

Intraoperative Triamcinolone Versus Bevacizumab as an Adjunct to Conjunctival Autograft in Primary Pterygium Surgery

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ABSTRACT

Introduction: Pterygium is a wing shaped fibrovascular growth from the bulbar conjunctiva onto the cornea. The treatment of pterygium is surgical excision but it has high recurrence rate. Considering the role of inflammation and angiogenic factors such as VEGF in the formation and recurrence of pterygium, this study was done to evaluate and compare the efficacy of subconjunctival injection of triamcinolone acetonide and bevacizumab as an adjunct to conjunctival autograft in primary pterygium surgery.

Material and methods: Patients with primary pterygium who underwent surgical excision with conjunctival autograft were randomized into three groups. Group A received intraoperative subconjunctival injection of 12 mg of triamcinolone. Group B received intraoperative subconjunctival injection of 2.5mg/0.1ml of Bevacizumab. Group C doesn't received any subconjunctival injection. Recurrence was defined as any fibrovascular growth of conjunctival tissue extending more than 1.5 mm across the limbus over the cornea.

Results: 58 patients (43 males and 15 females) were included in the study. Mean age of the patients was 39.2± 10.4 years. There were 20 patients in group A and 19 patients each in group B and C. Recurrence rate of pterygium in group A, B and C were 10%, 10.5% and 15.78% respectively.

Conclusion: Both triamcinolone and bevacizumab are equally effective in reducing the rate of recurrence of pterygium when used as an adjunct to conjunctival autograft, although this was statistically not significant. Triamcinolone may be preferred over bevacizumab due to cost effectiveness.

Keywords: Pterygium, Recurrence, Triamcinolone, Bevacizumab.

INTRODUCTION

Pterygium is a wing shaped fibrovascular growth from the bulbar conjunctiva onto the cornea. It is a very common ocular surface disorder and it is more prevalent in the people living in hot tropical climate. Although the exact etiopathogenesis of pterygium is not well understood, but exposure to ultraviolet rays is supposed to be a major risk factor for its occurrence.¹ Pathologically pterygium is a degenerative condition of subconjunctival tissue, which undergoes elastotic degeneration and proliferates as vascular granular tissue under the epithelium, it ultimately encroaches the cornea destroying the corneal epithelium, superficial stroma and Bowman's membrane.² Currently instead of being described solely as degeneration of conjunctiva, inflammation and fibrovascular proliferation are proven to be an important factor in its pathogenesis.³ Further recent studies suggest that immunological dysfunction leading to angiogenesis stimulated by ultraviolet radiation plays an important role.⁴

It has also been found that increased levels of pro angiogenic factors like basic fibroblast growth factor(BFGF), transforming

growth factor(TGF- β), vascular endothelial growth factor(VEGF) and platelet derived growth factor are responsible for formation and recurrence of pterygium, however the most prominent of these growth factor is VEGF.⁴

The treatment of pterygium is essentially surgical. Excision of pterygium with bare sclera method is associated with high rate of recurrence (55.5%- 89%).^{5,6} Various methods like application of Beta irradiation, use of Mitomycin- C, 5- Fluorouracil and thiotepa intraoperatively or post operatively has been tried as adjunctive therapy with varying success to prevent recurrence of pterygium.⁵⁻⁷⁻⁹ Furthermore recently conjunctival autograft is being extensively used as an adjunctive procedure with less recurrence rate.^{4,10}

One of the factors responsible for recurrence of pterygium after surgery is post operative conjunctival inflammation. It has been reported that persistent conjunctival inflammation around the surgical site after pterygium surgery is present in about 15% of cases of conjunctival autograft.¹¹ The role of corticosteroid in the prevention of post operative inflammation is well understood. Thus it was thought to use steroid injection (Triamcinolone acetonide) subconjunctivally at the site of surgery to suppress post operative conjunctival inflammation responsible for recurrence of pterygium.

Another factor supposed to be responsible for recurrence of pterygium after surgery is increased level of growth factor especially vascular endothelial growth factor.⁸ Bevacizumab is a humanized monoclonal antibody that inhibits VEGF, the main stimulant of angiogenesis.

Considering the role of inflammation and angiogenic factors such as VEGF in the formation and recurrence of pterygium, this study was done to evaluate and compare the efficacy of subconjunctival injection of triamcinolone acetonide and bevacizumab as an adjunct to conjunctival autograft in primary pterygium surgery.

MATERIAL AND METHODS

This prospective, randomized study included 64 eyes of 64 patients with primary pterygium who underwent surgical excision with conjunctival autograft between September 2013- August 2015. Patients were divided into three groups using random number table. Group A received intraoperative

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subconjunctival injection of 12 mg of triamcinolone (Steroid Group). Group B received intraoperative subconjunctival injection of 2.5mg/0.1ml of Bevacizumab (Bevacizumab group). Group C doesn't received any subconjunctival injection (control group). The study was approved by institute ethics committee of RIMS Ranchi, India. Informed consent was taken from all the patients after explaining to them the nature and consequences of the study.

A through complete ocular examination with best corrected visual acuity, slit lamp biomicroscopy, applanation tonometry and fundoscopy were performed in each patient before and after surgery. Preoperatively, pterygium was graded according to criteria described by Tan et al.²¹ Pterygia were graded as grade T1 (atrophic pterygium) in which episcleral vessels were clearly visible, grade T2 (Intermediate) with partially visible episcleral vessels and grade T3 (fleshy pterygium) in which episcleral vessels were not visible. All surgeries were done by a single surgeon (RG).

Surgical technique

Under peribulbar anaesthesia the pterygium was dissected and peeled off from the underlying cornea and 3-5 mm of conjunctiva covering head and body of pterygium were excised leaving bare sclera near the limbus. Minimal cautery was applied for hemostasis. After excision of the pterygium a conjunctival graft devoid of tenon's capsule was taken from the adjacent superior conjunctiva. It was placed over bare sclera, and was sutured with 10-0 nylon. At the end of surgery, Triamcinolone acetate (12 mg) and Bevacizumab (2.5mg/0.1ml) was injected subconjunctivally in Group- A and Group- B respectively. In Group-C no subconjunctival injection was given after conjunctival autograft. All the subconjunctival injections were given in inferior fornices in order to prevent flap contraction.

Post operatively a topical antibiotic moxifloxacin 0.5%, steroid drop betamethasone 0.1% and preservative free artificial tear (carboxy methyl cellulose 0.5%) each 4 times a day were given and was tapered over a period of 4-6 weeks. All sutures were removed after 2 weeks in post operative period in each group. Post operative follow up examination was performed on day-1, 1 week, 2 weeks, 1 month and 3,6,9 and 12 months after surgery. Patients completing at least 12 months of follow-up were included for analysis.

Recurrence was defined as any fibrovascular growth of conjunctival tissue extending more than 1.5 mm across the limbus over the cornea.

STATISTICAL ANALYSIS

All statistical analysis was done using the SPSS for Windows software (version 18.0, SPSS Inc., Chicago, IL, USA). Categorical data were compared between the study groups using Chi-square test and numerical data were compared using an independent sample-T test. P-values of 0.05 or less were considered as statistically significant.

RESULTS

Out of 62 patients enrolled in the study, 58 patients completed minimum 12 months follow-up. There were 43 males (74.1%) and 15 females (25.9%) patients. Mean age of the patients was 39.2± 10.4 years (range 24–56 years). Pterygium with grade T1

were seen in 11 eyes, grade T2 were seen in 31 eyes, grade T3 were seen in 16 eyes. There were 20 patients in group A and 19 patients each in group B and C. Table 1 shows age, sex and grade of pterygium between different study groups. There were no statistically significant differences in age, sex, and grade of pterygium between the three study groups (Table 1).

No intraoperative complication was noted in any patients in either group. The main outcome of the study was focused on postoperative recurrence. The recurrence of pterygium was seen in 2 patients each in group-A and B, and in 3 patients in group C. Thus the recurrence rate in group A, B and C were 10%, 10.5% and 15.78% respectively. This difference in recurrence of pterygium were statistically not significant ($p > 0.05$). All the recurrences occurred between 8-12 months after surgery. Average month of recurrence was 9.85 months. Further it was observed that recurrence was more in younger age group. Increased intraocular pressure was noted in two eye in group A which received subconjunctival injection of Triamcinolone, which was controlled medically. No any other complication was noted in any eye in either group during 12 months of follow-up.

DISCUSSION

This prospective randomized study was done to evaluate and compare the safety of triamcinolone and bevacizumab and its effect on recurrence rate of pterygium when used as an adjunct to conjunctival autograft.

In our study the recurrence rate was less in group A (10%) and B (10.5%), where subconjunctival injection of Triamcinolone and Bevacizumab was given with conjunctival autograft, while it was more in group-C (15.78%) where only conjunctival autograft was done. Although this difference was statistically not significant ($p > 0.05$).

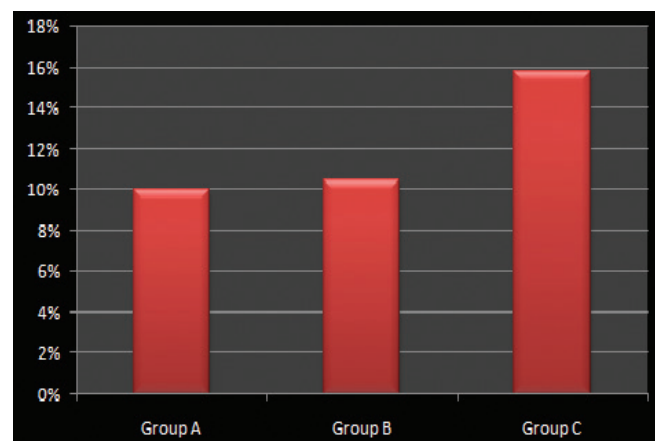


Figure-1: Showing recurrence rate of pterygium between different study groups

	Group A	Group B	Group C
No. of eyes	20	19	19
Age (Years)	40.1±9.6	39.3±9.9	38.1±10.5
Sex (Male/Female)	15/5	13/6	14/5
Pterygium grade (no. of eyes)			
T1	4	5	4
T2	10	10	11
T3	6	4	4

Table-1: Showing age, sex and grade of pterygium between different study groups:

A number of factors such as age, exposure to ultraviolet rays, environment factors, conjunctival inflammation, type of pterygium, various angiogenic factors are responsible for recurrence.^{4-6,14} Keeping in view of etiopathogenesis, several adjunctive therapies like conjunctival autograft, application of mitomycin-C, use of cyclosporine drug, subconjunctival injection of triamcinolone acetonide and bevacizumab along with excision of pterygium was tried to prevent recurrence rate.^{4-6,9,10,12}

The present study has been undertaken to explore the role of subconjunctival injection of triamcinolone and bevacizumab in the prevention of recurrence and any undesirable side effects when used as an adjunct to primary excision with conjunctival autograft.

Triamcinolone acetonide is an intermediate acting medium potency steroid, which is five times more potent than hydrocortisone having duration of action for 15-20 days in conjunctiva. Intraoperative injection of triamcinolone reduces the post operative conjunctival inflammation thereby reducing the rate of recurrence of pterygium.

In a study by A Kheirkhah et al¹³ use of intraoperative triamcinolone injection in pterygium surgery with a bare-sclera technique and mitomycin C application, did not significantly reduce postoperative conjunctival inflammation or pterygium recurrence.

In our study also use of intraoperative triamcinolone injection with conjunctival autograft was not associated with significant decrease in the rate of recurrence of pterygium.

Bevacizumab is a humanized monoclonal antibody that inhibits VEGF, the main stimulant of angiogenesis. It has been tried in treatment of pterygium as an adjunct to surgery. It has been used in both topical and injectable form with different dosing schedule with varying efficacy.¹⁵⁻²⁵

In a study by Razeghinejad MR et al¹⁹ use of bevacizumab after pterygium excision with a rotational conjunctival flap had no significant effect on recurrence rate of pterygium. In our study also use of intraoperative bevacizumab injection with conjunctival autograft was not associated with any significant decrease in the rate of recurrence of pterygium.

Increased intraocular pressure was noted in two patients who received Triamcinolone injection, which were controlled medically. Although various complications had been reported with use of bevacizumab including corneal epitheliopathy,¹⁹ corneal melt²⁶ and increased intraocular pressure²⁷, none of the patients in our study had any side effect related to use of bevacizumab. This could be due to use of low dose and single injection.

CONCLUSION

Both triamcinolone and bevacizumab are equally effective in reducing the rate of recurrence of pterygium when used as an adjunct to conjunctival autograft, although this was statistically not significant. Triamcinolone may be preferred over bevacizumab due to cost effectiveness. However further studies with larger number of patients are needed to know more about the role of triamcinolone and bevacizumab in the treatment of primary pterygium and its recurrence after surgery.

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