

Role of Intralesional 5-Flourouracil as Primary Treatment of Early Pterygium

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ABSTRACT

Objective: The primary objective of this study was to assess the impact of intralesional 5-FU in early stage pterygium in terms of size reduction, visual acuity improvement, intraocular pressure and efficacy of 5-FU.

Study Design: Quasi experimental study.

Place and Duration of Study: Ophthalmology Department, Fauji Foundation Hospital, Rawalpindi Pakistan, from Jun 2024 to May 2025.

Methodology: The study included 130 patients diagnosed with early-stage pterygium, treated with a single dose of intralesional 5-FU and follow-up assessments conducted at 1week, 1 month, 3 months and 6 months. Follow-up assessments included pterygium size, visual acuity, intraocular pressure and slit-lamp examination.

Results: The study included 130 participants with a mean age of 45.2±10.1 years, with 53.8% aged 45 years or younger. The gender distribution was nearly equal (53.8% males and 46.2% females). Most participants (73.1%) had unilateral pterygium, and 60% had Grade 1 pterygium. Treatment with intralesional 5-FU resulted in a significant reduction in pterygium size (3.1±1.2 mm pre-treatment to 2.0±0.8 mm post-treatment, $p<0.001$). Visual acuity improved from a pre-treatment log MAR score of 0.25±0.18 to 0.18±0.14 post-treatment ($p=0.02$). Efficacy was observed in 85.31% of patients, with higher efficacy in younger males and those with Grade 1 pterygium ($p<0.001$).

Conclusion: Intralesional 5-FU is an effective and safe primary treatment for early-stage pterygium, demonstrating significant reduction in lesion size and low recurrence rates. Further studies with longer follow-up and control groups are needed to validate these findings.

Keywords: Early-Stage Pterygium, Intralesional 5-Fu, Recurrence Rate, Size Reduction, Treatment Efficacy.

How to Cite This Article: Naz A, Haq RIU, Asfandyar, Obaid N, Nazir T, Majeed A. Role of Intralesional 5-Flourouracil as Primary Treatment of Early Pterygium. *Pak Armed Forces Med J* 2025; 76(Suppl-1): S339-S343. DOI: <https://doi.org/10.51253/pafmj.v76iSUPPL-1.13499>

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INTRODUCTION

Pterygium is a common ocular condition characterized by the growth of a fleshy, triangular tissue over the cornea beyond the stem cell limbus.¹ This abnormal growth, which typically starts at the nasal conjunctiva, can gradually extend onto the cornea, potentially causing visual impairment or discomfort.² The known prevalence worldwide reported in literature is 10.2%.³ The exact etiology of pterygium remains multifactorial, with environmental, genetic, and immune-related factors playing pivotal roles in its development.⁴ Prolonged exposure to ultraviolet (UV) light, dust, and wind, especially in individuals residing in areas with high sunlight exposure, has been widely recognized as a primary risk factor.⁵ Although pterygium is generally considered a benign condition, its progression can result in astigmatism, ocular irritation, and even visual impairment if left untreated. Thus, timely intervention

is crucial, particularly when the pterygium is in its early stages.⁶

Historically, the primary treatment for pterygium has been surgical excision, which remains the standard approach in cases where the condition leads to significant discomfort, vision impairment, or recurrent growth.⁶ However, the main challenge with surgical intervention is the risk of recurrence. The recurrence reported in multiple studies with surgical technique is up to 40%.⁷ The recurrence carries the disadvantage of being more invasive than primary and worse prognosis owing to refractoriness to treatment.⁸ To address this, various adjunctive therapies have been explored to reduce recurrence rates and improve surgical outcomes. Among the most promising of these therapies is the use of a chemotherapeutic agent i.e. intralesional 5-fluorouracil (5-FU).⁹ Intralesional 5-FU involves the injection of this cytotoxic drug directly into the pterygium lesion. Being a pyrimidine analogue, it interferes with DNA and RNA synthesis by inhibiting thymidylate synthase thus preventing proliferation of fibroblasts in scar tissue. Its usefulness has been published in various studies in terms of

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Received: 18 May 2025; revision received: 25 Jul 2025; accepted: 11 Sep 2025

efficacy to prevent regression of recurrence. Recent studies have suggested the use of intralesional 5-FU as a primary treatment for early pterygium as a promising alternative to surgical excision.¹⁰ It carries the theoretical advantage of being an outdoor procedure, eliminating the risk of infection, scarring and need for general anesthesia. To best of our knowledge, very limited work has been done to explore the utility as primary modality for treatment of primary pterygium. Evidence is available as systematic literature review suggesting the safety and probably efficacy of intralesional 5-FU in oculo-facial scars management. Furthermore, it suggested that so far existing literature lacks high quality randomized controlled trials to establish efficacy and best protocols for administration.

The rationale of this study is to ascertain the role of 5-FU as primary treatment in early-stage pterygium management. The objective of this study is to assess the role in terms of size reduction, visual acuity improvement, intraocular pressure and efficacy of 5-FU.

METHODOLOGY

This Quasi experimental study was carried out in Ophthalmology department Fauji foundation hospital Rawalpindi, from Jun 2024 to May 2025 after approval of synopsis. Hospital ethical review board approval was sought from committee vide approval letter no 841/RC/FFH/RWP dated 06 June 2024.

The sample size was calculated utilizing WHO sample size calculator, anticipating 87% efficacy of topical 5-flourouracil in patients of primary pterygium¹¹ (Confidence level 90%, Absolute precision 0.05), mandated 122 patients to be included as sample of study.

Inclusion Criteria: The individuals aged between 18 and 65 years with unilateral or bilateral early pterygium that had not yet caused significant corneal involvement.

Exclusion Criteria: Patients with recurrent pterygium, pre-existing ocular conditions such as glaucoma, and those who had undergone previous pterygium surgery were excluded from the study.

Patients were included as per non probability convenient sampling. The methodology is described in patient flow diagram (Figure). Each participant underwent a detailed ophthalmological examination, which included visual acuity testing, slit-lamp biomicroscopy, and measurement of pterygium size.

The size of the pterygium was defined as the extent of the conjunctival tissue encroaching onto the cornea, and only early-stage pterygium (grade 1 or 2) was included in the study, as classified by the Reckitt & Benckiser classification system.

Following the initial examination, all 130 patients were administered intralesional 5-FU injections. The dose of 5-FU was calculated based on the lesion size and was carefully injected under sterile conditions using a fine-gauge needle (insert gauge size). The drug was delivered directly into the base of the pterygium lesion, with each patient receiving a single injection. The injection was performed under local anesthesia to ensure patient comfort. Post-treatment, all patients were followed up at 1 week, 1 month, 3 months, and 6 months after the injection. Follow-up examinations included visual acuity testing, slit-lamp examination, and measurement of the pterygium size to evaluate the effectiveness of the treatment. Efficacy was defined as a significant reduction in pterygium size greater than 1.5 mm after treatment with intralesional 5-flourouracil (5-FU) (Figure).

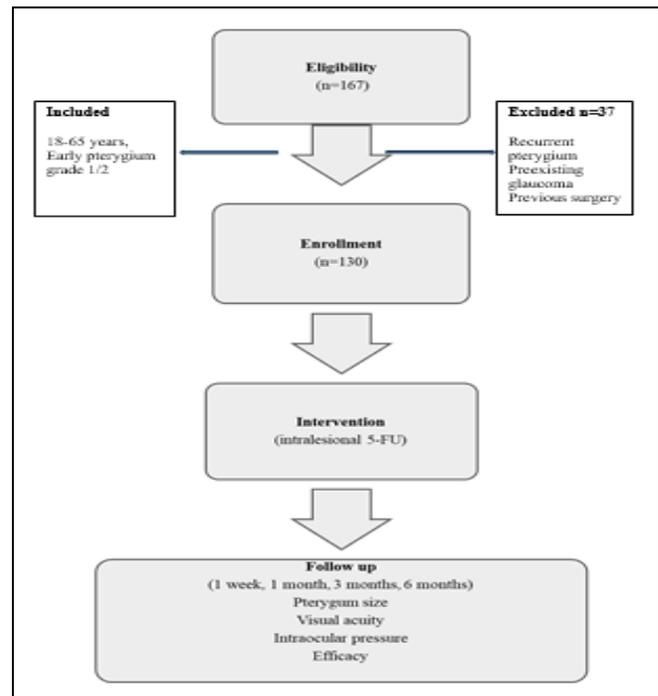


Figure: Patient Flow Diagram (n=130)

Statistical Package for Social Sciences for Mac 24 (Released 2016. IBM SPSS Statistics for Mac, Version 24.0; IBM Corp, Armonk, NY) was used for data analysis. The data analysis involved summarizing participant characteristics using descriptive statistics,

including Mean±SD and median with interquartile range (IQR) for continuous variables and frequencies for categorical variables. Paired t-tests were used to compare pre- and post-treatment values for pterygium size, and intraocular pressure, and Wilcoxon signed-rank test for visual acuity with a *p*-value of <0.05 considered significant. Chi-square tests were used to compare efficacy across demographic groups. Stratified analyses were conducted for age, gender, laterality, and pterygium grade, with statistical significance set at *p*≤0.05.

RESULTS

The study included 130 participants with a mean age of 45.2±10.1 years. Of these, 53.8% (70) were aged 45 years or younger, while 46.2% (60) were older than 45 years. The gender distribution was nearly equal, with 53.8% (70) males and 46.2% (60) females. Most participants (73.1%, 95) had unilateral pterygium, while 26.9% (35) had bilateral involvement. In terms of pterygium grade, 60% (78) of the cases were classified as Grade 1 (early-stage), and 40% (52) were classified as Grade 2 (early-stage) as given in table-I.

Table-I: Demographics of Study Participants (n=130)

Variable	Categories	n(%)
Age	(Mean±SD)	45.2±10.1
	≤45 years	70(53.8%)
	>45 years	60(46.2%)
Gender	Male	70(53.8%)
	Female	60(46.2%)
Laterality of Pterygium	Unilateral	95(73.1%)
	Bilateral	35(26.9%)
Pterygium Grade	Grade 1 (Early-stage)	78(60.0%)
	Grade 2 (Early-stage)	52(40.0%)

The treatment with intralesional 5-FU resulted in a significant reduction in pterygium size, with the mean initial size being 3.1±1.2 mm pre-treatment and decreasing to 2.0±0.8 mm post-treatment (*p*-value <0.001). Visual acuity also improved, with the pre-treatment log MAR score averaging 0.25±0.18 and improving to 0.18±0.14 post-treatment (*p*-value =0.02). However, intraocular pressure (IOP) did not show a significant change, with pre-treatment IOP at 14.2±2.3 mmHg and post-treatment IOP at 14.5±2.1 mmHg (*p*-value =0.15). Regarding treatment efficacy, 85.31% of patients (111) showed significant size reduction greater than 1.5 mm, while 14.69% (19) did not experience significant improvement (*p*-value <0.001) given in table-II.

The efficacy of intralesional 5-FU treatment varied based on demographic and clinical factors. In

terms of age, 88.57% of patients aged 45 years or younger showed efficacy, compared to 81.67% of patients over 45 years, with a statistically significant difference (*p*-value <0.001). For gender, a higher proportion of male patients (95.71%) experienced efficacy, while only 73.33% of female patients showed similar results, which was statistically significant (*p*-value <0.001). Regarding laterality of pterygium, 84.21% of patients with unilateral pterygium showed efficacy, compared to 88.57% of those with bilateral pterygium, with a statistically significant difference between groups (*p*-value =0.03). Finally, in terms of pterygium grade, 94.87% of patients with Grade 1 (early-stage) pterygium showed efficacy, whereas only 71.15% of patients with Grade 2 (early-stage) pterygium had similar results, with this difference being statistically significant (*p*-value <0.001).

Table-II: Outcome Variables of the Intralesional 5-FU Treatment (n=130)

Variables	Categories	Values	<i>p</i> -value
Initial Pterygium Size (mm)	Pre-treatment	3.1±1.2	<0.001
	Post-treatment	2.0±0.8	
Visual Acuity (logMAR Score)	Pre-treatment	0.3(0.2-0.6)*	0.02**
	Post-treatment	0.2(0.1-0.3)*	
Intraocular Pressure (mm Hg)	Pre-treatment	14.2±2.3	0.15
	Post-treatment	14.5±2.1	
Efficacy of Treatment (Size reduction >1.5 mm)	Yes	111(85.31%)	<0.001
	No	19(14.69%)	

*Median (interquartile range) **Wilcoxon ranked-sign test

Table-III: Efficacy stratified by Age, Gender, Laterality of Pterygium, and Pterygium Grade (n=130)

Variables	Categories	Efficacy (Yes) n=111	Efficacy (No) n=19	<i>p</i> -value
Age Group	≤ 45 years	62(88.57%)	8(11.43%)	<0.001
	> 45 years	49(81.67%)	11(18.33%)	
Gender	Male	67(95.71%)	3(4.29%)	<0.001*
	Female	44(73.33%)	16(26.67%)	
Laterality of Pterygium	Unilateral	80(84.21%)	15(15.79%)	0.03*
	Bilateral	31(88.57%)	4(11.43%)	
Pterygium Grade	Grade 1 (Early-stage)	74(94.87%)	4(5.13%)	<0.001*
	Grade 2 (Early-stage)	37(71.15%)	15(28.85%)	

*chi square test

DISCUSSION

Intralesional 5-fluorouracil (5-FU) has emerged as a promising adjunctive therapy, potentially offering an effective primary treatment for early-stage pterygium.¹² The reported efficacy in one of studies is 87.13% - 97.13% suggesting the need to explore this modality in further studies.^{12,13} This study explores the role of intralesional 5-FU in managing early pterygium

by examining its effects on lesion size reduction and recurrence rates. It also assesses the safety and feasibility of this approach as a non-surgical alternative.

In our study, the mean initial pterygium size was 3.1 ± 1.2 mm, which is comparable to the findings of Lee *et al.*, (2022), who reported that the mean initial pterygium size ranged from 2 to 4 mm in 57.2% of eyes treated with 5-FU.¹⁴ Furthermore, Valezi *et al.*, (2022) found that the mean initial pterygium size was 3.94 mm in their study cohort, which also falls within a similar range to our study's mean size. These results suggest that intralesional 5-FU is consistently applied in early-stage pterygium, with the average lesion size being between 2 and 4 mm in most cases. The proportion of unilateral pterygium in our study (73.1%) was consistent with Lee *et al.*, who reported that 80% of their cohort had unilateral pterygium, and Valezi *et al.*, who found that 72% of their participants had unilateral cases.^{14,15} In terms of visual acuity, our study demonstrated a significant improvement which aligns with the results of Shah *et al.* where the change in uncorrected distant visual acuity (UCVA) before and after treatment was minimal (0.162 ± 0.167 to 0.166 ± 0.168).¹¹ Our findings suggest that 5-FU treatment can lead to slight but meaningful improvements in visual acuity, as has been documented in other studies. Moreover, Prabhasawat *et al.*, also reported that intralesional 5-FU was successful in reducing recurrence rates in impending recurrent pterygium, though they did not specifically measure visual acuity.^{12,16}

In terms of efficacy of treatment, our study found that 85.31% of patients experienced significant pterygium size reduction greater than 1.5 mm, which is consistent with Lee *et al.*, who reported that postoperative intralesional injections of 5-FU effectively arrested progression in 81.3–96% of primary and recurrent pterygia. Additionally, Prabhasawat *et al.*, demonstrated that 5-FU improved the success rate and reduced recurrence in impending recurrent pterygium.^{16,17} Parveen *et al.*, observed significant improvement in 65.6% of patients treated with 5-FU, compared to just 6.3% in the Bevacizumab group, which aligns with our study's finding.¹⁸ Similarly, Ghazizadeh *et al.*, reported a 89% reduction in lesion thickness and improvement in redness, which correlates with our observation of a reduction in pterygium size from 3.1 ± 1.2 mm pre-treatment to 2.0 ± 0.8 mm post-treatment.¹⁹ Our study echoes these

findings, with a high efficacy rate of 85.31%, suggesting that intralesional 5-FU is highly effective in reducing the size of early-stage pterygium and preventing recurrence.

Rahman *et al.*, found that 5-FU injections resulted in regression of fibrovascular tissue, with no complications. Despite the smaller sample size in Rahman's study, the effectiveness of repeated 5-FU injections in recurrent pterygium was evident, which supports our observation of minimal recurrence after treatment.²⁰ Efficacy of the weekly 5-FU has been studied in one of the studies and has been reported to be 85.3%. Moreover, the study reported the effect was maintained over a prolonged follow up period of 17 months.²¹

Despite these advantages, there are some challenges and limitations to the use of intralesional 5-FU in the treatment of pterygium. The optimal dosage, frequency, and duration of 5-FU injections remain a topic of debate, as different studies have reported varying outcomes and is beyond the scope of this study. Additionally, the long-term effects of intralesional 5-FU on ocular tissues and the potential for complications with repeated treatment cycles have yet to be fully understood. Ongoing research and clinical trials are essential to refine treatment protocols, optimize outcomes, and fully understand the long-term impact of intralesional 5-FU on pterygium management.

LIMITATIONS OF STUDY

The study's limitations include the lack of long-term follow-up beyond six months, which may not capture the full scope of recurrence or late-onset side effects. Additionally, the single-center design may limit the external validity of the results, and the absence of a control group reduces the ability to compare the treatment directly with other interventions. The potential for bias in patient selection and reporting of outcomes should also be considered. However, the study's design allowed for comprehensive follow-up assessments at multiple time points, ensuring a thorough evaluation of treatment outcomes. Additionally, the inclusion of diverse demographic groups (age, gender, pterygium laterality) strengthens the analysis of treatment efficacy across various patient profiles.

CONCLUSION

Intralesional 5-FU demonstrates promising results in reducing pterygium size and recurrence in early-stage cases. This study supports its potential as a viable primary treatment for patients seeking an alternative to surgery. However, further research with longer follow-up and control groups is needed to confirm these findings and optimize treatment protocols.

ACKNOWLEDGMENT

To the dedicated team of ophthalmology department Fauji Foundation Hospital including paramedic staff, operation theatre assistants and Nurses.

Conflict of Interest: None.

Funding Source: None.

Authors' Contribution

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

AN & RIUH: Data acquisition, data analysis, critical review, approval of the final version to be published.

A & NO: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

TN & AM: Conception, data acquisition, drafting the manuscript, 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.

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