

# Effectiveness of Intralesional Bevacizumab in Grade I/II Pterygium as Primary Treatment

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## Abstract:

**Objective:** To determine the effect of Intralesional Bevacizumab in pterygium (grade I/II) as primary treatment in terms of mean change in size.

**Methods:** The quasi-experimental study was conducted in the Ophthalmology Department, Benazir Bhutto Hospital, Rawalpindi, over a period of 6 months, from July 2019 to January 2020. Thirty eyes of patients aged 25–70 years with primary grade I or II pterygium were enrolled using consecutive sampling technique. We measured a reduction in the pterygium size by comparing the baseline measurements with those obtained 1 week, 1 month and 3 months after intralesional injection of 0.1 mL of 2.5mg bevacizumab. We analysed the data using SPSS version 22. Paired sample t-test was applied to compare pre and post injection change in size of pterygium. p-value <0.05 was considered statistically significant.

**Results:** The mean age of total study population was calculated to be  $49.07 \pm 12.06$  SD years. 66.7% (n=20) patients were males and 33.3% (n=10) were females. The mean pterygium length at baseline was found to be  $2.26 \pm 1.05$  mm. We observed a statistically significant difference (p-value  $\leq 0.05$ ) in length of pterygium at 1 week, 1 month and three months after treatment when paired sample t-test was employed.

**Conclusion:** The size of pterygium following the use of intralesional injection of bevacizumab was found to be significantly less at 1 week, 1 month and 3 months, when compared with baseline values. *Al-Shifa Journal of Ophthalmology* 2026; 22(3): 123-129.

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## Introduction:

Pterygium is a prevalent ocular surface disorder featuring a fibrovascular growth of conjunctival tissue onto the cornea<sup>1</sup>. The prevalence of pterygium varies markedly across different geographic regions, ranging from 1 to 30%. Its global prevalence has been estimated at approximately 10.2%, with higher rates reported in populations exposed to ultraviolet radiation, particularly those living in tropical and subtropical climates<sup>2</sup>. This geographic fluctuation signifies the role of environmental factors in its development. Although pterygium is typically described as a degenerative condition of the conjunctiva, its exact pathogenesis remains unclear. Multiple risk factors are associated in the development of pterygium, including excessive exposure to ultraviolet radiation, sunlight, wind, dust, chronic irritation, trauma, and inflammation<sup>3</sup>.

Increasing evidence suggests that inflammation, fibrovascular proliferation, and angiogenesis play vital roles in its development<sup>4</sup>. Pterygium cells produce matrix metalloproteinases (MMPs), which have been implicated in the pathogenesis of pterygium by facilitating invasion into Bowman's layer and the corneal stroma<sup>5</sup>. Pterygium is also composed of actively proliferating fibrovascular tissue, suggesting that neovascularization plays a pivotal role in its formation and progression.

Multiple immunohistochemical studies have demonstrated significantly increased production of vascular endothelial growth factor (VEGF) in pterygium tissue compared with normal conjunctiva and cornea. This overexpression supports the role of angiogenesis in pterygium pathogenesis and identifies VEGF as a potential therapeutic agent<sup>6</sup>.

The primary goal in the management of pterygium is prevention of progression and recurrence. At present, no effective medical therapy exists to reliably halt disease progression, and surgical excision remains the definitive treatment in most clinical settings. However, recurrence rates remain highly variable, ranging from 50% to 80% following simple excision and 5% to 15% with more advanced surgical techniques and adjunctive therapies. Although reduced recurrence has been documented with the use of antifibrotic agents, their use is associated with potentially serious complications, making pterygium management a subject of ongoing debate<sup>7</sup>. Given the established role of VEGF in pterygium pathogenesis, anti-VEGF therapy has emerged as a promising treatment modality. Bevacizumab is a recombinant humanized monoclonal antibody that works by preventing VEGF–receptor interaction and thus inhibits all isoforms of VEGF<sup>8</sup>. A recent local study demonstrated that intralesional bevacizumab injections can reduce pterygium vascularity and size in both primary and recurrent cases, without

significant local or systemic adverse effects<sup>9</sup>. However, that study primarily evaluated bevacizumab as an adjunct to surgical management rather than as primary treatment modality. Evidence regarding the effectiveness of bevacizumab as an independent treatment modality for primary pterygium remains insufficient in the Pakistani population. Therefore, the present study evaluated the effect of intralesional bevacizumab as a primary treatment option, with reduction in pterygium size as the primary outcome. This approach may offer a minimally invasive alternative to surgical treatment, particularly in patients with early pterygium.

### Methods:

A quasi-experimental study was conducted in Ophthalmology Department, Benazir Bhutto Hospital, Rawalpindi, over a period of 6 months, from July 2019 to January 2020. The study included patients with primary pterygium (grade I/II). The sample size was calculated using the Open Epi sample size calculator based on a previous study. Assuming a 95% confidence level, 90% study power, and an effect size of 1.16, the required sample size was determined to be 30 eyes. Data was collected by consecutive sampling technique. Patients between 25 - 70 years of age with primary pterygium (grade I/II) causing symptoms like foreign body sensation, redness, itching and patients with cosmetic concerns were included in the study. Patients presenting with recurrent pterygium, having ocular surface disease like dry eye, ocular allergy, glaucoma, pregnant/lactating women and those allergic to bevacizumab were also excluded from study.

Prior to initiation of the study, approval was obtained from the Institutional Ethics Review Forum of Rawalpindi Medical University. Written informed consent was obtained from all participants. We performed a comprehensive clinical evaluation for each patient, including detailed history taking and documentation

of demographic characteristics such as age, sex, along with presenting ocular symptoms. A detailed ophthalmological examination was also performed for all the patients to exclude coexisting ocular conditions. The examination included assessment of best-corrected visual acuity (BCVA), slit-lamp biomicroscopic examination of the anterior segment, fundus evaluation, and intraocular pressure (IOP) measurement. We documented the site and size of the pterygium prior to intervention, with horizontal extension measured in millimeters using a standardized scale or Vernier caliper. Under strict aseptic conditions and following instillation of topical anesthesia, we injected 0.1 mL of bevacizumab (2.5 mg) into the body of the pterygium in the operating theater.

After the procedure, patients were discharged on topical medications consisting of a combined antibiotic–steroid eye drop administered four times daily, along with artificial tear substitutes four times daily for one week. Follow-up evaluations were performed at 1 week, 1 month, and 3 months post-injection. All clinical data was recorded on predesigned proformas. Pterygium size was used as the

primary outcome measure and reassessed at each follow-up visit for statistical analysis. The data was entered and analyzed using SPSS software version 22. The mean and standard deviations were calculated for Quantitative variables i.e. age, reduction in size of pterygium (baseline and 3 months) measured at baseline and post injection after 1 week, 1 month and 3 months. The 95% within-subject confidence intervals were calculated for pterygium size at baseline and at 1 week, 1 month, and 3 months after the injection. Paired sample t-test was applied to compare pre and post injection change in size of pterygium. P-value  $\leq 0.05$  was considered statistically significant. Effect modifiers like age, gender, grade were controlled by subgrouping. Paired sample t-test was applied to subgroups.

### Results:

We included a total of 30 eyes ( $n = 30$ ) with primary pterygium of grade I or II in the study. All patients presented with symptoms of foreign body sensation, redness, and itching. Demographic characteristics of the study population are shown in table I.

*Table I: Demographics characteristics of the Study Participants*

| Variable | Frequency (%) | Age (mean $\pm$ SD) |
|----------|---------------|---------------------|
| Male     | 20 (66.7%)    | 49.85 $\pm$ 12.20   |
| Female   | 10 (33.3%)    | 47.50 $\pm$ 12.28   |

The mean baseline pterygium size was  $2.26 \pm 1.05$  mm. A progressive reduction in pterygium size following intralesional bevacizumab injection was observed. The mean pterygium size measured  $1.64 \pm 0.69$  mm at 1 week,  $1.38 \pm 0.56$  mm at 1 month, and  $1.08 \pm 0.52$  mm at

3 months after treatment. The paired t-test demonstrated a statistically significant reduction in pterygium size at all follow-up visits compared with baseline ( $p \leq 0.05$ ). Table II presents the detailed statistical analysis.

*Table II: pterygium size at baseline and 1 week, 1 month and 3 months post treatment according to effect modifiers*

| Variables            | N  | Pterygium size<br>Baseline<br>(mm) | Pterygium size<br>1 week<br>(mm)<br>P value <0.001 | Pterygium size<br>1 month<br>(mm)<br>P value <0.000 | Pterygium size<br>3 months<br>(mm)<br>P value <0.000 |
|----------------------|----|------------------------------------|----------------------------------------------------|-----------------------------------------------------|------------------------------------------------------|
| Male                 | 20 | 2.20±1.02                          | 1.65±0.70<br>P value <0.001                        | 1.37±0.51<br>P value <0.000                         | 1.09±0.52<br>P value <0.000                          |
| Female               | 10 | 2.38±1.15                          | 1.63±0.72<br>P value <0.004                        | 1.41±0.66<br>P value <0.004                         | 1.08±0.55<br>P value <0.002                          |
| < 50 years           | 15 | 2.27±1.03                          | 1.63±0.68<br>P value <0.002                        | 1.34±0.48<br>P value <0.000                         | 1.06±0.52<br>P value <0.000                          |
| >50 years            | 15 | 2.25±1.11                          | 1.65±0.73<br>P value <0.002                        | 1.43±0.64<br>P value <0.001                         | 1.11±0.54<br>P value <0.000                          |
| Grade 1<br>Pterygium | 20 | 2.05±1.07                          | 1.46±0.68<br>P value <0.000                        | 1.26±0.59<br>P value <0.000                         | 0.98±0.56<br>P value <0.000                          |
| Grade 2<br>Pterygium | 10 | 2.68±0.92                          | 2.00±0.61<br>P value <0.019                        | 1.63±0.41<br>P value <0.003                         | 1.28±0.39<br>P value <0.000                          |

In four (13.3%) patients, subconjunctival hemorrhage at the injection site was observed. The condition was self-limiting and resolved spontaneously without any intervention. Subgrouping was performed for potential effect modifiers including age, gender, and pterygium grade. Paired sample t-test analysis applied to subgroups demonstrated a statistically significant reduction in mean pterygium size at 1 week, 1 month, and 3 months following treatment ( $p \leq 0.05$ ).

### **Discussion:**

Pterygium is an ocular surface degeneration in which fibrovascular proliferation and chronic inflammation play a significant role in its pathogenesis. Multiple immunological and genetic factors are implicated in disease progression, and growing evidence suggests that an imbalance between angiogenic and anti-angiogenic factors is central to its development<sup>10, 11, 12</sup>. Immunohistochemical studies have demonstrated increased expression of vascular endothelial growth factor (VEGF) in pterygium tissue compared to normal conjunctiva. Consequently, abundant VEGF expression provides a rationale for anti-VEGF therapy

aimed at regression of neovascularization and reduction in pterygium size<sup>13</sup>.

In recent years, several studies have evaluated the effect of local bevacizumab therapy in both primary and recurrent pterygium<sup>12,14</sup>. Our study assessed the effect of intralesional bevacizumab as a primary treatment modality in Grade I and II pterygium, with the aim of introducing a minimally invasive and cost-effective treatment option for the local population. Our results demonstrated a statistically significant reduction in pterygium size following treatment compared to baseline. Additionally, significant associations were observed with effect modifiers such as age, grade, and gender. No serious ocular or systemic adverse effects were observed.

A systematic review and network meta-analysis by Zeng et al., 2017 reported that subconjunctival bevacizumab has been administered in doses ranging from 1.25 mg to 7.5 mg as an adjunctive treatment for pterygium. The 2.5 mg dose used in our study falls within this reported therapeutic range. This meta-analysis reported that intralesional injection of bevacizumab was associated with a 62% reduction in the odds of pterygium recurrence compared with placebo<sup>10</sup>.

Our findings are consistent with the updated meta-analysis of randomized controlled trials by Zhang et al., 2021 which included 1124 patients and reported that subconjunctival bevacizumab at 2.5mg dose, effectively reduces pterygium size by suppressing fibrovascular proliferation. The meta-analysis also demonstrated that bevacizumab reduces the risk of pterygium recurrence and improves overall clinical outcomes, supporting its role as an effective therapeutic option in the management of pterygium<sup>15</sup>.

Similarly, Aziz et al., 2021 demonstrated that intralesional bevacizumab significantly reduced pterygium size and vascularity. Their study included 30 patients with primary pterygium, similar to the present study, and their findings were consistent with our results<sup>16</sup>.

In the present study we observed a reduction in pterygium size (measured in millimeters) along with decreased congestion on gross examination. Ghooz et al., 2019 reported that intralesional injection of 0.2ml of bevacizumab (5mg/ml) combined with 5-fluorouracil significantly reduced the pterygium vascularity and size ( $P < 0.005$ ). However, despite these favorable clinical outcomes, the treatment did not result in a significant reduction in pterygium-induced astigmatism<sup>17</sup>.

In contrast to our findings, Liu et al., 2017 in a systematic review and meta-analysis, reported that subconjunctival bevacizumab did not significantly reduce pterygium recurrence when used as an adjunct to surgery<sup>18</sup>. However, their analysis focused on postoperative recurrence, whereas our study evaluated changes in pterygium size, vascularity, and symptoms following subconjunctival bevacizumab injection. The observed difference may be explained by the different outcome measures and the higher bevacizumab dose used in our study (2.5 mg vs. 1.25 mg in most studies included in the meta-analysis).

Parveen et al., 2023 found that 0.1ml injection of bevacizumab (2.5mg/ml)

offered a favorable safety profile, with no cases of punctate epithelial keratitis, unlike 5-fluorouracil, despite the latter showing greater efficacy in reducing pterygium progression<sup>19</sup>.

The literature regarding bevacizumab use in recurrent pterygium remains controversial. Ghiasian et al., 2022 reported that topical and subconjunctival bevacizumab provide only limited benefit in recurrent pterygium, and current evidence does not support their routine use<sup>20</sup>. Conversely, Mansour et al., 2009 described effective control of inflammation in residual pterygium tissue following subconjunctival anti-VEGF therapy. Similarly, Teng et al., 2009<sup>22</sup> reported transient regression of inflammation and hyperemia following subconjunctival bevacizumab injection in a patient with inflamed primary pterygium<sup>21</sup>. In the present study, our patients experienced symptomatic relief within one week of injection, accompanied by a significant reduction in pterygium size.

Bevacizumab has been used as an adjunct to pterygium surgery. In a prospective randomized controlled trial, Sayadi et al., 2022 reported that preoperative intralesional bevacizumab administered one month before surgery significantly reduced the risk of pterygium recurrence compared with surgery alone<sup>13</sup>. The study also demonstrated significantly improved pterygium color intensity, with 53.3% of patients demonstrating mild color intensity after treatment ( $P = 0.001$ ). Mohamed et al., 2024 reported that preoperative subconjunctival bevacizumab administered before pterygium excision with conjunctival autografting significantly reduced the postoperative recurrence rate, supporting its role as an effective adjunct to surgical management<sup>4</sup>.

In conclusion, intralesional/subconjunctival bevacizumab significantly reduced the size, vascularity, and symptoms of Grade I and II primary pterygium, demonstrating its potential as a safe and effective minimally invasive

treatment, particularly in early-stage disease. The treatment was well tolerated, with no serious adverse effects observed. Although bevacizumab may not replace surgical excision in advanced or progressive cases, it may serve as a useful therapeutic option for selected patients who are poor surgical candidates or prefer a nonsurgical approach. The main limitations of this study were the relatively small sample size, short follow-up period, and the lack of detailed assessment of post-treatment visual acuity and corneal astigmatism. Future multicenter, adequately powered randomized controlled trials with standardized outcome measures and extended follow-up are warranted to determine the optimal dosing strategy, treatment schedule, long-term efficacy, safety, and cost-effectiveness of intralesional/subconjunctival bevacizumab in the management of primary pterygium.

### Conclusion:

The study concluded that the size of pterygium following the use of intralesional/subconjunctival injection of bevacizumab was found to be significantly less at 1 week, 1 month and 3 months, when compared with baseline values.

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