ORIGINAL ARTICLE

Recurrence Rate of Pterygium Following Surgical Excision with Intraoperative Versus Postoperative Mitomycin-C

Atiya Rahman, Kamran Yahya and Khwaja Sharif-ul-Hasan

ABSTRACT

Objective: To compare the rate of recurrence and complications of pterygium following surgical excision by applying 0.02% mitomycin-C intraoperatively or using topical 0.02 % mitomycin-C drops postoperatively.

Study Design: Randomized clinical trial.

Place and Duration of Study: Baqai Medical University Hospital, Department of Ophthalmology, from January 2001 to July 2005.

Methodology: Eighty-four eyes of 65 patients, aged between 20-70 years, with primary pterygium were randomly allocated into two groups using random tables. Patients with bilateral disease were treated with an interval of 10-14 days and randomized separately. In group-I, 0.02 % mitomycin-C was applied intraoperatively for 3 minutes after pterygium excision. Group-II received mitomycin-C 0.02 % eye drops twice a day for 2 weeks after pterygium excision. Patients were followed-up for pterygium recurrence for one year. Variables were compared for significance, using Pearson chi-square test.

Results: In Group I, recurrence of pterygium was seen in 4 (10.0%) eyes and superficial punctate keratitis in 4 (9.5%) eyes, while 8 (19.0%) eyes developed avascularization of sclera at the pterygium excision site. In group II, 8 (20.51%) eyes had pterygium recurrence (p=0.38), 13 (31.0%) eyes had superficial punctate keratitis and tenon cyst was seen in one (2.4%) eye. One (2.4%) eye in each group developed scleral thinning.

Conclusion: There was no significant difference in pterygium recurrence rate intraoperatively or postoperative application of 0.02% mitomycin-C. Complications were comparatively less following application of intraoperative 0.02% mitomycin-C for 3 minutes.

Key words: *Pterygium. Mitomycin-C. Bare Scleral Excision. Recurrence.*

INTRODUCTION

Pterygium is a conjunctival degenerative disorder.[1] It is more common in tropical and subtropical countries.[2] It is a fibrovascular growth of actinically damaged conjunctiva that extends across the limbus and invades the cornea.[3] The stimulus, which causes pterygium to grow, is excessive exposure to sunlight.[4] Ultraviolet rays cause mutation in limbal basal stem cells, which produce an abnormal p53 protein, excessive tissue growth factor–β and various cytokines are responsible for various pathological changes in pterygium.[5]

The primary surgical indication for pterygium removal is decreased visual acuity due to encroachment of the pterygium into visual axis, irregular astigmatism, discomfort, irritation, restricted ocular motility, difficulty in wearing contact lens, refractive surgery and cosmetic deformity. There are many different surgical approaches for the management of pterygium. The simplest technique is the bare scleral technique, first described by Ombrian,[6] but its rate of recurrence is 37 to 91%.[3]

The recurrence rate of pterygium could be decreased by using mitomycin-C.[7] It is an anti-neoplastic antibiotic agent isolated from the fermentation filtrate of Streptomyces caespitosus[8] and inhibits the synthesis of DNA and cellular RNA.[9] The use of mitomycin-C is sometimes associated with complications, such as scleral necrosis, secondary glaucoma, corneal perforation,[10] iritis and sudden onset of mature cataract.[7] The use of mitomycin-C in pterygium recurrence control has not been studied in local context, so far.

The aim of this study was to compare the recurrence rate of pterygium following surgical excision by applying 0.02% mitomycin-C intraoperatively for three minutes or using topical 0.02 % mitomycin-C drops postoperatively twice daily for two weeks and also compare the rate of complications between the two.

METHODOLOGY

This study was conducted at the Department of Ophthalmology, Baqai Medical University Hospital, Karachi, from January 2001 to July 2005. The study included 84 eyes of 65 patients aged between 20-70

Department of Ophthalmology, Baqai Medical University Hospital, Karachi.

Correspondence: *Dr. Atiya Rahman, IV-A, 9/1, Nazimabad, Karachi.*
E-mail: atiyaky@yahoo.com

Received October 2, 2007; accepted May 23, 2008.

years. Sample size was estimated for the difference between the two population proportion choosing confidence interval (1–α) = 95%, absolute precision (d) of 0.07, anticipated population proportion I (P1) 0.07, and (R) anticipated population proportion II (P2) at 0.033.

The calculated sample size was 77, adding 10% to this for the anticipated follow-up loss, it became 84. Eyes with primary pterygium, satisfying the inclusion criteria were randomly allocated into two groups, 42 eyes in each group using random tables. Patients with bilateral disease were treated with interval of 10 -14 days and randomized separately.

The inclusion criteria were patients older than 20 years and primary pterygium invading more than 2 mm on the cornea from the limbus. The exclusion criteria were any history of previous pterygium surgery, external ocular diseases, such as atopic keratoconjunctivitis, ocular rosacea, herpetic keratitis and single-eye patients.

A complete ocular examination including visual acuity was recorded by using Snellen's chart. The intraocular pressure was measured by applanation tonometer (Haag Streit) after instillation of local anesthetic drops proparacaine hydrochloride 0.5% and using fluorescein strips. Anterior segment was examined using slit lamp (Nidek SL–450) and posterior segment examination was done by slit lamp biomicroscopy using double aspheric 90 D lens (Volk).

In group I patients, surgical excision of pterygium was performed using bare scleral technique under an operating microscope. After pterygium excision, no cautery was applied on the sclera, and area of bare sclera on average measuring 5 x 6 mm was left behind. After excision, mitomycin-C 0.02% was applied intraoperatively for 3 minutes at the corneoscleral site by a sterile sponge 5 x 5 mm soaked in 8-10 drops of mitomycin-C. After 3 minutes, the eye was irrigated with 10 ml of normal saline. The mitomycin-C drops were freshly prepared on the day of surgery, under sterile conditions, from commercially available injectable 2 mg vial diluted with 10 ml of distilled water to achieve the concentration of 0.02%.

Patients in group II received mitomycin-C 0.02% eye drops after pterygium excision postoperatively twice a day for two weeks, these drops were prepared freshly on the day of surgery as for intraoperative application and were dispensed in a sterile dropper. Patients were asked to refrigerate it for one week after which on the follow-up visit, they were given freshly prepared for the next week.

Patients were followed-up on day 1, 7, 15 and then monthly for 6-12 months. They were evaluated for ocular pain, foreign body sensation and photophobia. After recording visual acuity, slit lamp examination was done using fluorescein stain to look for superficial punctate keratitis and scleral defect. Anterior chamber reaction, recurrence of pterygium and intraocular pressure were also recorded.

Mean age between gender and two groups were calculated using student's t-test. Frequency of recurrence and complications were compared using chi-square test. SPSS version 15 was used for statistical analysis. P-value ≤ 0.05 was considered statistically significant.

RESULTS

Eighty-four eyes of 64 patients underwent pterygium excision followed by mitomycin-C 0.02 % (0.2 mg/ml) application. Out of those 64 patients, 53 were males and 31 females. The mean age of patients was 45.57 years (ranging from 20–80 years, Table I). Those 84 eyes were divided into two groups; 42 eyes in each group. All the patients had primary pterygia which were present on the nasal side. The patients were followed up for one year.

Table I: Demographic characteristics of patients.

	Intraoperative MMC Group-I	Postoperative MMC Group-II	p-value	95% confidence interval of the difference
Number of eyes	42	42		
Age (years) mean ±SD	45.57±14.77	45.83±11.05	0.927	-5.927 – 5.403
Gender				
Male	29	24	0.366	
Female	13	18		

Out of 84 eyes, 5 eyes were lost to follow-up. Two belonged to group I and 3 to group II. Table II summarizes the intraoperative and postoperative complications. In group I, superficial punctate keratitis was seen in 4 (9.5%) eyes after fluorescein staining on the slit lamp. Avascularized sclera were observed within the first postoperative month in 8 (19.0%) eyes and scleral thinning in the bare area was seen in 1 (2.4%) eye during the second week. In group II, superficial punctate keratitis was seen in 13 (31.0%) eyes and scleral thinning and tenon cyst was noted in 1 (2.4%) eye.

Table II: Postoperative complications.

Complications	Intraoperative MMC Group-I (n=40)	Postoperative MMC Group-II (n=39)	* p-value
Superficial punctate Keratitis	04 (9.5%)	13 (31.0%)	
Avascularised sclera	08 (19.0%)	00 (0%)	
Scleral thinning	01 (2.4%)	01 (2.4%)	0.003
Tenon cyst	00 (0%)	01 (2.4%)	
No complications	27 (64.3%)	24 (57.15)	

** pearson chi-square*

In group I, pterygium recurrence was seen in 4 (10.0%) eyes, and in group II, recurrence was seen in 8 (20.51%) eyes. The fibrovascular growth extended 2-2.5 mm on the cornea. Statistically, the recurrence rate between the two groups was not found to be significant (p=0.38).

Statistically significant difference was observed in the complication rate between the two groups p=0.00.

DISCUSSION

Pterygium frequently recurs after simple surgical removal, various adjunctive measures have been devised to prevent the recurrence, these include sliding conjunctival flap to cover pterygium site, conjunctival autograft transplantation, β–irradiation and use of topical and intraoperative mitomycin-C.[11]

Mitomycin-C significantly reduces the rate of pterygium recurrence following its excision to less than 10 %[12] by inhibiting the proliferation of fast growing cells, such as fibroblasts and vascular endothelial cells.[4] Use of mitomycin-C for pterygium surgery was first described by Kunitomo and Mori in Japan in 1963 and in the United States by Singh *et al.* in 1988.[3] Hayasaka *et al.* reported the use of 0.02% mitomycin-C as safe and effective for preventing pterygium recurrence.[4]

In these patients, following the application of mitomycin-C 0.02% intraoperatively for 3 minutes after pterygium excision, recurrence was 10.0%. Recurrence rate of 33.3% after intraoperative application of mitomycin-C has been reported by Avisar *et al.*,[13] which is very high as compared to the presently reported recurrence rate. Mastropasqua *et al.* reported recurrence rate of 12.5% following pterygium excision and intraoperative application of 0.02% mitomycin-C for 3 minutes.[11] Frucht-Pery *et al.* reported recurrence rate of 6% following the intraoperative application of 0.02% mitomycin-C for 3 minutes.[14]

Among these patients the recurred pterygia were proliferation of fibrovascular tissue involving 2 - 2.5 mm of cornea. Amano *et al.* has defined recurrence as postoperative regrowth of fibrovascular tissue crossing corneoscleral limbus.[11]

Among the patients, who were given topical mitomycin-C 0.02% drops twice a day for two weeks, pterygium recurred in 8 (20.51%) eyes. Oguzi *et al.* reported the recurrence rate of 20% following the use of 0.02% mitomycin-C eye drops four times a day for one week,[4] which is almost same as ours. Manning *et al.* used 0.02% mitomycin-C drops postoperatively and reported 22.2% recurrence.[4] Recurrence of 1.36% has been reported by Fahmi *et al.* following the use of mitomycin-C 0.02% drops twice daily for 3 days.[15]

Intraoperative and postoperative application of mitomycin-C is associated with various complications such as punctate keratopathy, corneal perforation, iritis,[14] scleral melting, glaucoma and cataract formation.[3]

In this study, superficial punctate keratitis was observed in 4 (9.5%) eyes following intraoperative application and mild avascularity of bare sclera was found among 8 (19.0%) eyes, which was treated by applying lubricants till resolution. No such avascularized scleral area was seen among the patients who were given topical mitomycin-C 0.02% eye drops. Raiskup *et al.* reported avascularized scleral zone in 6.9% eyes following pterygium excision and intraoperative application of mitomycin-C for 5 minutes and 23.2% among those patients who were given postoperative mitomycin-C 0.02% drops twice a day for 5 days.[12] Superficial punctate keratitis was seen in 13 (31.0%) eyes in patients who used topical mitomycin-C 0.02% eye drops. Rachmiel *et al.* has reported the rate of superficial punctate keratitis as 7.9% after topical mitomycin-C 0.02% application.[7]

Avascularized scleral bed and superficial punctate keratitis that appeared in our patients could be attributed to the toxic and antimetabolic effects of mitomycin-C on the stem cells, particularly vascular endothelial cells and limbal pleuripotent stem cells as hypothesised by Rubinfeld.[7]

Scleral thinning in the bare area of sclera was observed in 1 (2.4%) eye belonging to each group after 2 weeks. The scleral defect responded to topical antibiotics and ocular lubricants. Tenon cyst occurred in 1 (2.4%) eye following topical mitomycin-C use and the lesion resolved spontaneously after seven weeks. The reason for high rate of complications among patients belonging to group II could be due to the uncontrolled and prolonged use of the drug by these patients. Single intraoperative application of mitomycin-C 0.02% is comparatively safer as it localizes the effect on the tissue, do away problem of patients' poor compliance and prevents dose dependent complications caused by inappropriate use.[11]

CONCLUSION

In this study, following pterygium excision, application of mitomycin-C in concentration 0.02% intraoperatively for 3 minutes or postoperatively topically mitomycin-C 0.02% eye drops twice a day for two weeks, did not show a statistically significant difference in the recurrence rate of pterygium among the two groups. The postoperative complications were less with intraoperative application of 0.02% mitomycin-C for 3 minutes, showing that it is safe adjunctive treatment for primary pterygium excision.

Acknowledgement: The authors are thankful to Dr. Bader Faiyaz Zuberi for statistical help who voluntarily participated in this study.

REFERENCES

1. Ahmad I, Untoo RA, Ahmad SS. Complications following use of intraoperative mitomycin-C in pterygium surgery. *JK Science* 2004; **6**: 34-6.

2. Saleem M, Muhammad L, Zia-ul-Islam. Pterygium: an epidemiological study. *Pak J Ophthalmol* 2004; **20**:17-22.
3. Donnenfeld ED, Perry HD, Fromer S, Doshi S, Solomon R, Biser S. Subconjunctival mitomycin-C as adjunctive therapy before pterygium excision. *Ophthalmology* 2003; **110**:1012-6.
4. Oguz H, Basar E, Gurler B. Intraoperative application versus postoperative mitomycin-C eye drops in pterygium surgery. *Acta Ophthalmol Scand* 1999; **77**:147-50.
5. Barraquer R. Updated management of limbal dystrophies and degenerations – Part 1. *Highlights Ophthalmol* 2005; **33**:7-8.
6. Mahar PS, Nwokora GE. Role of mitomycin-C in pterygium surgery. *Br J Ophthalmol* 1993; **77**:433-5.
7. Rachmiel R, Leiba H, Levartovsky S. Results of treatment with topical mitomycin-C 0.02% following excision of primary pterygium. *Br J Ophthalmol* 1995; **79**:233-6.
8. Cano-Parra J, Diaz-Llopis M, Maldonado MJ, Vila E, Menezo JL. Prospective trial of intraoperative mitomycin-C in the treatment of primary pterygium. *Br J Ophthalmol* 1995; **79**:439-41.
9. Boyd S. Application of mitomycin-C during pterygium surgery. *Highlights Ophthalmol* 2002; **30**: 26.
10. Mastropasqua L, Carpineto P, Ciancaglini M, Enrico Gallenga P. Long-term results of intraoperative mitomycin-C in the treatment of recurrent pterygium. *Br J Ophthalmol* 1996; **80**: 288-91.
11. Amano S, Motoyama Y, Oshika T, Eguchi S, Eguchi K. Comparative study of intraoperative mitomycin-C and β-irradiation in pterygium surgery. *Br J Ophthalmol* 2000; **84**: 618-21.
12. Raiskup F, Solomon A, Landau D, Ilsar M, Frunch Pery J. mitomycin-C for pterygium: long-term evaluation. *Br J Ophthalmol* 2004; **88**:1425-8.
13. Avisar R, Gaton D, Loya N, Appel I, Weinberger D. Intraoperative mitomycin-C 0.02% for pterygium: effect of duration of application on recurrence rate. *Cornea* 2003; **22**:102-4.
14. Frucht–Pery J, Raiskup F, Ilsar M, Landau D, Orucov F, Solomon A. Conjunctival autografting combine with low dose mitomycin-C for prevention of primary pterygium recurrence. *Am J Ophthalmol* 2006; **141**:1044-50.
15. Fahmi MS, Sayed J, Ali M. After removal of pterygium role of mitomycin and conjunctival autograph. *Ann Abbasi Shaheed Hosp Kar Med Dent Coll* 2005; **10**:257-61.