Comparative Study on the Use of Conjunctival Autograft With or Without Mitomycin-C in Pterygium Surgery

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ABSTRACT

Objective: To compare the recurrence rate after conjunctival autograft alone versus conjunctival autograft with mitomycin-C in the treatment of primary and recurrent pterygium.

Methods: This was a prospective, randomized, interventional comparative study of patients with primary and recurrent pterygium who were randomized to receive either simple excision with conjunctival autograft (CA) or simple excision with CA and mitomycin-C applied. They were followed up for 6 months and observed for recurrence of the pterygium. Statistical analyses were used to compare the 2 groups.

Results: Fifty-eight patients (62 eyes) diagnosed with primary and recurrent pterygium were evaluated. The mean age was 44.81 ± 12.35 years (range 25 to 70 years). Thirty eyes were treated with conjunctival autograft (15 primary, 15 recurrent) and 32 eyes (17 primary, 15 recurrent) with conjunctival autograft combined with intraoperative application of low-dose mitomycin-C (0.02% for 3 minutes). The mean follow-up period was 25 ± 1.40 months (range 24 to 28 months). There was a 3.22% recurrence rate (2 eyes) from the recurrent pterygium group. There was no significant difference in the rate of recurrence ($p = 0.53$) between the 2 treatments for both primary and recurrent pterygium. No mitomycin C-related complication was observed during the length of the study.

Conclusion: Conjunctival autograft surgery alone for primary and recurrent pterygium is effective and safe in reducing the recurrence rate of pterygium within 6 months.

Key Words: Pterygium, Recurrent pterygium, Mitomycin-C, Conjunctival autograft

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A pterygium is an elastotic degeneration of the conjunctival tissue and hyalination of the subepithelial tissue resulting in a triangular fibrovascular outgrowth from the conjunctiva encroaching on the cornea.[1] The worldwide incidence of pterygia appears to be increased in areas within 36 degrees north and south of the equator, popularly known as the pterygium belt, where the Philippines is located.[2,3] The most common cause of pterygium is the exposure to ultraviolet B or UVB rays. Other possible causes include hereditary factors such as the p53 oncogene, a marker for the pterygium gene seen among families, and dry eyes due to abnormalities in the tear film causing proliferation of cells for new growth.[4]

Pterygia are graded according to translucency.[5] Atrophic pterygium (T1) is defined as a fleshy conjunctival mass where episcleral vessels are unobscured. Intermediate pterygium (T2) is where episcleral vessels are partially obscured. Fleshy pterygium (T3) is where episcleral vessels are completely obscured by the conjunctival mass. When the lesion progresses to involve the central cornea, it causes significant astigmatism, obstruction of the visual axis, and corneal scarring.

Indications for excision are vision loss secondary to proximity to the visual axis or astigmatism, eye movement restriction, atypical appearance, progressive growth, and cosmetic concerns.[4] As early as 1800's, several techniques have been formulated to remove pterygia. Recurrence has always been a primary concern. Most ophthalmologists define pterygium recurrence as regrowth of fibrovascular pterygium-like tissue crossing the limbus onto the cornea with the fibrovascular recurrence attaining the same degree of corneal encroachment as the original lesion or regrowth exceeding 1 mm onto the cornea.[4]

In the hope of preventing recurrence among patients who underwent simple pterygium excision, adjunctive therapies were introduced such as beta-irradiation and thiotepa application, which are no longer used because of serious complications.[6] Mitomycin-C (MMC) is an antibiotic-antineoplastic drug that alkylates DNA and produces crosslinks, inhibiting DNA synthesis. In 1994, MMC was introduced as an adjunct therapy in treating recurrent pterygium.[7]

To our knowledge, there have been limited reports comparing the efficacy of conjunctival autograft (CA) alone versus CA with intraoperative MMC as an alternative pterygium treatment. This study determined the recurrence rate of CA with and without MMC in the treatment of primary and recurrent pterygium.

METHODOLOGY

All patients were evaluated at the Department of Ophthalmology and Visual Sciences of the Philippine General Hospital. The inclusion criteria were: 1) age 18 to 70, with unipolar primary or recurrent pterygium invading 2.0 mm or more of the cornea with ocular complaints; 2) for recurrent pterygium, enrollment should be at least 6 months since the patient's last surgery for pterygium; and 3) gave a written informed consent. Exclusion criteria included: 1) glaucoma and dysfunctional tear syndrome; 2) history of any previous ocular surgery aside from pterygium excision; and 3) refusal to give consent to the study.

The following demographics were gathered: age, gender, address, occupation, history of any systemic disease, history of previous ocular surgery, best-corrected visual acuity, tonometry, refraction, Schirmer's I and tear break-up time measurements, and slit lamp examination. An image of the patient's cornea was recorded for baseline comparison prior to surgery. The size of the pterygium was also recorded. Pterygia with at least 2.0 mm size were included in the study.

Patients who fulfilled the inclusion criteria were divided into two groups: primary and recurrent pterygium. Those with primary pterygium were randomly assigned to two groups: group 1 underwent simple excision with CA and group 2 underwent simple excision with CA and intraoperative low-dose MMC. The recurrent pterygium group was also randomized into either group 3 representing simple excision with CA and group 4 for simple excision with CA and intraoperative low-dose MMC. Randomization was done using sealed envelope type.

Three surgeons performed the surgeries following the same method. In the surgical technique, retrobulbar anesthesia was administered using an equal mixture of 3 mL of 1% lidocaine HCl and 3 mL of 4% bupivacaine HCl. Partial thickness of the 12 o'clock limbal area was bridled using spatulated vicryl

6-0 suture. The pterygium head was carefully dissected from the cornea using a blade 15, and the body was dissected from the conjunctiva using Wescott tenotomy scissors. During the process, the rectus muscle was identified and not disturbed. The conjunctival edge was trimmed using tenotomy scissors. The defect was measured (in mm) with a caliper at primary gaze. The superior bulbar conjunctiva was exposed and marked with gentian violet with a measurement 1mm greater than the conjunctival defect. Lidocaine-epinephrine was injected subconjunctivally to the donor conjunctiva using a gauge 30 needle. Careful dissection and excision of the conjunctiva from the Tenon's was done. The free graft was placed over the scleral bed, epithelium side up, and anchoring sutures were placed on the four corners of the graft using nylon 10-0. Additional sutures were evenly placed to secure the donor conjunctiva. Tobramycin-dexamethasone eye ointment was applied over the sutured area, and pressure eye patch was placed and retained for 24 hours.

The operative technique for conjunctival autograft with MMC application was essentially the same except for the application of 0.02% MMC in the bare sclera and head of the pterygium for 3 minutes and then washed off with 30 mL of normal saline solution after excision of the pterygium.

Patients were given tobramycin-dexamethasone drops four times a day postoperatively and tapered slowly during the course of follow up. Sutures were gradually removed after 3 weeks.

A single examiner, who was blinded to the procedure, did the follow up after 1 day, 1 week, 1 month, 2 months, 3 months, and every 6 months thereafter. In this study, the presence of pterygium recurrence was observed during the entire length of the study. Recurrence was defined as any fibrovascular proliferation encroaching onto the cornea coming from the original pterygium site.

Data were encoded and tallied in SPSS version 10 for Windows. Descriptive statistics were generated for all variables. For nominal data, frequencies and percentages were computed. For numerical data, mean, standard deviation, and the median were generated. Comparison of the different variables under study was done using chi-square, t-test, Mann-Whitney U test, and Fisher's Exact test.

The research ethics board of PGH has reviewed and approved the protocol.

RESULTS

Demographic and clinical characteristics are summarized in Table 1. Sixty-two eyes of 58 patients were included in the study. The mean age was 44.81 ± 12.49 years and 48.97 ± 12.35 years in the primary and recurrent pterygium groups respectively. There were no differences between the ages (p = 0.63) and gender (p=0.96) of the two groups. There was also no difference in the duration of follow up (p=0.10).

Table 1. Demographic characteristics of study population (N=58).

Characteristics	Group 1	Group 2	Group 3	Group 4	P value
Number of eyes	15	17	15	15	--
Age (years) Mean ± SD	44.73 ± 11.99	44.88 ± 3.29	49.60 ± 11.31	48.33 ± 13.68	0.63
Follow up (months) Mean ± SD Median	24.93 ± 1.16 24	25.47 ± 1.92 24	24.24 ± 0.56 24	25.00 ± 1.31 24	0.10
Gender Female Male	 9 6	 9 8	 9 6	 9 6	0.96

Group 1 - Primary pterygium CA without MMC
Group 2 - Primary pterygium CA with MMC
Group 3 - Recurrent pterygium CA without MMC
Group 4 - Recurrent pterygium CA with MMC

The recurrent rates of the different groups are shown in Table 2. Two patients had recurrence of the pterygium, both belonging to the recurrent group. In group 3 (without MMC), the pterygium recurred in a 41-year old laundrywoman with the fibrovascular proliferation on the nasal side of the cornea 2.0 mm from the limbus noted 2 months post-surgery. In group 4 (with MMC), the recurrence was noted in one eye of a 30-year old seafarer with bilateral recurrent pterygium 1 month post-surgery. In this study, the rate of recurrence was 3.22% and there was no difference between the use of MMC or not in both the primary & recurrent groups (p=0.53).

Table 2. Recurrence rates of pterygium.

Recurrence	Group 1 n (%)	Group 2 n (%)	Group 3 n (%)	Group 4 n (%)
Positive	0	0	1 (7.14)	1 (7.14)
Negative	15	17	14 (92.86)	14 (92.86)

One patient complained of occasional eye discomfort characterized as sensation of "heaviness" in the affected eye 3 weeks after surgery. On slit-lamp examination, there was note of superficial punctate keratitis with good graft uptake. Patient was started on topical lubricant four times a day with resultant relief.

Table 3. Complications.

Complications	Conjunctival autograft n (%)	Conjunctival autograft + 0.02% MMC n (%)
Steroid-induced increased IOP	1 (3.3%)	0
Tenon's cyst	1 (3.3%)	0
None	28 (93.3%)	32 (100%)

There was no difference (p = 0.23) in the proportion of patients with postoperative complications among the groups (Table 3). Steroid-induced increase in intraocular pressure (IOP) (25 to 30 mmHg on week 3) was noted in one patient diagnosed with primary pterygium who underwent CA alone. The steroid was tapered and discontinued within 2 weeks and at 8 weeks post-surgery, IOPs returned to normal. No anti-glaucoma medications were given. Tenon's cyst was observed in one patient who underwent CA alone. There was no associated limitation of movement of the globe and no medications were given. The plan was to observe.

DISCUSSION

Pterygium occurrence is increasing and is more prevalent in countries along the equatorial zone. Our results showed no difference between the number of males and females who were diagnosed with pterygium. An almost equal distribution in our study could be attributed to an increasing female workforce working outdoors and possibly to an underestimation of the male population seeking consult for pterygium in a tertiary hospital.

The management of pterygium recurrence has been a challenge for ophthalmologists for centuries. It has been a source of frustration for both surgeons and patients. Bare sclera and primary closure techniques were frequently performed, with high rates of recurrence.[4-6]

The introduction of intraoperative MMC to bare sclera has been shown to reduce pterygium recurrence with only minimal complications.[7-9] The decreased contact time of the drug to the bare sclera is an important factor to minimize complications. In a 5-year follow-up evaluation of post-pterygium surgery in human eyes using intraoperative MMC, it was found that the use of 0.02% MMC intraoperatively for 3 minutes was safe with no serious complications.[8] Another recent study using 0.04% MMC intraoperatively for 1.5 minutes reported no serious complications, such as persistent avascular zones, ulcer or thinning of the sclera, corneal edema, corneal perforation, and scleral calcification.[9]

After the safety of the use of low dose MMC in pterygium excision has been established in 1994, studies thereafter have been conducted to prove its efficacy in reducting pterygium recurrence. Recurrence rates ranged from 4.7% to 33% when combining this adjunct drug with simple pterygium excision.[10-14] In a study by Lam, the recurrence was greatly reduced by increasing the concentration and length of exposure of the drug to bare sclera, but this also increased the complications. He reported two cases of scleral melt among patients who had exposure to 0.02% MMC for 5 minutes.[14] Thereafter, many have concluded that it was safer to use MMC in moderation and combine it with another effective surgical procedure in reducing recurrence. These studies were the basis for choosing the concentration & exposure time of MMC in this study.

Conjunctival autograft (CA), developed in 1985, is a common surgical procedure that was initially performed for treatment of advanced and recurrent pterygium.[15] Currently, it is gaining popularity as a treatment for primary pterygium, with recurrence rates ranging from 13.3% to 20.8%.[10,13,16,17] For recurrent pterygium, recurrence rates varied from 13.6% to 31.2%.[13,16,17] Studies on mitomycin-C as adjunct therapy to CA have reported further decrease in recurrence rates. Wong compared CA alone versus CA with intraoperative MMC in primary pterygium and reported a significant difference ($p<0.03$) in recurrence rates between the 2 groups. He concluded that in those with pterygium encroaching one-third to one-half of the cornea, the rate of recurrence was more than double in the CA group.[16] Most of the recurrence was noted at the 7th to 9th month of follow up. In another study involving primary pterygium, there was a significant reduction in the recurrence rate when combining CA with MMC compared to CA alone.[10] In our study, we not only compared the

recurrence rates of CA alone versus CA with MMC in primary but also in recurrent pterygium. Our results showed that recurrence occurred only in the recurrent pterygium group, and that treatment effect was not significantly different between the groups (p=0.53).

Risk factors for pterygium occurrence included younger age and frequent sun exposure. For pterygium recurrence, aside from those mentioned earlier, surgeon's skill and experience in removing the pterygium could affect the recurrence rate. This was supported by the study of Farrah and coworkers who concluded that the surgeon's experience could influence the success rates and complications of CA for pterygium treatment.[18]

One limitation of our study was the short follow-up period. Dela Hoz and associates showed that without MMC, recurrence of pterygium after CA peaked at around 3 to 6 months. If MMC was applied, recurrence was observed at 36 months.[19] Our results showed recurrence as early as the first month after surgery in the recurrent pterygium group treated with CA and MMC. Surgeon's experience and the aggressive nature of the pterygium might explain this early recurrence. Moreover, the patient was a seaman who was constantly exposed to the elements of the sun and wind. Longer follow up is recommended for our study sample to ascertain those that would develop recurrence later.

Complications noted were steroid-induced intraocular pressure elevation and Tenon's cyst formation. These were not considered to be related to the use of MMC.

In summary, our study showed that conjunctival autograft alone could decrease the recurrence rate among primary and recurrent pterygium, with no significant difference seen with the addition of intraoperative low-dose MMC with a 6-month follow up. Further follow up, however, is recommended to observe for late-onset recurrence and complication.

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