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ORIGINAL ARTICLE

Management of Patients of Recurrent Pterygium by Intralesional Injection of 5 Fluorouracil

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ABSTRACT

Background: Management of recurrent pterygium using intralesional injection of 5-fluorouracil (5-FU) is an emerging technique aimed at reducing recurrence and inflammation without the need for repeated surgical intervention.

Objective: To manage the patients of recurrent pterygium by intralesional injection of 5 fluorouracil.

Methodology: This prospective study was conducted at Teaching Hospital, Loralai from 1st January 2023 to 30th June 2023 and 100 patients (100 eyes) including recurrent pterygium on clinical diagnosis were enrolled. The primary outcomes of the study were progression arrest, reduction of redness/lesion vascularity and secondary outcomes were cosmetic benefits, improvement of redness, irritability as well as astigmatism effects. A comprehensive eye examination was performed as baseline. Following the injections, visual acuity was evaluated, corneal topography was performed. All injections were administered in the outpatient clinic using a slit lamp. Ten minutes prior to the procedure, topical anesthesia (1% w/v tetracaine minims, Bausch & Lomb, UK) and 5% w/v povidone iodine eye drops (Bausch & Lomb, UK) were instilled. A pre-loaded 1 ml syringe containing 0.3 ml of 5FU (2.5 mg per 0.1 ml) was used to inject 0.1–0.2 ml (equivalent to 2.5–5 mg of 5FU) into the body of the pterygium using a 30-gauge needle. The formation of a bleb confirmed intra-lesional delivery of the drug. After the injections, 1–2 drops of 0.5% chloramphenicol were applied topically and continued four times daily for three days post-injection. All patients had 24-hour access to an emergency eye care service and could contact the investigators with any concerns during the study.

Results: The mean age of the patients was 55.1±3.5 years with 60% males and 40% females. The progression arrest was noticed in 100% cases. However, 4 cases presented recurrence and later had to opt surgical interventions. The pterygium length was reduced in 60% cases with a mean difference of vector magnitude up to 0.10mm. Optical coherence tomography (OCT) measurements showed a reduction in pterygium thickness in 85% of patients, while the remaining patients exhibited no change. Among the patients who demonstrated a reduction in clinical grade, 90% showed an improvement of one grade, while 10% improved by two grades. The mean clinical grade decreased from 2.313 before the injection to 1.630 after the injection ($P < 0.001$; 95% CI: 0.368–1.007). The pterygium length was clinically graded as reduced in 65% cases while it remains in same grade in 35% ofcases. The photographic images of the patients showed reduction in the vascularity of the eye and redness with the injections.

Conclusion: The application of intralesional 5 fluorouracil injections is significantly effective in recurrent cases, only 25% cases recurrence.

Keywords: Management, Recurrent Pterygium, Intralesional injection, 5 Fluorouracil

INTRODUCTION

The elastotic degeneration of subconjunctival tissue is known as pterygium which effects the bulbar conjunctiva exposed at the nasal and the temporal regions.[1-3] Its major effect observed when fibro-vascular tissues progressed through the limbus as well as visual axis of eye resulting into corneal steeping and ocular inflammation in addition to astigmatism irregularities restricting the ocular movement.[4]

The pterygium etiology remains dependent on the various factors including environmental dryness, inheritance or immunology however the other significant factors include proliferation of fibro-vascular subconjunctiva. The enhanced expression of various growth factors including insulin-like growth factor, epidermal growth factors (EGF), basic-fibroblast growth-factor (bFGF), transforming growth factor-beta, connective tissue growth factor, vascular endothelial growth factor (VEGF), has been described in primary as well as recurring pterygia.[5,6]

Surgical removal is considered as the gold standard including the auto-conjunctival grafting for the pterygium treatment.[7] Various researchers have shown a recurrence rate as 0 to 14.29 percent [8]. Literature has supported intralesional 5-flurocil (5FU) application to seize the pterygium disease advancement and may lead to non-surgical management.[9-12]

The present study was designed to manage pterygium through intralesional 5 fluorouracil injections. The result of the study clearly identified the potential outcomes of the aforesaid management. This study provided evidential support in opting the intralesional 5 fluorouracil injections for the management of pterygium disease.

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MATERIALS AND METHODS

This prospective study was conducted at Teaching Hospital, Loralai from 1st January 2023 to 30th June 2023 and included 100 patients (100 eyes) including recurrent pterygium on clinical diagnosis. An informed consent was taken from each patient for its participation in the study. The sample size was generated by using sample size web-based calculator applying the 80% power of test, 95% CI and 5% margin of error. The inclusion criteria consisted of clinically confirmed progressive recurrent cases of pterygium who sought intervention having no previous surgical treatment history for aforesaid condition. While exclusion criteria consisted of omitting all children and women of childbearing age (unless using contraception). The primary outcomes of the study were progression arrest, reduction of redness/lesion vascularity and secondary outcomes were cosmetic benefits, improvement of redness, irritability as well as astigmatism effects. A comprehensive eye examination was performed at baseline and following the injections. Visual acuity was evaluated using LogMAR charts, followed by assessment of pupil reactions and a biomicroscopic examination of the anterior segment. Corneal topography was conducted to measure corneal astigmatism, while optical coherence tomography (OCT) was performed at two fixed

locations to assess tissue thickness. Intraocular pressure was measured, and a fundus examination was also conducted. All injections were administered in the outpatient clinic using a slit lamp. Ten minutes prior to the procedure, topical anesthesia (1% w/v tetracaine minims, Bausch & Lomb, UK) and 5% w/v povidone iodine eye drops (Bausch & Lomb, UK) were instilled. A pre-loaded 1 ml syringe containing 0.3 ml of 5FU (2.5 mg per 0.1 ml) was used to inject 0.1–0.2 ml (equivalent to 2.5–5 mg of 5FU) into the body of the pterygium using a 30-gauge needle. The formation of a bleb confirmed intra-lesional delivery of the drug. After the injections, 1–2 drops of 0.5% chloramphenicol were applied topically and continued four times daily for three days post-injection. All patients had 24-hour access to an emergency eye care service and could contact the investigators with any concerns during the study. The length of the pterygium, from the limbus to the apex, was measured before and after the injections using Image J software (Version 1.31, Maryland, USA). Any complications or adverse events were documented. Anterior segment photographs were taken at each follow-up visit to monitor treatment response, particularly regarding redness and progression. A standardized protocol was used for both anterior segment photography and OCT imaging. Pterygia were graded based on appearance:

- **Severe**: predominantly red with extensive vascularization, dilated vessels, and a fleshy appearance;
- **Moderate**: more white than red, showing moderate vascularity with narrow vessels and less fleshiness;
- **Mild**: thin, atrophic, and minimally vascularized.

These grades were assigned scores of 3, 2, and 1, respectively. Astigmatic changes were analyzed using the Vector Analyzer software, with the magnitude of the difference vector calculated accordingly. The data was analyzed using GraphPad Prism 7.03 (GraphPad Software La Jolla, CA, USA) as well as SPPS version 26.0 using Wilcoxon ad hoc test for determining pterygium length.

RESULTS

The mean age of the patients was 55.1±3.5 years with 60% males and 40% females. The mean age was between 25-70 years (Table 1). The side effects of injecting intralesional of 5 fluorouracil injection presenting no stinging in patients however all patients had sub-conjunctival and intra lesion hemorrhage which subsided after 2 weeks (Table 2).

The progression arrest was noticed in100% cases. However, 4 cases presented recurrence and later had to opt surgical interventions. The pterygium length was reduced in 60% cases with a mean difference of vector magnitude up to 0.10mm. Optical coherence tomography (OCT) measurements showed a reduction in pterygium thickness in 85% of patients, while the remaining patients exhibited no change. The average decrease in thickness was 35.7±31.30 µm, with a median of 29 µm ($P < 0.001$; 95% CI: 11.7-59.9) [Table 3].

Among the patients who demonstrated a reduction in clinical grade, 90% showed an improvement of one grade, while 10% improved by two grades. The mean clinical grade decreased from 2.313 before the injection to 1.630 after the injection ($P < 0.001$; 95% CI: 0.368-1.007). The pterygium length was clinically graded as reduced in 65% cases while it remains in same grade in 35% of the cases (Fig. 1). The photographic images of the patients showed reduction in the dilation of the eye and reddishness with the injections. A total of 5 injection of intralesional of 5 fluorouracil were administered wherein the positive outcomes were initiated post 3rd injection in majority of the cases (Fig. 2).

Table 1: Age and gender distribution within patients (n=100)

Demographic variables	No.	Range
Age in years (Mean±SD)	55.1±3.5	25-70 years
Male	60 (60%)	--
Female	40 (40%)	--

Table 2: Side effects of intralesional of 5 fluorouracil injection (n=100)

Side effects	No.	Resolution
Stinging during injection	-	--
Subconjunctival	100	2 weeks
Intra-Lesion hemorrhage	100	2 weeks

Table 3: The outcomes of intralesional of 5 fluorouracil injection among enrolled patients

Variable	No. (n=100) (Eyes= 100)	Mean Magnitude of Difference	P value	95% CI
Progression Arrest	100 (100%)	-	-	-
Pterygium length (reduction)	60 (60%)	0.10 mm ± 0.1	0.041	0.025-0.178
Astigmatism (reduction)	25 (25%)	10.2	0.351	--
No difference in astigmatism	10 (10%)	1.0	0.020	--
Astigmatism (increase)	26 (26%)	5.0	0.025	--

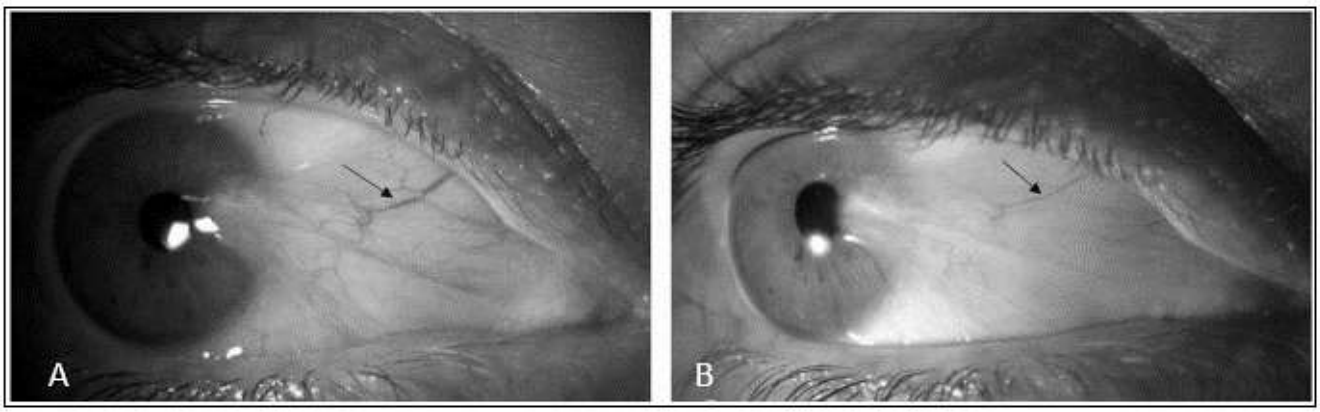

Fig. 2: Photographic Imaging of the pre (A) and Post (B) injection difference in vessels dilations followed by reduction in vascularity

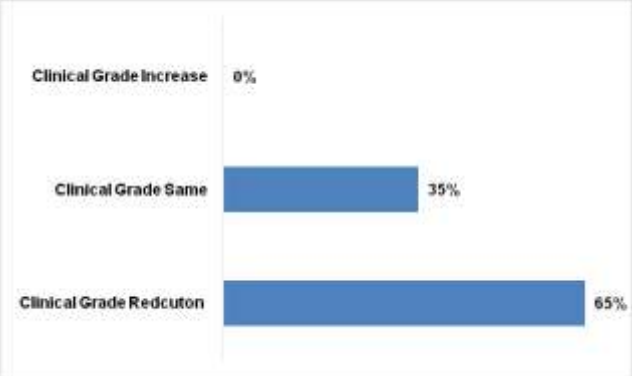

Fig. 1: Frequency of pterygium length clinical grading

DISCUSSION

Various interventions have been employed to reduce the recurrence of pterygium after surgery, whether for primary or recurrent cases. These include autologous conjunctival grafting and the intraoperative use of antimetabolites such as 5-fluorouracil (5-FU). In addition, intralesional injections of antimetabolite drugs have been used to manage recurrent pterygium.[11-14] Encouraged by their effectiveness in treating recurrence, both 5-FU and anti-VEGF agents have also been applied individually in primary pterygium with considerable success [8]. 5-FU works by inhibiting DNA synthesis and fibroblast proliferation[15], while anti-VEGF antibodies prevent angiogenesis by binding VEGF isoforms and blocking VEGF-receptor interactions.[13]

In the present study, intralesional 5-FU injections were administered for the treatment of primary pterygium. The treatment led to a reduction in clinical grade, thickness, and vascularity of the lesions.[16,17] By targeting both major pathological mechanisms—fibrosis and angiogenesis—this approach may have a synergistic effect. A slight decrease in pterygium length was also observed in some patients, likely due to thinning at the apex; however, the reduction was minimal (around 0.2 mm) and not clinically significant. Importantly, progression of the pterygium was halted in all cases, with noticeable cosmetic improvement. Some patients may not require surgery as a result, highlighting the clinical relevance of this approach.[18,19]

Interestingly, astigmatism increased in most patients post-injection. This may be attributed to contraction of fibrotic tissue exerting increased mechanical pull on the cornea, leading to further distortion. In contrast, previous studies that used weekly 5-FU injections (0.1 ml of 5 mg for 4 weeks) reported a reduction in astigmatism, alongside improvement in clinical appearance. The discrepancy may be due to variations in tissue response and injection protocol. Nevertheless, most studies agree that 5-FU can safely improve the appearance, colour and surface area of pterygium.[20]

CONCLUSION

The application of intralesional 5 fluorouracil injections is significantly effective and minimized the recurrent cases with only 20% cases recurrence. The reduction in pterygium length was observed in 65% patients. The improvements in reddishness, tissue vascularity and fibroblast collagen were evident. However long-term follow up on its management results is essential.

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