 49.46 years. 11(56.67%) were female while 10 patients (43.34%) were males. Female to male ratio was 1.34: 1.

There was no statistically significant difference ($p>0.05$) in visual acuity. Visual acuity remained same or improved postoperatively in both the groups. No worsening of vision was noted. There was a shift of patients from worse to better vision, probably due to a reduction in astigmatism.

Majority of patients presented to us with complaints of redness, mass, and itching. There was a significant reduction in symptoms after injection ($P = 0.0018$). Pain and photophobia were gone, and there was a decrease in redness, itching, watering, and irritation.

Systolic and diastolic blood pressure at different time intervals showed no significant difference ($p>0.05$).

There was a significant reduction in mean surface area and grading which was done according to system used by Tan et al.

Apart from subconjunctival hemorrhage which occurred in 4 patients (19%) and resolved within 2 weeks, no ocular surface toxicity, persistent epithelial defects, corneal abrasion, infections, or uveitis were reported during the study.

The change in the grades of pterygium on day 7, day 28 and day 90 is as per table 1 and summary of changes from baseline to day 90 are as per table 2.

Table 1: Weekly Observations

Time interval	Grade I	Grade II	Grade III
Baseline	0	11 (52.38%)	10 (47.62%)
Day 7	4 (19.05%)	11 (52.38%)	6 (28.57%)
Day 28	8 (38.10%)	9 (42.86%)	4 (19.04%)
Day 90	9 (42.86%)	10 (47.62%)	2 (9.52%)

Table 2: Summary of changes

S No.		III	II	I	Change
1.	Grade III (10)	02	04	04	08/10
2.	Grade II (11)		06	05	05/11
3.	Total (21)	02	10	09 (42.8%)	19/21

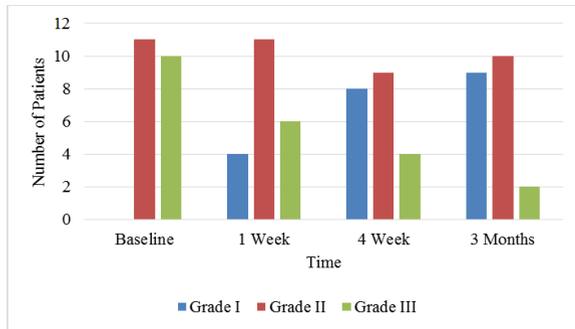


Fig. 1: Pterygium grades after subconjunctival bevacizumab injection

Discussion

On an overview, of the total 21 cases of pterygium in the study population that underwent subconjunctival injection of bevacizumab, 09 cases (42.8%) showed significant decrease in vascularity getting into Grade I.

But on analyzing the 10 cases with Grade III on enrollment, It may be seen that 08 (80%) of these pterygium have shown a decrease in vascularity with half of them graded as II and the remaining half as grade I.

On analyzing the 11 cases of Grade II pterygium at baseline, 05 (45%) cases changed to grade I by day 90.

Pterygium is a triangular growth of subconjunctival tissue of which surgical removal may be required due to irritation, cosmetic blemish, or reduction of vision due to astigmatism or blocking of pupillary area. It may recur after excision. The major goal of pterygium treatment is avoiding recurrence, but complication rates and cosmetic results have also to be considered. There is no gold standard procedure known for pterygium treatment. However pterygium excision with a graft is regarded the best treatment modality.¹⁴ But even the best techniques have the risk of recurrence and complications.¹⁵ Femtosecond assisted flap has been introduced but that would only modify the quality of the conjunctival flap.¹⁶ Mitomycin C and 5-fluorouracil are the antimetabolites which have been found to reduce the chance of recurrence; but can cause undesirable complications like scleral necrosis.¹⁷

In relation to the role of VEGF in the pathogenesis of pterygium and consequently the usefulness of anti-VEGFs in the treatment becomes relevant. There have been studies on pterygium management by the use of both topical and subconjunctival bevacizumab.¹⁸

In this study bevacizumab has been used subconjunctivally in patients of pterygium who had not been subjected to any treatment. The treatment was matched with the grades of pterygium and the improvement. In this study the change of symptoms was also noted. Majority of patients in this study presented with complaints of redness, mass, and itching. Post-injection there was a significant decrease in symptoms after injection ($P = 0.0018$). Pain and

photophobia were gone, and there was a reduction in irritation, redness, itching and watering.

Management of pterygium is a complex issue. Any management which would reduce the symptomatology and postpone surgery is always a welcome situation. This study suggests that the subconjunctival bevacizumab is beneficial in pterygium management.

Conclusion

This study concluded that sub-conjunctival injection of bevacizumab was found beneficial in treatment of grade II and III pterygium with no local or systemic adverse effects.

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