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Management of Primary Pterygium with Intralesional Bevacizumab (AVASTIN) Injection

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ABSTRACT

Objective: To determine the management of primary Pterygium with intralesional Bevacizumab (AVASTIN) Injection.
Study Design: Quasi-Experimental Study
Place and Duration of Study: Armed Forces Institute of Ophthalmology, Rawalpindi Pakistan, from Oct 2019 to Mar 2020.
Methodology: Sixty patients of Primary Pterygium with Grades 1, 2, and 3 were included. Pre-Intralesional injection evaluation includes the Ocular surface disease Index (OSDI), grading of Pterygium and ophthalmic examination, refraction, slit lamp bimicroscopy, fundoscopy, tonometry, and corneal topography. After four weeks of intralesional injection, reassessment was done.
Results: A total of 60 participants with the mean age of the participants was 44.06±14.83 years were included in the study. In 26(43.3%) patients, grittiness, epiphora, redness, and photophobia were reported, and 16(26.6%) patients reported blurring of vision that improved in 100% of patients after intralesional injections. There was statistical significance (p-value ≤0.05) in means of K1, Sim K astigmatism, Surface asymmetry index, Surface Regularity Index, Grade of Pterygium, and Ocular surface disease index before and after the intralesional injection of Bevacizumab. However, no significant difference was recorded in Uncorrected Visual Acuity, Best Corrected Visual Acuity, and K2 parameters in pre and post-injection states (p-value ≥0.05). Only 7(11.6%) patients reported subconjunctival haemorrhage after the procedure.
Conclusions: Treatment of Primary Pterygium with intralesional Bevacizumab injection successfully improves symptoms, Ocular Surface Disease Index, and reduces corneal astigmatism with minimum complications.

Keywords: Bevacizumab, Ocular surface disease index, Primary pterygium.

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INTRODUCTION

From the Greek pterygos meaning "wing," Pterygium is a common limbal conjunctival lesion that gradually involves the cornea.[1] Lesion of the nasal limbus is more common than the temporal, often resulting in a characteristic wing-like shape.[2] Fleshy fibrovascular tissue crosses the corneal visual axis when it advances across the limbus.[3] In tropical and subtropical regions, it is one of the most common ocular surface diseases.[4] Squamous metaplasia and goblet cell hyperplasia characterize the pterygium epithelium surrounding the cornea centripetally. A Bowman's layer breakdown also contributes to this condition.[5] With a global prevalence of 0.7% to 33%,[6,7] it affects adults older than 20, with males more frequently than females. In the general population, it affects 7-13% of individuals.[8] Depending on the population studied, other studies have reported a worldwide prevalence ranging from 1 to 25 percent.[9] There is a wide range of pterygium prevalence in India, ranging from 8.4 to 42%.[10] In Pakistan, 7.4% of cases of Pterygium were recorded in a regional study.[8] There is still no definitive explanation for the cause of Pterygium; however, several environmental factors, including ultraviolet light exposure, dryness, occupational exposure to irritants, ocular inflammation, and genetic and immunological factors, are involved in its development.

VEGF receptors, along with other angiogenesis-related molecules. Asvastin® contains Bevacizumab, a recombinant humanized monoclonal IgG1 antibody that can bind to all isoforms of VEGF-A. Binding to and neutralizing VEGFs prevents their interaction with endothelial cell receptors. Primary, perioperative, and early recurrent pterygium treatments have been performed with anti-VEGF agents. Intralesional injection of Bevacizumab (Avastin) was used in this study to evaluate the clinical outcome of primary pterygia without surgical intervention Treatment of patients can be improved by reducing symptoms, Corneal astigmatism and the need for more invasive surgical excision.

METHODOLOGY

The quasi-experimental study was conducted from October 2019 to March 2020, at Armed Forces Institute of Ophthalmology, Rawalpindi Pakistan, after taking approval from the Institutional Review Board.

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The sample size was calculated with the help of the WHO sample size calculator software.

Inclusion Criteria: Patients either gender, aged 20 to 70 years with Grades 1, 2 and 3 primary pterygium were included in our study.

Exclusion Criteria: Patients with an indication of any Ocular Disease except Refractive Errors, Recurrent Pterygium, pseudo pterygium, Conjunctival Intraepithelial Neoplasia, and Prior Ocular Surgery, inability to follow-up during the study period were excluded from the study.

Before enrolling all patients, we obtained their written informed consent, and the confidentiality of the patients was ensured at all levels. A single investigator took detailed Ocular and systematic histories and performed full ophthalmic evaluation, including Refraction, Slitlamp Bimicroscopy, Fundoscopy, Tonometry, and Corneal Topography by ZIEMER Galilei G4 Topographer.[11] The Ocular Surface Disease Index (OSDI),[12] of each patient was calculated.

Grading of the Pterygium was Done according to Ping Huang *et al*.[13] Grade-1: There is translucent tissue under the body of the Pterygium, and episcleral vessels can easily be seen. Veins are slightly dilated. Grade-2: Pink colour is present due to the mild density of dilated vessels within the pterygium tissue. It is still possible to identify the episcleral vessels despite some obscuration. Grade-3: The Pterygium is red; the vessels under the Pterygium are engorged and tortuous; the episcleral vessels beneath the body of the Pterygium are obscured and indistinct.

After taking written informed consent, predesigned proformas were used to collect patient details. In the operation theatre, after installing Topical anaesthetic and 5% Povidone Iodine in the eye, 0.1 to 0.2ml of Bevacizumab (2.5-5mg) was injected in the body of Pterygium, post-injection 1 to 2 drops of Moxifloxacin 0.5% were instilled topically. Following injection, the Patient continues topical antibiotic (Moxifloxacin 0.5%) four times daily for a week. Patients were followed after one week to rule out any injection-related complications. In the fourth week, a post-injection ocular assessment of each patient was performed. It included Refraction, Slitlamp bimicroscopy, Tonometry, and Corneal Topography by ZIEMER Galilei G4 and OSDI.

Data were analyzed using Statistical Package for the social sciences (SPSS) version 22.00 software. Mean ±SD was calculated for continuous variables. Frequency and percentage were calculated for categorical variables. Paired t-test was used. The *p*-value of ≤0.05 was considered significant.

RESULTS

A total of 60 people participated (30 males and 30 females). The mean age of study participants was 44.06 ±14.83 years. 26(43.3%) participants have grittiness, epiphora, redness, and photophobia symptoms, and 16 (26.6%) have blurring vision before applying intralesional Bevacizumab injection. However, symptoms improved in 100% of individuals after intralesional inject ion. Before the injection, 26(43.3%) individuals had mild dry eyes, 31(51.6%) had moderately dry eyes, and 3 (5%) had severe dry eyes, according to the ocular surface disease index. This improved after the Bevacizumab injection, where 25(41.6%) individuals had a normal eyes (no dryness) and 35(58.3%) had only mild dry eyes. Grade of Pterygium also showed improvement post intralesional injection where 15(25%) individuals had Grade-1, and 45(75%) had Grade-2 pterygium compared to the preinjection phase where 2(3.3%) individuals had Grade-1 and 49(81.6%) had Grade-2, and 9(15%) individuals had Grade-3 pterygium. In addition, 53(88.3%) individuals reported no complication post-procedure, whereas 7(11.6%) individuals showed subconjunctival haemorrhage. As seen from the above table, there was statistical significance (*p*-value ≤0.05) in means of K1, Sim K astigmatism, SAI, SRI, Grade of Pterygium, and OSDI before and after the intralesional injection of Bevacizumab. However, no significant difference was recorded in UCVA, BCVA, and K2 parameters in pre and post-injection states (Table).

Table: Comparison of Before and After Intralesional Bevacizumab injection in Primary Pterygium (n=60)

Parameters	Intralesional Bevacizumab Injection in Primary Pterygium		*p*-value
	Pre-Injection	Post-Injection	
Uncorrected visual acuity (UCVA)	3.62±1.439	3.43±1.691	0.505
Best-corrected visual acuity (BCVA)	1.53±0.676	1.25±0.437	0.010
K1	39.11±3.497	41.06±3.191	0.001
K2	43.52±2.43	43.33±2.59	0.060
SimkAstigmatism	-4.41±4.14	-2.26±2.75	0.001
Surface asymmetry index (SAI)	2.31±1.25	1.51±0.66	0.001
Surface regularity index (SRI)	1.16±0.51	0.96±0.33	0.001
Grade	2.12±0.41	1.75±0.43	0.001
Ocular Surface Disease Index (OSDI)	1.62±0.585	0.58±0.497	0.001

DISCUSSION

This study aimed to use anti-VEGF therapy in intralesional Bevacizumab to treat Pterygium. Managing Pterygium can be very challenging due to frequent recurrence. Angiogenesis, proliferation by VEGF, and endothelial cell migration is the important cause of recurrence after pterygium surgery.[12,13] Anti VEGF therapy causes the regression of blood vessels & prevents angiogenesis leading to a decrease in the size of Pterygium.[14,15]

Although Pterygium has unclear pathogenesis, one of the important factors in its formation and progression is neovascularization. It has been proposed that a change in the ratio of an angiogenic stimulator to an inhibitor determines their development.[16] In addition, recent studies have suggested that genetic components, cytokines, extracellular matrix remodelling, antiapoptotic mechanisms, immunological mechanisms, and growth factors may influence the development of the disease. In Pterygium, there is increased expression of several growth factors, includeing epidermal growth factor (EGF), basic fibroblast growth factor (bFGF), vascular endothelial growth factor (VEGF), transforming growth factorbeta, connective tissue growth factor, nerve growth factor, & insulin like growth factor. Jin *et al*. stated that pterygia contain a high level of VEGF, a significantly lower pigment epithelium derived factor (angiogenic inhibitor).[11]

In 2001, Lee *et al*. demonstrated that VEGF might play a role in the development of Pterygium.[17] Thus, administering anti-VEGF like Bevacizumab may reduce fibroblast proliferation and the recurrence rate. Our study showed that 100% of the individuals showed improvement in symptoms post-Bevacizumab injection, and no recurrence was reported after four weeks. Our study showed a change in pterygium grade after four weeks of intralesional Bevacizumab injection, similar to the study carried out by Felipe *et al*.[18] In our study, Visual acuity either remained the same or improved post injection. However, there was no report of worsening vision in any of the 60-patients. There was a noticeable shift in vision, likely due to decreased astigmatism. Mean sim K astigmatism was reduced after the Bevacizumab injection, which was in coherence with another study.[19] We experienced 100% improve-ment in the symptoms of grittiness, epiphora, redness, & photophobia in the majority of our patients.

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LIMITATION OF STUDY

We excluded recurrent cases; further studies are recommended in the recurrent cases, and the post-operative effect of Intralesional Bevacizumab Injection (AVASTIN) should be studied in such cases.

CONCLUSION

Treatment of primary Pterygium with intralesional Bevacizumab injection successfully improves symptoms, Ocular surface disease index and reduces corneal astigmatism with minimum complications.

Conflict of Interest: None.

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

IM & MS: Data acquisition, critical review, approval of the final version to be published.

MA & MM: Conception, study design, drafting the manuscript, approval of the final version to be published.

AR & ZUB: Data analysis, data interpretation, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Bano S, Khan S, Waqar M, Iqbal M, Bhatti HW, Raza A. Effect of pterygium excision on mean corneal curvature. Professional Med J 2021; 28(04): 568-571. doi: 10.4103/ijo.IJO_2747_20
2. Chu WK, Choi HL, Bhat AK, Jhanji V. Pterygium: new insights. Eye (Lond) 2020; 34(6): 1047-1050. doi:10.1038/s41433-020-0786-3.
3. Ghoz N, Britton J, Ross AR, Mohammed I, Hogan E, Said DG, et al. Management of primary pterygium with intra-lesional injection of 5 flurouracil and Bevacizumab (Avastin). Eye 2019; 33(11): 1776-1183. doi: 10.1038/s41433-019-0493-0.
4. Fonseca EC, Rocha EM, Arruda GV. Comparison among adjuvant treatments for primary pterygium: a network meta-analysis. Br J Ophthalmol 2018; 102(6): 748-756. doi: 10.1136/bjophthalmol-2017-310288.
5. Mohamed TA, Soliman W, Fathalla AM, El Refaie A. Effect of single subconjunctival injection of Bevacizumab on primary pterygium: clinical, histopathological and immunohistochemical study. Int J Ophthalmol 2018; 11(5): 797-800. doi: 10.18240/ijo.2018. 05.13
6. Malik S, Khan MS, Basit I. Comparison of primary versus recurrent pterygium after intralesional 5-Fluorouracil. J Pak Med Assoc 2016; 66(1): 559-562.
7. Khan MS, Malik S, Basit I. Effect of intralesional 5 fluorouracil injection in primary pterygium. Pak J Med Sci 2016; 32(1): 130. doi: 10.12669/pjms.321.8169.
8. Haq I, Durra M, Tahir M, Khan MA. Prevalence of Pterygium among Welders in Okara District. Ophthalmol Update 2020; 18(2): 252-257.
9. Supanji S, Purbonegoro T, Dianratri A, Jati KDP, Saputro A, Wibowo AA, et al. Age and gender distribution of pterygium cases from the pterygium surgery social service program. J Community Empower Health 2021; 4(2): 133-139. doi: 10.22146/jcoemph.62285.

10. Graue-Hernandez EO, Córdoba A, Jimenez-Corona A, Ramirez-Miranda A, Navas A, Serna-Ojeda JC, et al. Practice patterns in the management of primary pterygium: a survey study. Cornea 2019; 38(11): 1339-1344. doi: 10.1097/ICO.0000000000002091.
11. Jin J, Guan M, Sima J, Gao G, Zhang M, Liu Z, et al. Decreased pigment epithelium-derived factor and increased vascular endothelial growth factor levels in pterygia. Cornea 2003; 22(5): 473-477.
12. Stival LR, Lago AM, Figueiredo MN, Bittar RH, Machado ML, Nassaralla JJ, et al. Efficacy and safety of subconjunctival bevacizumab for recurrent pterygium. Arq Bras Oftalmol 2014; 77: 4-7. doi:10.5935/0004-2749.20140003
13. Huang P, Huang J, Tepelus T, Maram J, Sadda S, Lee OL, et al. Validity of a new comprehensive pterygia grading scale for use in clinical research and clinical trial. Int Ophthalmol 2018; 38(6): 2303-2311. doi: 10.1007/s10792-017-0722-0
14. Linaburg T, Choi D, Bunya VY, Massaro-Giordano M, Briceño CA. Systematic Review: Effects of pterygium and pingueculum on the ocular surface and efficacy of surgical excision. Cornea 2021; 40(2): 258-267. doi: 10.1097/ICO.0000000000002575.
15. Gordon CR, Rojavin Y, Patel M, Zins JE, Grana G, Kann B, et al. A review on Bevacizumab and surgical wound healing: An important warning to all surgeons. Ann Plast Surg 2009; 62(1): 707-709. Doi: 10.1097/SAP.0b013e3181828141.
16. Singh P, Sarkar L, Sethi HS, Gupta VS. A randomized controlled prospective study to assess the role of subconjunctival Bevacizumab in primary pterygium surgery in Indian patients. Ind J Ophthalmol 2015; 63(10): 779-784. doi: 10.4103/0301-4738 0017 1508.
17. Lee AJ, Lee J, Saw SM, Gazzard G, Koh D, Widjaja D, et al. Prevalence and risk factors associated with dry eye symptoms: a population based study in Indonesia. Br J Ophthalmol 2002; 86(12): 1347–1351.
18. Felipe AF, Siong RL, Uy HS. Subconjunctival injection of bevacizumab for treatment of pterygium. Philipp J Ophthalmol 2009; 34: 44–50.
19. Zhang X, Jiang Y, Fu Q, Zhang X, Chen Y. Efficacy of bevacizumab in the treatment of pterygium: An updated meta-analysis of randomized controlled trials. Int Immunopharmacol 2021; 98: 107921. doi: 10.1016/j.intimp.2021.107921.