Original Article

Risk Factors Involved in Pterygium Recurrence after Surgical Excision

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Purpose: To assess the influence of size and type of growth, age and gender of the patient and the duration of intraoperative mitomycin-C (MMC) application, on the recurrence of pterygium after surgical excision.

Material and Methods: This retrospective, descriptive case series was carried out at the department of ophthalmology, Aga Khan University Hospital, Karachi. One hundred forty seven patient's (147 eyes) data files were analyzed from 1999 to 2009, who underwent surgical removal of pterygium using bare sclera method with MMC in concentration of 0.2 mg / ml (0.02%) with variable exposure time of 1-5 minutes. Ninety nine male and 48 female with mean age of 46.4 years (range 16 to 60 years) were included in the study. The classification of subjects was done according to the age, gender, MMC application time and type and size of pterygium. The main outcome measure was comparison of pterygium affected eye for any kind of recurrence after a minimum of 12 months of the follow up.

Results: The pterygium recurrence rate was 8.8% in our case series at the mean follow of 1 year. The factors such as younger age (< 50 years) at presentation (P = 0.04, Pearson chi square test) and the presence of secondary pterygium (P = 0.05) correlated significantly with the recurrence of pterygium. There was a definite trend of lesser recurrence seen with MMC application time of greater than 3 minute as well as for a lesser size of the pterygium. However, statistical significance could not be achieved because of the small sample size.

Conclusions: These results suggest that a younger age of < 50 years coupled with increased size as well as history of multiple recurrences and MMC application time of less than 3 minutes are risk factors for pterygium recurrence after surgical excision.

Pterygium is one of the most common conjunctival surface degenerative disorders seen in subtropical and tropical areas[1-3]. Apart from causing cosmetics blemish, it alters the smoothness of the anterior surface of the eye ball with disruption of the normal tear film. It can also induce corneal astigmatism and if allowed to proceed over the pupillary area, reduces the vision[2]. A number of different surgical approaches have been proposed for the treatment of pterygium. The most common method has been the bare scleral excision technique, first described by Ombrian[4]. However, the major limitation to simple excision is the high rate of postoperative recurrence[5]. Therefore a number of adjunct therapies have been advocated along with excision to varying levels of success during the last three decades. The use of topical Mitomycin C (MMC) as an adjunct therapy to prevent pterygium recurrence has considerably increased since its first introduction by Kunitomo and Mori of Japan[6] and its subsequent usage in US by Singh and associates[7].

A number of research studies have been carried out to document the appropriate dosage and efficacy of MMC in treating pterygium and preventing its recurrence. However relatively few studies have evaluated the role of other factors such as age, gender, MMC exposure time, as well as the size and extent of

pterygium encroaching on the cornea[8-10]. Hence to prove the hypothesis that the above mentioned factors also play an important role in pterygium recurrence, we undertook this study to evaluate the role of these factors.

MATERIAL AND METHODS

This retrospective, case series study was carried at Ophthalmology Department, Aga Khan University Hospital (AKUH), Karachi – Pakistan. The patient's data files were analyzed starting from the period of 1999 till 2009. Only those patients fulfilling the following criteria were enrolled in the study, informed consent from the patient, individuals of all ages with established diagnosis of either unilateral or bilateral progressive pterygia of different sizes, supervised surgical excision by bare scleral technique and MMC administration, with minimum follow-up period of 12 months. The patients lost to the follow up or having any suspicious growth other than the pterygia and corneal scarring were excluded.

All patients had their detailed medical history taken, with complete ocular examination including best corrected visual acuity (BCVA), slit-lamp examination of anterior segment with Goldman applanation tonometry and fundus examination with +90 DS lens. The pterygia were classified either as primary or secondary on the basis of first time episode or recurrence respectively.

The pterygium size was graded depending on the extent of corneal involvement: Grade 1 – pterygium encroaching over cornea for 2 mm. Grade 2 – head of the pterygium covering cornea of more than 2 mm but sparing the visual axis and Grade 3–involving the visual axis.

A total of 147 patients (147 eyes) based on our inclusion criteria were incorporated in the study who had minimum follow up of 12 months, while 26 patients were lost to the follow-up, during the study period were excluded from the study. Ninety-nine male and 48 female (Male to Female ratio 2:1) aged between 16 and 60 years (mean age 46.4 years) were included in the study. Primary pterygium was present in 120 patients while secondary pterygium was diagnosed in 27 patients. One hundred two eyes (69.4%) were affected by grade 1 pterygium, 24 eyes (16.3%) had grade 2 and 21 eyes (14.3%) were having grade 3 pterygium. In 129 eyes (87.7%), pterygium was located on the nasal side, with 16 eyes (10.9%) had it on the temporal side and 2 eyes (1.4%) were affected on the either side. Out of 147 eyes with pterygium, 66 belonged to the right eye and 81 to the left eye. The baseline characteristics of patients are shown in (Table 1).

Pterygium excisions were performed on an outpatient basis by the same surgeon using the same technique[11]. After excision with bare scleral technique under topical anesthetic (Proparacaine – Alcon Belgium), a sterile sponge (5x5 mm) soaked in 8 – 10 drops of 0.2 mg/ml MMC (0.02%) (Mitomycin – C, Kyowa – Japan) was applied over corneo-sclera and the area from where pterygium was excised with variable duration of 1 – 5 minutes. The sponge was removed and eye irrigated with 20 ml of Normal saline 0.9%. This was followed by topical administration of Dexamethasone 0.1% + Tobramycin 0.3% (Tobradex-Alcon, Belgium) and Hydroxypropyl Methylcellulose (Tear Naturale II – Alcon, Belgium) four times a day for 4 weeks. The dosage of MMC was calculated in line with the international recommendations[12-14]. Patients were regularly followed up at the interval of 3 months after the procedure. Any Adverse effect or physical findings were noted on each visit for a minimum of one year period. The recurrence of pterygium was defined as an encroachment of fibrovascular connective tissue across the limbus and onto the cornea for any distance in the position of the previous lesion.

The classification of subjects was done according to the age, gender, MMC application time, type and grading of the pterygium. Subjects were divided into two age groups (1) ≤ 50 years in age (2) > 50 years. The time duration of topical application of MMC was divided into five groups, ranging from 1 to 5 minutes. The potential factors were also classified accordingly (Table 2).

The study protocol was reviewed and approved by an ethics committee at the study centre and the study was carried out in accordance with the declaration of Helsinki of 1975 as revised in 1983. The primary outcome measure was the comparison of pterygium affected eye for any kind of recurrence after excision, along with the assessment of the potential role of MMC and grading of the pterygium with other factors in pterygium recurrence after a minimum of 12 months of follow up.

The data was entered in Statistical Package for Social Sciences (SPSS) version 16 and analyzed using frequencies, proportions, group means, standard deviation, Pearson Chi square test and Fisher exact

test. Alpha level of 0.05, confidence interval of 95% and power of 0.8 were selected for the analysis.

Table 1: Baseline characteristics of patients

Characteristics of Patients	No. of Patients (N = 147)	Frequency n (%)
Sex		
Male	99	67.3
Female	48	32.7
Affected eye*		
Right	66	44.9
Left	81	55.1
Grading of Pterygium*	120	81.6
Primary		
1	85	70.8
2	21	17.5
3	14	11.7
Secondary	27	18.4
1	17	63
2	03	11.1
3	07	25.9
Site of Pterygium		
Nasal	129	87.8
Temporal	16	10.9
Central	02	1.4
Recurrence		
Yes	13	8.8
No	134	91.2

* Bilaterally affected eyes have been classified into right and left respectively

* Grading of pterygium has been done as given in methods

RESULTS

Out of 147 eyes (147 patients), the recurrence of pterygium was seen in 13 eyes (8.8%) of 13 patients with mean time of recurrence of 6.77 months.

Out of 13 recurrences, 12 patients were in the age group below 50 years (P = 0.04, Pearson Chi Square test). Similarly there was a higher tendency of recurrence in male (10.1%) as compared to female (6.2%) though this was not statistically significant (P = 0.547). Most of the recurrence was seen on the nasal side (9.3%) while 6.2% of pterygia recurred on either side (P = 1.00).

Table 2: Potential risk factors in Pterygium recurrence

Variable	Recurrence n (%)		P-value*
	Yes	No	
Type of Pterygium			
Primary	08 (6.7)	112 (93.3)	0.05
Secondary	05 (18.5)	22 (81.5)	
Grading of Pterygium			
1°	06 (5.9)	96 (94.1)	0.06
2°	05 (20.8)	19 (79.2)	
3°	02 (9.5)	19 (90.5)	
Gender			
Male	10 (10.1)	89 (89.9)	0.547
Female	03 (6.2)	45 (93.8)	
Age (Years)			
Mean ± Std. Dev.	46.4 ± 1.23		0.04
< 50	12 (13.5)	77 (86.5)	
> 50	01 (1.7)	57 (98.3)	
MMC (Application Time)			
1 min	01 (50)	01 (50)	0.213
2 min	07 (9.9)	64 (90.1)	
3 min	04 (9.8)	37 (90.2)	
4 min	01 (3.7)	26 (96.3)	
5 min	00 (00)	06 (100)	
Concurrent Cataract			
Yes	02	29	0.737
No	11	105	
Pterygium Location			
Nasal	12 (9.3)	107 (90.7)	1.00
Central	01 (6.2)	15 (93.8)	
Temporal	00 (00)	02 (100)	

In the group with recurrent pterygia, the recurrence rate was greater (18.5%) than in the group with primary pterygium (6.7%) (P = 0.05) with mean (std.dev) time of 3.20 months as compared to 9.00 months. A definite trend of recurrence was also noted on further stratification of the subjects on the basis of the corneal involvement, with a higher rate of recurrence seen in subjects with higher grades of

corneal involvement (P = 0.06). Similarly, when subjects with primary pterygia were graded according to the size, there was a highly significant recurrence seen with higher grades of pterygium (P = 0.008). However, the same was not seen in participants with secondary pterygia (P = 0.334). The role of pterygium grading in recurrence of pterygiais shown in Table 3. Mitomycin – C application time was also noted for its relevance to the recurrence and there was a decreased rate of recurrence from 50% in 1 minute group to no recurrence seen in 5 minutes group (P = 0.213).

Corneal nebular opacity was the frequent finding seen in most patients postoperatively with one patient developing conjunctival cyst at the site of excision. No major complication like scleral thinning, ulceration or necrosis was seen in our patients

Table 3: Effect of Pterygium grading system on recurrence

Grading of Pterygium	Recurrence n (%)		P-value*
	Yes	No	
Primary			
1°	02 (2.4)	83 (97.6)	
2°	04 (19)	17 (81)	0.008
3°	02 (14.3)	12 (85.7)	
Secondary			
1°	04 (23.5)	13 (76.5)	
2°	01 (33.3)	02 (66.7)	0.334
3°	00 (00)	07 (100)	

DISCUSSION

The recurrence of the pterygium remains an important health care issue in patients[1] in Asian countries. The present study was motivated by the invariably high recurrence of pterygium not only in Pakistan but world over[5, 15].

The recurrence rate of pterygium in the present study was 8.8%. In a recent clinical trial carried out in the Pakistani population, Rahman et al[16] estimated a recurrence of pterygia in 10% of the population. In another prospective study, Cheng et al[17] observed a recurrence of 7.9% in subjects with primary pterygia and a recurrence of 19.2% in subjects with recurrent pterygia. However comparison between our study and others is likely to be biased attributed to the different study population, setting and criteria used for grading pterygium. The age was significantly related to recurrence of pterygium in our study, with rising cases of recurrence in younger age groups of < 50 years. Similar conclusions have been drawn from various studies carried throughout the globe[18-20]. The female gender was not related to recurrence in the target group, presumably due to the fact that women in Pakistan are most of the time housewives whereas men are commonly exposed to the occupational and environmental hazards, leading to higher rate of recurrence.

The site of the pterygium was also investigated for its role in recurrence, mainly because of the fact that in most of the cases, pterygia is always present on the nasal side; however there was no significance of site with recurrence.

The secondary pterygium has been recognized as a risk factor for higher recurrence in various studies[17, 18, 19]. Similarly, in the present study a highly significant rate of recurrence of 18.5% was observed in the secondary recurrent group as compared to 6.7% in the primary pterygium group. In a recent prospective study carried out by Diaz et al[21], no recurrence was observed on follow-up in group of patient with previous recurrent pterygia treated with intra-operative MMC. A lot of grading systems are currently being used for grading pterygium but in our study we have used the grading system based on the extent of corneal involvement by the fibrous pterygium. There was a higher tendency of recurrence seen in participants with higher grades of corneal involvement with rate of recurrence of 5.9% in 1° group as compared to 21% in 2° group. Similar results have been obtained in studies across Europe where a high rate of recurrence has been associated with increased fleshiness of the pterygia[22], though the grading system used in these studies is slightly different, with translucency and vascularity being used as a criterion for grading. Nonetheless in both the studies, a higher grade is increasingly being recognized as a risk factor for recurrence. In the secondary pterygium group, the same results could not be achieved, though a definite trend has been noted possibly due to the small sample size. The possible difference in the effect on recurrence of pterygium by the application of intra-operative topical MMC can be attributed to the difference in concentration as well as its application time. In a dose response study related to MMC, Robin et al[23] have shown that duration of exposure appears to be more important than the concentration of MMC. In the present study, there was no recurrence seen in patients

treated with topical MMC for 5 minutes, however a high recurrence rate of 50% was seen in patients treated for 1 minute. Other groups had a recurrence rate in between these two extremities. Similar results were also documented in a randomized trial carried out by Lam et al[15]. In their work, at a mean follow-up time of 30 months, a recurrence rate of 8.3% was seen in the patients applied 0.02% MMC for 5 minutes as compared to 42.9% seen in the group applied 0.02% MMC for 3 minutes. Though there was no recurrence seen in the 5 minute MMC application group, most cases of corneal nebular opacity were seen among these patients. The results of our study hold important implications for further work on MMC, as probably, duration of administration of MMC, holds the key in its effect on pterygium recurrence.

CONCLUSION

Our study found significant associations of recurrence with higher grade as well as with secondary pterygia. There was a lesser recurrence with old age. The results of this study, suggests using MMC application time of greater than 3 minute for high risk recurrent pterygia.

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