

The use of mitomycin C with autologous limbal-conjunctival autograft transplantation for management of recurrent pterygium

Mohamed A Fakhry

Department of Ophthalmology,
Kasr El Aini Hospital, Cairo University,
Cairo, Egypt

Purpose: The purpose of this study is to evaluate and compare recurrence rates upon using mitomycin C (MMC) with limbal-conjunctival autograft for treating recurrent pterygia.

Methodology: An interventional, prospective, comparative clinical study was performed in 30 eyes (26 patients) with recurrent pterygia, allocated into two groups: Group A (19 eyes) operated by pterygium excision and limbal-conjunctival autograft transplantation (L-CAT) without MMC and Group B (20 eyes) operated with injection of 0.1 mL of MMC 0.15 mg/mL 1 month before L-CAT surgery. Exclusion criteria included patients with symblepharon, cicatricial conjunctival diseases, limbal stem cell deficiency, and other intraocular diseases.

Results: A total of four cases of recurrences for Group A ($P = 0.012$) and one case of recurrence for Group B ($P < 0.001$) were recorded.

Conclusions: Preoperative injection of MMC in low dose and concentration improves the results of L-CAT in recurrent pterygium.

Keywords: recurrent pterygium, limbal autograft, conjunctival autograft, mitomycin C

Introduction

A pterygium is a wing-shaped growth of fibrovascular conjunctiva onto the cornea. Its incidence varies across geographical locations. Several hypotheses have been ascribed to its etiology. Currently, it is believed that the pterygium is a growth disorder characterized by conjunctivalization of the cornea due to localized ultraviolet-induced damage to the limbal stem cells. Aggressive pterygial fibroblasts are also responsible for corneal invasiveness.¹

The indications for surgery include reduced vision due to encroachment on the visual axis and irregular astigmatism, chronic irritation, recurrent inflammation, restrictive ocular motility, and cosmetic purposes. Numerous surgical techniques including bare sclera excision with or without the use of adjuncts like beta irradiation, thiotepa eye drops, intra- or postoperative mitomycin C (MMC), amniotic membrane transplantation, and conjunctival autograft have been described.² Pterygium represents a local limbal deficiency. Thus, inclusion of limbal epithelium in the conjunctival graft for pterygium surgery would achieve better anatomic and functional reconstruction after pterygium removal by restoring barrier function of the limbus.³

MMC is an antitumor antibiotic that was first isolated from *Streptomyces caespitosus* by Wakaki et al⁴ in 1958, and it acts by inhibiting DNA synthesis. The mechanism of action seems to be inhibition of fibroblast proliferation at the level of the episclera.⁵ The benefit of MMC is that it has the prolonged if not permanent effect which indicates its toxicity to the cells.⁶ Adjunctive MMC for pterygium surgery was first

Correspondence: Mohamed A Fakhry
14 Abou-Hazem St, Madkour,
Elharam, Giza 12111, Egypt
Tel +20 2 35862810
Email fakhryref@hotmail.com

described by Kunitomo and Mori⁷ in Japan in 1963 and in the United States by Singh et al⁸ in 1988 as postoperative topical MMC of concentration ranging from 0.4 to 1 mg/mL.

Although multiple studies have reported recurrence rates of ~5%–12% with the use of topical MMC,^{9,10} this technique has been associated with rare but significant conjunctival, sclera, and corneal toxicity.⁹ In an attempt to decrease ocular morbidity, intraoperative use of MMC was suggested.¹¹ Advantages of this technique include decreasing the MMC dosage and application directly to the area of pathology rather than to the entire ocular surface. A combined pterygium removal with intraoperative MMC and conjunctival autografting was described.¹²

The purpose of this study was to evaluate the role of MMC injection directly into the surgical site 1 month before limbal-conjunctival autograft transplantation (L-CAT) in recurrent pterygia.

Subjects and methods

A prospective, comparative, interventional clinical study was carried out. This study included 39 eyes (33 patients; 27 unilateral and 6 bilateral) complaining of recurrent pterygium of variable size, duration, and number of recurrences, which are mentioned in Table 1. All recurrences happened at least 3 months prior to the MMC injection. Surgeries carried out prior to our study were bare sclera technique for 28 eyes and conjunctival rotational flap for 11 eyes. None had free conjunctival graft or MMC application.

Exclusion criteria were patients with symblepharon, cicatricial conjunctival diseases, limbal stem cell deficiency diseases, and other intraocular diseases. Subjects were recruited from outpatient clinic of Kasr El Aini University and International Eye Hospital in Cairo. They were allocated into 2 groups: Group A included 19 eyes of 15 patients (11 males and 4 females; 4 bilateral and 11 unilateral) all operated by pterygium excision and free autologous limbal-conjunctival autograft transplantation (L-CAT) without MMC and Group B included 20 eyes of 18 patients (9 males

and 9 females; 2 bilateral and 16 unilateral) all had injection of MMC 1 month before L-CAT surgery.

Preoperative assessment

Both uncorrected and best-corrected visual acuities (UCVA and BCVA, respectively) were measured using decimal system with equivalent standard logarithm of the minimum angle of resolution values. Full ophthalmic examination was performed including intraocular pressure measurement with Goldmann's applanation tonometry and indirect ophthalmoscopy for fundus.

Pterygium examination was performed to identify its nature (fleshy or fibrotic) and its corneal encroachment. It was graded according to growth onto the cornea: Grade 1 (0–2 mm), Grade 2 (2–4 mm), and Grade 3 (more than 4 mm).

Surgical technique

- Anesthesia was given by peribulbar injection of Debocaine[®] 2.0% (lidocaine HCL 20 mg; El Nasr Chemicals, Cairo, Egypt) and Marcaine[®] (bupivacaine HCL 0.5%; AstraZeneca AB, Sodertartalje, Sweden) in a ratio of 1:1. Subconjunctival injections at the pterygium and graft sites help in dissection.
- Dissection of the pterygium head was carried out with a crescent knife.
- Resection was carried out from the underlying sclera or medial rectus.
- Excision of the whole pterygium was carried out followed by hemostasis using wet-field cautery.

In Group A, a superficial circumferential incision (around 100- μ m depth) in the cornea, 0.5-mm from the superotemporal limbus, was performed to include limbal epithelium to the conjunctival graft. The limbal-conjunctival graft was placed in the correct orientation in the scleral bed and sutured using eight 8/0 vicryl anchoring sutures, conjunctiva-episclera-conjunctiva.

- Dressing was carried out with antibiotic-steroid mixtures ointment plus eye cover.
- Postoperative treatment given was mixed antibiotic-steroid drops (Dexaflox[™], ofloxacin 3.0 mg/mL and dexamethasone 1.0 mg/mL; Jamjoom, Jeddah, Saudi Arabia) and ointment (Tobradex[®], tobramycin 0.3 mg/mL and dexamethasone 1 mg/mL; Alcon, Cairo, Egypt) with gradual tapering of medications over 1 month postoperatively.

In Group B, 1 month before carrying out the previously described surgery, under an operating microscope and by using a 30-gauge needle, 0.2 mL of 1% lidocaine anesthetic

Table 1 Showing descriptive data for both groups

Data in mean \pm SD	Group A	Group B
Number of recurrences	1.33 \pm 0.2	1.93 \pm 0.3
Duration passed since last recurrence (months)	4.3 \pm 0.5	5.1 \pm 0.2
Length (mm)	7.00 \pm 2.66	5.23 \pm 1.56
Width (mm)	3.9 \pm 0.94	3.56 \pm 0.62
Grade	1.73 \pm 0.79	1.60 \pm 0.82

with epinephrine was injected into the head of the pterygium at the limbus, which caused mild swelling of the conjunctiva. Five minutes after the lidocaine injection, subconjunctival injection at site of pterygium was done using a 30-gauge needle on a tuberculin syringe containing MMC (0.1 mL of 0.15 mg/mL), followed by previously described eye drop and ointment for 1 week.

Evaluation

Patients were examined at postoperative days 1, 7, 14, and 30, then every 3 months for 1 year with the exception of 9 eyes which completed only 6 months follow-up. Evaluation is for the occurrence of any complications, such as corneal epithelial toxicity, sclera thinning, or graft sloughing, and for recurrences. Figures 1 and 2 show photographs for 2 cases of Groups A and B, respectively. Recurrence was defined as progressive fibrovascular corneal encroachment after surgery.

Results

Data were coded and entered using the statistical package SPSS (version 17; SPSS Inc, Chicago, IL). Data were summarized in percentage for qualitative variables. Comparisons between groups were done using χ^2 test. P value ≤ 0.05 was considered statistically significant.

Descriptive results

The study included 39 eyes of 33 patients (20 males and 13 females). Age ranged from 15 to 65 years (mean 43 ± 1.5 years) for Group A and from 27 to 59 years (mean 39 ± 2 years) for Group B.

Visual acuity

Preoperatively, mean UCVA measured for Groups A and B was 0.6 ± 0.1 and 0.56 ± 0.2 , respectively. Mean BCVA

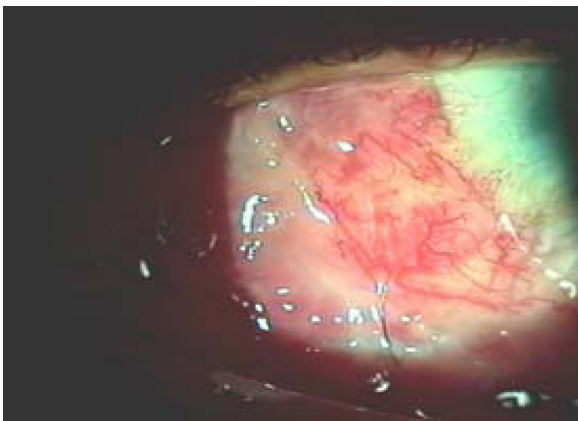


Figure 1 Postoperative photograph of a case of Group A.



Figure 2 Postoperative photograph of a case of Group B.

measured for Groups A and B was 0.9 ± 0.07 and 1 ± 0.1 , respectively.

Postoperatively at 1 month follow-up, mean UCVA measured for Groups A and B was 0.58 ± 0.08 and 0.57 ± 0.15 , respectively. Mean BCVA measured for Groups A and B was 0.87 ± 0.09 and 1.1 ± 0.08 , respectively.

Intraocular pressure

In Group A, the mean of 16 ± 0.5 mm Hg measured preoperatively changed postoperatively at 1 month follow-up to a mean of 15.8 ± 0.2 mm Hg. In Group B, the mean of 17.1 ± 0.4 mm Hg measured preoperatively changed postoperatively at 1 month follow-up to a mean of 16.9 ± 0.1 mm Hg.

Recurrence

A total of four cases of recurrences were recorded for Group A, two at 3 months, one at 6 months, and one at 12 months follow-up. One case of recurrence was recorded for Group B at 6 months follow-up.

Incidence and P value

For Group A (19 cases), recurrence in 4 cases (21.1%) ($P = 0.012$, within the group) was observed. For Group B (20 cases), recurrence in 1 case (5%) ($P < 0.001$, within the group) was observed. The incidence of recurrence in Group A (4 cases) represents 80% of the total recurrent cases (5 cases) and in Group B (1 case) represents 20% of the total recurrent cases. Comparing the recurrence incidence of the two groups was favorable for Group B (only 1 case of recurrence), but P value was 0.134 (statistically nonsignificant); however, it should be stated that the low number of recurrences in this study may have affected the statistical results of comparing the 2 groups. Figure 3 shows a bar graph with number of recurrences for each group.

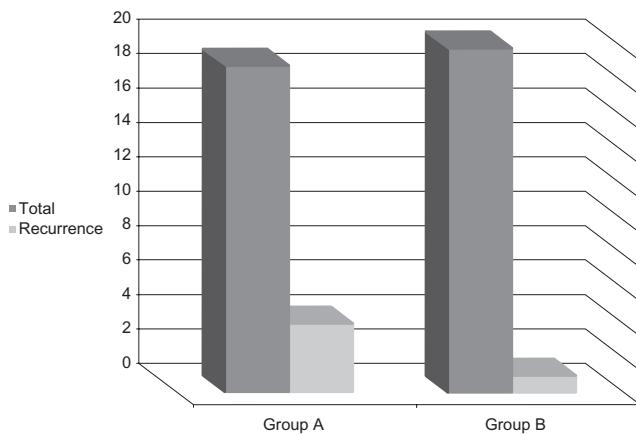


Figure 3 A bar graph showing recurrences in both groups; Group A (without MMC) and Group B (with MMC).

Abbreviation: MMC, mitomycin C.

Discussion

Pterygium, a worldwide degenerative corneal disease with a multifactorial etiology, is particularly common in tropical countries; the main complication of pterygium treatment is the unpredictable rate and timing of recurrences.^{13,14}

The pterygia recurrence rate reported for patients treated with the bare sclera technique ranges from 24% to 89%,^{15,16} whereas that reported after conjunctival autograft transplantation ranges from 1.6% to 33%.^{17,18} Amniotic membrane graft has been used as an alternative to conjunctival autograft transplantation, but the recurrence rate was still as high as 37.5% for recurrent pterygia.¹⁹

Recurrent pterygium presents a significant surgical problem. Conjunctival shortening or symblepharon caused by multiple surgeries is especially challenging. Repeated surgical intervention in the limbal area causes severe barrier function destruction. To treat this complicated disorder, both suppression of the subconjunctival fibrosis and the reconstruction of limbal barrier are required. Conjunctival transplantation, lamellar keratoplasty, and limbal autograft transplant have been performed.²⁰

In our study, the idea of using MMC 1 month preoperatively is to further decrease the dosage and morbidity associated with MMC when applied as topical or at time of surgery and to increase its effectiveness by applying the medication in a low concentration and low volume (0.1 mL of 0.15 mg/mL) subconjunctivally 1 month before surgery directly to the target tissue of activated fibroblasts.

Over a follow-up period of 12 months, four cases of recurrences (21.1%) for Group A and one case (5%) for Group B were reported. The superiority of using MMC could

be explained by its inhibitor and toxic effect on fibroblasts, and using it 1 month before surgery maximized its effect despite the low dose used.²¹

Other studies showed rather similar results compared to this study. Donnenfeld and colleagues reported a recurrence rate of 6% on using MMC as a single injection 1 month before surgery with same concentration used in our study; however, all cases operated were primary pterygia.²¹ Boberg-Ans and colleagues²² proposed limbal autograft transplantation for the treatment of recurrent and advanced pterygia and reported a 7.4% recurrence rate. However, Gris and colleagues² noted no recurrences after L-CAT. Akura and colleagues²³ also investigated a smaller excision graft combination employing a 4-mm window excision with subepithelial pterygium removal, but used intraoperative MMC. Their technique produced no recurrences in 66 patients with follow up ranging from 6 to 32 months.

Conclusion

Although the combined MMC injection followed by L-CAT procedure is time consuming and technically demanding, our reported favorable recurrence rate encouraged us to use this technique for recurrent pterygium treatment.

No broad consensus exists on the best treatment for recurrent pterygium. Further long-term, multicenter, and randomized trials with higher numbers of cases are needed to determine the best treatment method. The results of our study show that both treatment modalities achieved success in the prevention of recurrent pterygium.

Disclosure

The author reports no conflicts of interest in this work.

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