

## PREVENTION OF PTERYGIUM RECURRENCE BY USING INTRA-OPERATIVE 5-FLUOROURACIL

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### ABSTRACT

**Objective:** This study was aimed to determine the role of intraoperative application of 5-Fluorouracil in the prevention of pterygium recurrence.

**Design:** A prospective clinical trial

**Place and Duration of Study:** The study was conducted at Eye Department, Military Hospital, Rawalpindi from February 2000 to August 2001.

**Patients and Methods:** A total number of one hundred and fifty patients were selected for the study and they were divided into two groups on a random basis. Control Group included 75 patients who underwent conventional pterygium excision. 5-Fluorouracil Group included 75 patients who received a single application of 5-Fluorouracil (25 milligram per milliliter) for five minutes immediately after pterygium excision

**Results:** Follow up was conducted in case of both the groups for at least six months. During follow up period, recurrence of pterygia was seen in thirty one patients (41.33%) in the control group while recurrence was seen in 25 patients (33.33%) in the 5-FU group. This shows a slight decrease in recurrence rate ( $P < 0.05$ ) but it significantly delayed the onset of recurrence ( $P < 0.05$ ).

**Conclusion:** It can be concluded that a single intraoperative application of 25 milligram per milliliter of 5-Fluorouracil can be considered as an adjunct treatment in pterygium surgery to prevent its recurrence.

**Keywords:** Prevention, pterygium, recurrence, 5-flourouracil.

### INTRODUCTION

Pterygium is a degenerative condition of the subconjunctival tissues which proliferates as vascularized granulation tissue to invade the cornea destroying the superficial layers of stroma and Bowman's membrane. Pterygia typically develop in patients who have been living in hot climates. It is quite common in Pakistan. The main factor in its development seems to be actinic (ultraviolet) exposure although a strong causal relationship has been documented with dryness, inflammation; exposure to wind, dust and other irritants. Pterygium recurrence following surgical excision is a fairly common problem which

leads to disability especially in high risk population groups. It is therefore highly recommended that adjunctive measures should always be taken in all the patients undergoing pterygium surgery.

Surgical excision is recommended as the only way of treating an established case of pterygium but excision is indicated only in cases of progression towards the visual axis or for cosmetic reasons. The recurrence rate is significant and recurrent pterygia are often worse than primary ones [1]. Many treatment modalities have been recommended for prevention of pterygium recurrence. These include intra-operative application of antimetabolites e.g. mitomycin-C [2-11] and 5-Flourouracil [12-15], conjunctival autografts

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[16-18] and beta radiation with strontium 90 [19].

5-Fluorouracil is one of the older antimetabolites which have been in use for decades against many cancers like skin cancer and a variety of adenocarcinomas. It is one of the pyrimidine antagonists. It is normally given intravenously to treat the cancers. However, in ophthalmology, it is topically applied for a few minutes to avoid recurrence in procedures like trabeculectomy. In vitro studies have shown that a single intraoperative 5 minute exposure to 5-Fluorouracil and mitomycin-C considerably delays the proliferation of human ocular fibroblasts in cell cultures. In vivo study of rabbit tissue has revealed that subconjunctival and scleral fibroblasts grown from area treated with 5-Fluorouracil do not recover for several days. Hence there was a need to study its efficacy in prevention of pterygium recurrence.

This study was aimed to determine the role of intraoperative application of 5-Fluorouracil in the prevention of pterygium recurrence.

## PATIENTS AND METHODS

It was randomized prospective clinical study. It was conducted at Eye Department, Military Hospital, Rawalpindi. The patients selected for the study were both serving and retired armed forces personnel and their families. A total number of 150 patients were included in the study and the study was carried out from February 2000 to August 2001. The patients were divided into two groups randomly after meeting the selection criteria.

### Inclusion Criteria:

- Patients having no history of previous ocular surgery.
- Primary progressive pterygia causing visual or cosmetic problems.

### Exclusion Criteria:

- Patients having diseases of eye lids e.g. ectropion
- Cases in whom pterygium had involved less than 1.5 mm of cornea.
- Patients having ocular infection
- Patients having corneal vascularization.
- Atrophic pterygia.

A total number of one hundred and fifty patients were selected for the study and they were randomly divided into two groups.

### Control Group:

It included 75 patients who underwent conventional pterygium excision.

### 5 – Fluorouracil (5 – FU) Group:

It included 75 patients who received a single application of 5-Fluorouracil (5-FU) 25 milligrams per milliliter for five minutes immediately after pterygium excision.

Pterygium was excised under local anesthesia with subconjunctival injection of 0.5–1 milliliter of 2% xylocaine with 1:100,000 adrenaline beneath and around the pterygium with 25 gauge needle. Topical anesthetic (0.5% proparacaine) drops were also used three times with an interval of 1–2 minutes before the subconjunctival injection of 2% xylocaine. After draping the patient, a wire speculum was introduced to keep the lids open during surgery.

Pterygium excision was started from corneal side using No. 15 surgical blade. Then, rest of the pterygium tissue along with adjacent Tenon's capsule was excised with the help of spring (action) scissors. And the sclera beneath was left exposed (bare sclera technique).

In 5-FU group (group-II) patients, a 5 mm x 5 mm piece of triangular sponge was placed in contact with the residual pterygium tissue and the exposed scleral surface for 5 minutes after it was soaked in 25 mg/ml concentration of 5-fluorouracil. After removing the piece of

triangular sponge, the 5-FU treated area was thoroughly rinsed with balanced electrolyte solution (BES) for one minute to prevent further contact of 5-FU with ocular tissues.

The eye was padded for 24 hours after topical steroids and topical antibiotics were instilled into the eyes of patients of both the groups. There was no difference in postoperative management. Both the groups were given similar treatment. Postoperative local treatment included 0.5% chloramphenicol (Econochlor) eye drops four times a day and dexamethasone (Mexidex) eye drops four times a day. Mefenamic acid 250 mg (Ponstan) tablets were used for analgesia only if patient complained of pain. Generally two tablets were given initially. Dosage was adjusted according to the requirement of the patient subsequently.

The grading was done on the basis of post operative appearance as shown in table No 3 and all the cases were divided into following three groups.

- Grade-I: No recurrence i.e. normal appearance.
- Grade-II: Which showed slight evidence of fibrovascular proliferation upto the limbus but not extending into the clear cornea.
- Grade-III: Frank recurrence with fibrovascular proliferation which also involves the clear cornea.

## RESULTS

A total number of 150 patients were included in the study. They were divided into two groups Group-I and Group-II. Each group had 75 patients, the number of patients being equal in both the groups. They were 94 males and 56 females patients.

In group-I (control group), 46 patients were males and 29 patients were females and in group-II (5-FU group) 48 patients were males and 27 patients were females

Age distribution of the patients in both the groups (table). Minimum age was 20 years and maximum age was 63 years. Average age in control group was  $35.5 \pm 12.3$  years and in 5-FU treated group was  $36.4 \pm 13.9$  years. There was no statistical differences between the age and sex distribution of the two groups ( $P > 0.05$ ).

In group-I (control group) 72 patients were having nasal pterygia while three patients were harboring temporal pterygia. In group-II (5-FU group) 73 patients were harboring nasal pterygia while only two patients had temporal pterygia.

Follow up was conducted in case of both the groups for at least six months. During follow up period of this study, recurrence of pterygia was seen in thirty one patients (41.33%) in the control group (group-I) while recurrence was seen in 25 patients (33.33%) in the 5-FU group (group-II). This shows a slight improvement ( $P < 0.05$ ). Also, the recurrence started after about 4-6 months in the control group (with mean  $\pm$  SD of  $5.4 \pm 1.0$ ) while the recurrence started after about 7-8 months in case of group-II (with mean  $\pm$  SD of  $7.5 \pm 1.5$ )

**Table: Age distribution.**

Age	No of Patients	Percentage
20-30	31	20.67
30-40	36	24
40-50	45	30
50-63	38	25.33

which shows that 5-FU delays the onset of recurrence ( $P < 0.05$ ).

## DISCUSSION

Pterygium is defined as excessive proliferation of fibrovascular tissue over the exposed ocular surface and is responsible for almost irreversible visual loss. This disease is particularly common in tropical and sub tropical regions including our country. High ultra violet light exposure, chronic inflammation and tear film abnormalities are presumed to be the causative factors.

Several modalities of treatment have been tried e.g. thiotepa, topical steroids and beta

radiation, but only surgical treatment has offered permanent relief. The non surgical modalities of treatments do not relieve the patient of the problem permanently and also cause complications. The surgical excision is associated with a high rate of recurrence. Recurrence is an encroachment of fibrovascular connective tissue across the limbus and into the cornea for any distance in the position of previous pterygium.

The time of pterygium recurrence has been described previously as to be within six months to a year [20]. 50% to 97% recurrences occur in 4 – 12 months period respectively following surgery. The process of recurrence is continuous under the simulation of unexcised abnormal pterygium tissue in susceptible cases. 5-FU was found to be effective at this level by inhibiting abnormal fibrovascular proliferation in these unexcised abnormal pterygium tissue [12-14].

The recurrence of pterygium after its surgical excision is a challenge for years. Various surgical procedures - prevent these recurrences. 5-FU is an antimetabolite the role of which is well established as an adjunct chemotherapy in glaucoma filtration surgery to prevent bleb failure in high risk glaucoma patients. Antimetabolite 5-FU inhibits mitosis by interfering with the S-phase and G-II phase of cell cycle. In vitro studies have shown that a single intra operative 5 minutes exposure to 5-FU and MMC considerably delays the proliferation of human ocular fibroblasts in cell culture. Excision of pterygium using 25 mg/ml intra operative 5-FU as an adjunct chemotherapy in primary pterygium surgery although reduces the recurrence; it does not do so very effectively [15]. A recent study has revealed recurrence rate of 32.5% with the intra operative use of 5-FU after pterygium surgery. However it carries much less risk of corneal complication as compared to post operative instillation of MMC [8-11].

In vivo study have shown that subconjunctival and scleral fibroblasts do not recover for several days if grown from the

area treated with 5-FU. So keeping this in mind, this study was carried out to find out measures of pterygium recurrence reduction. In this study pterygium was excised using the bare sclera technique followed by a single intra operative application of 25 mg/ml 5-Fluorouracil for five minutes over the residual pterygium tissue and the adjacent bare sclera to inhibit fibrovascular proliferation. The residual 5-Fluorouracil was washed out immediately with balanced electrolyte solution from the area of application to avoid toxic effects on corneal epithelium. The patients were followed up meticulously till the epithelialization of the bare tissue. The aim of this prospective study was reducing the rate of pterygium recurrence and delaying the onset of recurrence. The rate of pterygium recurrence in patients treated with 5-fluorouracil (33.33%) was slightly reduced as compared to the control group (41.33%) [12,15]. The onset of recurrence was delayed in 5-fluorouracil treated group as compared to the control group.

## CONCLUSION

This study, aimed at reducing recurrence following excision of pterygium, showed that by single intraoperative application of 25 milligram per milliliter of 5-Fluorouracil, the rate of pterygium recurrence following pterygium excision can be reduced. There was a slight decrease in the recurrence rate however it did not approach significance but it significantly delays the onset of recurrence. So it can be concluded that a single intraoperative application of 25 milligram per milliliter of 5-Fluorouracil can be considered as an adjunct treatment in pterygium surgery to prevent its recurrence.

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