

Role and Clinical efficacy of Subconjunctival Injection Bevacizumab in Nonsurgical Management of Pterygium

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ABSTRACT

Introduction: Pterygium progression and recurrence is a common complication. In various studies conducted on role of subconjunctival depot injection of bevacizumab, nothing has been standardized with regards to dosage and its frequency. The study was done with aim to assess role and clinical efficacy of subconjunctival injection of bevacizumab as a non surgical treatment modality for pterygium.

Material and Methods: 80 cases of pterygium were included in this study. Study was done over a period of 12 months from December 2018 to November 2019 at a tertiary care ophthalmic centre of Northern India. In this study, three doses of 2.5 mg of bevacizumab were administered sub-conjunctivally at monthly interval under topical anaesthesia on Outdoor Patient Department basis. Standard aseptic measures were observed.

Results: Cases were followed up next day after each injection and thereafter on monthly basis for three months and finally after 06 months of first injection. Progression of pterygium was noted in 8 cases. Subconjunctival haemorrhage was noted in 41 cases. Conjunctival cyst was seen in three cases which were punctured in OPD, however recurrence was noted after one month in one case. No rise in Intra Ocular Pressure (IOP) was noted.

Conclusions: Subconjunctival injection of bevacizumab is useful in treatment of patients with pterygium without local or systemic adverse effects.

Keywords: Pterygium, Anti VEGF, Subconjunctival Injection, Bevacizumab

INTRODUCTION

Pterygium is known to be a degenerative disorder of subconjunctival tissue with fibrovascular proliferation and encroachment over cornea.¹ The common site is the nasal limbus parallel to interpalpebral fissure.² Its presence leads to ocular surface disorders, astigmatism and media opacity.³ The most commonly executed treatment modality is surgical excision but its recurrence isn't uncommon. This recurrence can be minimised by autograft or Amniotic Membrane Transplantation, as a popular modality. Other modalities are augmentation with mitomycin- C, 5- fluorouracil and other antimetabolites. Irradiation with beta particles has also been tried. All these augmentations come with a baggage of possible complications like sclera melting, punctate epitheliopathy, etc.^{4,5}

Histologically, pterygium is a fibrovascular tissue and is abundant with vascular endothelial growth factor (VEGF).⁶ Blocking VEGF with anti VEGF agents may induce regression of newly formed blood vessels and thereby preventing the pterygium growth. Various anti VEGF agents

are being used as an adjuvant therapy in management of neoplastic tissues in lungs, breasts, brain and ovaries. Bevacizumab, a recombinant humanized murine monoclonal immunoglobulin G1 (IgG1) blocks the VEGF-A isoform and thereby angiogenesis.⁷ Bevacizumab, has been widely used in the management of various vascular retinopathies and corneal vascularization. Its usage has been restricted by various governments for intraocular purposes and has not been FDA approved.⁸

In various studies conducted on role of subconjunctival depot injection of bevacizumab, nothing has been standardized with regards to dosage and its frequency.

The study was done with aim to assess role and clinical efficacy of subconjunctival injection of bevacizumab as a non surgical treatment modality for pterygium.

MATERIAL AND METHODS

A cross sectional study was done at a tertiary care ophthalmic centre of North India over a period of one year from December 2018 to November 2019 to assess the role and efficacy of subconjunctival Injection bevacizumab was done. Cases with less than 2 mm of of nasal pterygium, recurrent pterygium and patient unwilling for surgery were selected for this study. Patients with chronic infective conditions like dacryocystitis, recurrent blepharitis, glaucoma, pregnancy or lactation, auto immune disorders were excluded from this study. Sample size was calculated by using formula

$$ss = \frac{Z^2 \times (p) \times (1-p)}{C^2}$$

Where:

Z = Z value (e.g. 1.96 for 95% confidence level)

p = percentage picking a choice, expressed as decimal (.5 used for sample size needed)

c = confidence interval, expressed as decimal

We recorded the patients age, sex, profession, exposure to sun per day, exposure to snow capped areas or sea, best corrected visual acuity, symptoms like irritation, itching, pain, redness

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and watering. Pterygium length and breadth was measured. Keratometry was performed using Zeiss auto-refractometer and intraocular pressure was assessed using Topcon Non Contact Tonometer. Since there is no standardized dosage for sub conjunctival administration of bevacizumab, we took help from other studies and administered 2.5 mg of bevacizumab underneath the head and neck of pterygial mass so that a bleb was formed. Entire procedure was done on OPD basis under due aseptic measures and topical anaesthesia using eye drops proparacaine hydrochloride 0.5% w/v. A 26 gauge hypodermic needle was used to administer the drug. Post injection individuals were warned to not to rub there eyed for at least one day. Topical antibiotic drops ciprofloxacin hydrochloride 0.3% w/v was given at six hour interval for five days, to prevent any infection. Cases were followed up next day after each injection and thereafter on monthly basis for three months and finally after 06 months of first injection. Statistical analysis was performed using SPSS software version 26 (SPSS, Inc., Chicago, IL). To compare the results between the groups, the Mann–Whitney U test was performed.

RESULTS

A total of 80 eyes of 57 patients were enrolled. All patients completed follow up visits, except two who were lost to follow-up at month three and another subject at month six. The patients were evaluated for the risk factors like age, sex, outdoor activities and residential background and visual acuity. It was found that more young adult males with rural background and outdoor activities and substandard visual acuity reported to us in OPD than otherwise. (Table 1) Cases with higher risk of failure (n=35) were inflamed pterygium (n=4), recurrent pterygium post excision (n=12)

Variable		
Age	Upto 20/21-40/41 and above	0/44/34
Sex	Male/ Females	49/29
Profession	Indoor/ Outdoor	12/66
Background	Rural/Urban	45/33
BSCVA (logMAR)	Less than-0.2/-0.1 to -0.5/-0.6 to -1.0	46/25/07

Table-1: Risk factors

High Risk Cases	No of cases
Inflamed Pterygium	04
Recurrence post excision	12
Arcus senilis	19

Table-2: High risk cases

Progression	1week	1 months	3 months	6 months
BSCVA < -0.2/-0.1 to -0.5/-0.6 to -1.0	48/24/08	53/20/05	54/19/05	54/19/05
Subconjunctival haemorrhage	41	3	0	0
Conjunctival cyst	03	01	01	01
Progression in size (primary/recurrence)	0/0	0/0	01/03	01/03
Hyperemia, pain, itching, watering	23	3	2	0
Switching over to surgery	0	0	0	2

Table-3: Follow up of cases following three injections of sub conjunctival bevacizumab

and arcus senilis (n=19). (Table 2)

Subconjunctival haemorrhage was noted in 41 cases. Conjunctival cyst was seen in three cases which were punctured in OPD, however recurrence was noted after one month in one case. Improvement by one to two lines in Visual acuity on logMAR chart was noted in some cases. This improvement was gradual and was stretched over the entire period of our study. No rise in Intra Ocular Pressure (IOP) was noted. There were no cases of ischemia, necrosis, corneal or scleral melting or infection. Progress was noted in two cases which were later subjected to surgery. (Table 3)

DISCUSSION

In our study we evaluated the efficacy and safety aspect of subconjunctival injection of bevacizumab (7.5 mg in equally divided doses on monthly basis) in prevention of progress of nasal pterygium. In this study, the cases were observed for six months on monthly basis following the third injection. We found our results comparable with other studies. Fallah et al reported delaying of recurrence in cases managed with topical dexamethasone and bevacizumab following pterygium excision.^{7,8,9} In our study only four cases showed continued growth beyond two millimeters despite injections within a span of six months of follow up.

Anti VEGF agents work like a double edged sword. It does come with a baggage of potential adverse effects. In a study wherein topical bevacizumab (12.5 mg/ml) was instilled twice a day for three months in cases with corneal vascularization, they noticed epithelial defects, epitheliopathy and stromal thinning.^{10,11,12} Corneal melting has also been reported in a case of corneal vascularization post penetrating keratoplasty. Studies with intralesional injection of bevacizumab generally had fewer complications. Majority of the complications were intralesional haemorrhage and heaviness for a day or two.^{13,14}

CONCLUSIONS

Subconjunctival injection of bevacizumab is useful in treatment of patients with pterygium without local or systemic adverse effects.

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