ORIGINAL ARTICLE

Comparison of primary versus recurrent pterygium after intralesional 5-Fluorouracil

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Abstract

Objective: To compare the mean change in corneal astigmatism and clinical appearance after intralesional injection of 5-Fluorouracil in primary and recurrent pterygia.

Methods: The quasi-experimental study was conducted at the Armed Forces Institute of Ophthalmology, Rawalpindi, Pakistan, from June 2014 to April 2015. The patients were categorised into two groups. Group1 named GP comprised primary pterygia patients, while those of recurrent pterygia were in Group 2 named GR. All the patients were treated with 0.1ml intralesional 5-Fluorouracil 5mg weekly injections for 04 weeks. Ophthalmic clinical evaluation included uncorrected distant visual acuity, keratometery and slit lamp examination was performed before and 04 weeks after the treatment.

Results: There were 86 eyes of 64 patients in the study. Mean uncorrected distant visual acuity of patients was 0.12±0.13 in GP and 0.26±0.17 in GR. Mean astigmatism before treatment was 1.75±1.08 in GP and 2.92±2.28 in GR. Same parameters 04 weeks after last injection were 1.66±1.17 and 2.64±1.78 in GP and GR respectively. All eyes had a statistically significant change in clinical appearance.

Conclusion: Intralesional 5-Fluorouracil injection improved cosmesis of primary as well as recurrent pterygia, but did not have statistically significant effect on corneal astigmatism.

Keywords: Pterygium, Recurrent pterygium, 5-fluorouracil. (JPMA 66: 559; 2016)

Introduction

Pterygium is a wing-like triangular, elevated, fibrovascular growth of degenerative conjunctiva into the cornea over limbus and is commonly seen on the nasal side.[1] It affects individuals older than 20 years of age affecting males twice as commonly as females with global prevalence of 0.7% to 33%.[2,3] Although exact aetiology of pterygium is not known, but various factors like outdoor work, ultraviolet (UV) light exposure, occupational exposure to irritants, ocular inflammation and dryness are said to be associated with its incidence and high prevalence.[4,5]

The mainstay of treatment for pterygium is surgical excision. It is indicated when there is progression threatening the visual axis, induced astigmatism, restriction of eye movement, chronic irritation, and poor cosmesis. The gold standard among the surgical techniques is surgical excision of the pterygium with an autologous conjunctival graft.[6,7]

Most common undesirable treatment outcome of pterygium surgery is recurrence. Recurrence rates of pterygium range from 10% to 80% depending on the surgical procedure carried out. Bare sclera technique has the highest recurrence rate which is reported to be as high as 82% in some studies. Recent studies reported the overall recurrence rate of 18%.[8,9] Various intraoperative and postoperative modalities, including b-irradiation, topical thiotepa, mitomycin C and 5-fluorouracil (5-FU) have been introduced to decrease the recurrence rate of pterugium surgery.[10,11]

5-FU is a pyrimidine analogue which interferes with deoxyribonucleic acid (DNA) and ribonucleic acid (RNA) synthesis and inhibits proliferating fibroblasts. Due to its anti-fibrotic and anti-scarring properties, it has been widely used in ophthalmology.[10,11] Pterygium recurrence is believed to be secondary to migration and proliferation of fibroblast cells and, hence, the use of 5-FU can halt pterygium progression and recurrence.[12,13]

The current study was planned to compare the short-term effects of 5-FU in patients with primary versus recurrent pterygia, and to observe the visual outcome as this may help in tailoring the use of 5-FU to a specific subgroup of patients.

Patients and Methods

The quasi-experimental study was conducted at the Armed Forces Institute of Ophthalmology, Rawalpindi, Pakistan, from June 2014 to May 2015. The sample size was calculated on the basis of Open EPI info calculator using pre-treatment and post-treatment mean values. Patients included were those who presented with pterygium of 2 or more millmeter over cornea, giving thick, fleshy appearance and obscuring the underlying

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episcleral vessels (Donald Grade 3). Patients with corneal degeneration, ectasia, scarring or history of trauma were excluded. Informed written consent was taken and patients were divided into two groups. Patients who had primary pterygia were included in Group 1 (GP) while those with recurrent pterygia after surgical excision were grouped in Group 2 (GR). Two eyes of the same patient were treated separately. Patients in both the groups underwent ophthalmic clinical examination that included uncorrected distant visual acuity (UCVA), keratometery with Auto Ref-keratometer (RK-F1, Canon) and slit lamp examination to grade the pterygium. Pterygia that obscured the underlying episcleral vasculature completely and partly were classified as grade 3 and grade 2 respectively, while those in which the underlying episcleral vessels were clearly visible were categorised as grade 1. Patients were recalled after 04 weeks of the last injection and a detailed examination including UCVA, autokeratometery and slit lamp examination of pterygium was performed.

Patients in both the groups were treated with 0.1 ml of 5FU (5mg) weekly injections for 04 weeks. 5FU solution is available in preformed strength of 50mg/ml in an ampoule containing 10ml, and 0.1ml of this solution was injected into the belly of pterygium approaching from superior border towards the centre. During the injection, care was taken to avoid puncturing any large blood vessel and spillover while retrieving the needle. The injection was given under topical anaesthesia (proparacaine hydrochloride 0.5%, Alcon) in the outdoor patient department (OPD) using a slit lamp. After the injection, topical 1 drop of chloramphenicol 0.1% was instilled thrice daily for a week.

For statistical analysis, SPSS 17was used. Data was described in terms of mean ± standard deviation (SD). The induced change in astigmatism comparing the preoperative and postoperative measures were evaluated statistically with sample t-test and paired sample test ($p<0.05$ significance level). Preoperative and postoperative clinical appearance and grading of pterygium was compared in the two groups by Chi square test and frequency distribution were used to determine significance level.

Results

There were 86 eyes of 64 patients in the study. Of the patients, 22(33%) were females and 42(67%) were males. GP had 54(63%) eyes of 42(67%) patients, while GR had 32(37%) eyes of 22(33%) patients. Mean age of GP patients was 39.57±5.127 years, while that of GR patients was 37.7±4.99 years (Table-1). Mean astigmatism before treatment was 1.75±1.08 in GP, and 2.92±2.28 in GR. Same parameters 04 weeks after the last injection were

Table-1: Mean value of corneal astigmatism in both groups.

Variables	(GP) Primary Pterygium	(GR) Recurrent Pterygium
Age	39.57±5.127	37.7±4.99
Pre-treatment Astigmatism	1.75±1.08	2.92±2.28
Post-treatment Astigmatism	1.66±1.17	2.64±1.78
Induced change	0.152±1.19	0.28±1.00
P- value	0.351	0.124

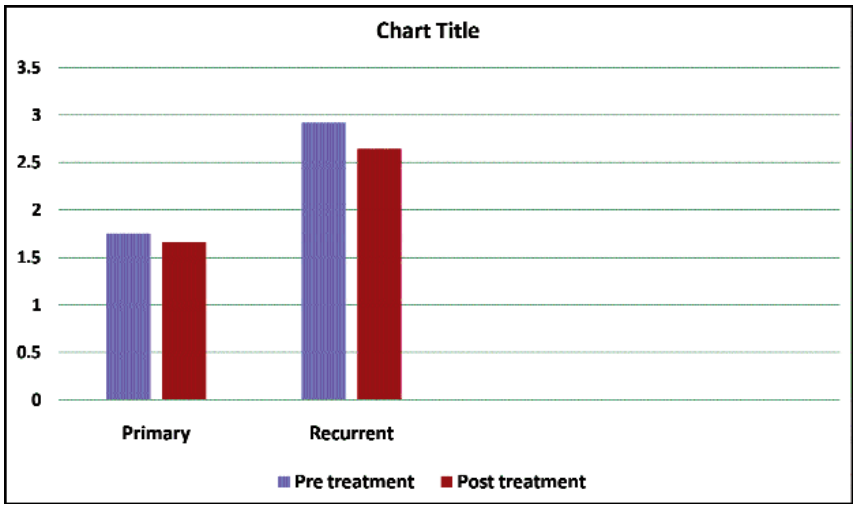

Figure: Comparison of astigmatism before and after treatment.

Table-2: Frequency distribution of various grades of pterygium before and after treatment.

Clinical Appearance	(GP) Primary Pterygium		(GR) Recurrent pterygium		P value
	Pre treatment	Post treatment	Pre treatment	Post treatment	P < 0.001
Grade 1	0	26	0	14	P < 0.001
Grade 2	12	20	10	12	P < 0.001
Grade 3	42	8	22	6	P < 0.001

1.66±1.17 and 2.64±1.78 in GP and GR respectively. Comparison of pre- and post-astigmatism was also done (Figure). Patients were evaluated one month after the last injection to evaluate change in clinical grade (Table-2).

Discussion

Although surgery is the gold standard treatment for pterygium, but recurrence remains a problem and is the most undesirable outcome after successful excision.[14,15] Recurrence is characterised by growth of fibrovascular tissue onto the cornea over the limbus and results from proliferation of fibroblasts.[16] The rate of recurrence varies from 10-80% and depends mainly on the surgical approach; simple excision leaving bare sclera has the highest rate while conjunctival autograft has the lowest rate of recurrence.[17]

5-FU and mitomycin C (MMC) are the two anti-proliferative and anti-fibroblastic agents which came into use as medical adjunct to surgery in order to reduce the frustration one faces after seeing recurrence in a case which appeared perfectly normal at the time of surgery. Besides, 5-FU is a pyrimidine analogue that inhibits DNA synthesis and affects rapidly proliferating cells.[18]

We compared the effect of 5-FU in primary versus recurrent pterygia. Like Akarsu C et al and Prabhasawat P et al, statistically significant improvement ($p<0.001$) in fibrovascular tissue growth and fleshy appearance of pterygia was noticed in both the groups as evident by change in Donald's grades.[19,20] Though some authors like Maldonado et al. revealed that intraoperative use of 5-FU is ineffective in preventing recurrence, considering their methodology this conclusion was probably due to inadequate dosage and a single intraoperative use.[21] Like us, Pikkel J et al. also concluded that 5-FU is effective in inducing regression of fibrovascular tissue of pterygiumin recurrent cases.[22]

In addition to clinical appearance, other important parameter that we analysed was induced corneal astigmatism. The results were somewhat variable in both the groups. Some patients developed worsening of corneal astigmatism, while others showed significant improvement. However, the results were not statistically significant in either group ($p>0.05$).

Despite the ineffectiveness of 5-FU in improving vision and corneal astigmatism to a significant level, it is worth mentioning that most of the patients acknowledged remarkable symptomatic improvement and relief from irritation and watering in both the groups.

Clinical appearance and cosmesis of the pterygium is another important variable that we considered in our study. Most of the patients with pterygium are concerned about the cosmesis and clinical appearance so it is an important medical as well as surgical target and endpoint. We found 85.2% patients in GP group and 81.25% in GR group who showed improvement in clinical appearance of pterygium after treatment with 5-FU.

Like Akarsu C et al. and Pikkel J et al., 5-FU appeared to be a safe and efficient medication for primary as well as recurrent cases and, fortunately, we did not find any serious complications secondary to its use during the follow-up period.[20,22]

Conclusion

The use of 5-FU in improving clinical appearance of both primary and recurrent pterygium was safe and effective. The findings are important, but further studies need to be conducted on a larger sample size not only to confirm our findings, but also to consider surgical need and outcome after using 5-FU.

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