

Original Article **Comparison between conjunctival autograft and intraoperative mitomycin C in surgical treatment of pterygium according to the recurrence rate**

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ABSTRACT

Background: pterygium is a common disease that affect many people in the world especially in the tropics and in an equatorial zone between 30° north and south latitudes. Egypt is one of the highly affected contraries. The most important problem in treatment of pterygium is high recurrence rate.

Aim: to compare conjunctival autograft and intraoperative mitomycin C to determine the best technique that can reduce the recurrence rate.

Methodology: this prospective interventional study comprised 40 eyes of 40 patients with primary pterygium included from the outpatient clinics of the ophthalmology departments at Al-Zahraa University Hospital and The Italian Military Hospital over a period of 15 months (from March 2019 to May 2020). They were randomized into two groups according to the adjuvant used: (1) intraoperative 0.02% MMC for 3 minutes or (2) conjunctival autografting technique. Patients were followed for recurrence and complications for a period of 6 months.

Results: 40 eyes of 40 patients their age ranged from 21 and 65 years in group (1) and between 27 and 60 years in group (2) with a male predominance of 30 cases (75%). There were 2 recurrences (10%) in MMC group and 1 recurrence (5%) in conjunctival autograft group. There was no statistically significant difference in the recurrence rate between the two groups. There were 2 cases of granuloma one case in each group and one case of partial graft dehiscence in group 2.

Conclusion: Both conjunctival autograft and intraoperative mitomycin C techniques are effective treatment modalities for treatment of primary pterygium and for reduction of recurrence rate. There is no significant difference between both techniques as regards the recurrence rate.

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INTRODUCTION

The term “pterygium” is a Latinized word that was taken from the Greek term “pterygion” that means “small wing”. It is an abnormal growth of the epithelium and the fibrovascular tissue from the corneoscleral limbus that invades the cornea toward the pupil, causing ocular surface inflammation and potential vision impairment. It usually develops nasally, rarely temporally, and very infrequently both sectors simultaneously ^[1].

The pathogenesis of pterygia is partially understood. Histologically, there is basophilic degeneration (actinic or senile elastosis) that was detected in the substantia propria of the epithelium of the pterygium. There are a variety of secondary changes that may be found in the epithelium of the pterygium such as orthokeratosis, acanthosis, and dyskeratosis, and mast cells which can be found in several pterygia. In long-standing nasal pterygia in elderly individuals at the level of Descemet’s membrane

and the endothelium deep corneal changes, such as reduced endothelial cell density may be seen [2]. A fully developed pterygium presents as an “apex” or “head” (apical aspect overlying the cornea), a “body” (conjunctival aspect extending between the limbus laterally and the canthus medially), and a “neck” (limbal aspect) [3].

The incidence of pterygium was noted to increase in the tropical areas and in the equatorial zone between 30° north and south latitudes. The possible risk factors are chronic sun exposure (ultraviolet light), older age, male sex, and outdoor activity [4]. For prevention of the development of pterygium; risk factors such as sunlight, wind and dust must be avoided by wearing ultraviolet rays protecting sunglasses and hats. After pterygium surgery using of the previous protective measures may also lead to decrease recurrence rate [5].

In mild cases of pterygium, medical treatment may be effective as artificial tear, topical lubricating drops, non-preserved ointments and short-term use of topical corticosteroids may be used to relieve the symptoms [6].

In severe cases where pterygium affects vision or causes severe symptoms of irritation, surgery is the treatment of choice. The main challenge to successful surgical treatment of pterygium is recurrence. Many surgical techniques have been used such as bare sclera technique, conjunctival autograft, amniotic membrane graft and intraoperative, pre and postoperative mitomycin C, but none of these previous techniques are accepted worldwide because of the variable recurrence rates [7].

Conjunctival autografting is known as the procedure of choice for treatment of both primary and recurrent pterygium, due to its suitability and lower recurrence rates (2%-39). Amniotic membrane graft technique is effective as conjunctival autograft in decreasing the recurrence rate [8].

Mitomycin C is an antineoplastic and antibiotic agent that was isolated from bacterium *Streptomyces caespitosus* which is found in the soil. It works by inhibiting Deoxy ribonucleic acid (DNA) synthesis; this leads to genotoxic injury to the cell that caused by the alkylation effect of mitomycin C which leads finally to the cell death. It acts against the cell during any stage of the cell cycle even the cells that are not synthesizing DNA. It can be used pre or postoperative or during the surgery, applied by sponge or in the form of eye drops. It prevents pterygium recurrence by inhibiting the proliferation of the fibroblasts in the episcleral region [9]. Mitomycin C may cause a serious complication if used for a long duration or used in high concentrations such as necrotizing scleritis, scleral calcification, corneal edema, ulceration, iritis and hypotony which happened due to injury of the ciliary body and its damaging effect on

corneal epithelium and endothelium. With the most commonly used dose, of 0.02% for 2-3minutes, no severe complications were reported [10]

The current study was conducted to compare the effectiveness of both conjunctival autograft and intraoperative mitomycin C in reducing the recurrence rate of primary pterygium.

PATIENTS AND METHODS

This study was a prospective, interventional and a non-randomized study. All patients in this study signed an informed written consent after proper explanation of the study. It was held at Al Zahraa University Hospital and The Italian Military Hospital. It was conducted in a period of 15 months (from March 2019 to May 2020). It included 40 eyes with primary pterygium of 40 patients. Patients were divided into two groups depending on the type of the surgical technique by which pterygium excision was done.

Group 1: included 20 eyes of 20 patients. Pterygium excision was done using the bare sclera technique supplemented by intraoperative 0.02% MitomycinC.

Group2: included 20 eyes of 20 patients. Pterygium excision was done using the conjunctival auto grafting technique.

Inclusion criteria were patients with primary pterygium, progressive pterygia (non-cosmetic indication for pterygium excision). Pterygia were 2-4 mm on the horizontal axis of the nasal aspect of the cornea. Age was above 20 years old.

Exclusion criteria were recurrent pterygium, non-progressive pterygium, pterygium associated with other chronic ocular surface disorders and patients with previous history of any conjunctival surgery.

All the patients were subjected to complete ophthalmic evaluation which including: Personal history (e.g. name, age, sex and occupation), present history (onset, course and duration of the symptoms), past history (history of ocular trauma or previous eye surgeries) and family history of similar conditions.

All patients were subjected also to ophthalmological examination including visual acuity (uncorrected visual acuity (UCVA) and best corrected visual acuity (BCVA)), slit Lamp examination, Tear Breakup Time (TBUT) and corneal fluorescein staining.

All surgeries were done under local anesthesia by installation of 0.4% benoxinate hydrochloride (Benox, Egyptian Int. pharmaceutical industries co. (E.I.P.I.CO.) -Egypt) 3 times at 2 minutes interval, then sub-conjunctival infiltration of 2% Lidocaine HCl (Xylocaine 0.5ml, FereseiusKabi-USA) under the body of the pterygium using 27 gauge needle to balloon out the

conjunctiva. The excision was done by detaching of the head of the pterygium from the underlying cornea and separation of the body of the pterygium from the overlying conjunctiva and then they were excised together with the affected conjunctiva and the underlying subconjunctival fibrovascular tissue and tenon's capsule using Westcott scissors (Bausch & Lomb-New York, USA). In group 1, intraoperative mitomycin C (MMC) (Cadila pharmaceuticals Ltds-India) (0.02%) was applied to the site of pterygium excision on the bare sclera using a sterile Weckcel sponge (Aegis Life Sciences Pvt Ltd-India) for 3 minutes. The site of application was then completely irrigated by 10-20 ml of a sterile balanced salt solution.

In group 2, the site of the excised pterygium was measured. A free conjunctival graft was excised from the superior temporal conjunctiva approximately 1 mm larger than the site of the excised pterygium. At the limbal margin of the graft we dissect it toward the cornea to include part the superficial limbus. The free graft was cautiously transmitted to the recipient site and take care to preserve the polarity of the tissue, then it was fixed with interrupted 8.0 vicryle sutures (Ethicon US).

Postoperatively, antibiotic, corticosteroid eye drops like Dexamethasone 1 mg + Neomycin (as sulphate) 3.5 mg + Polymyxin-B-sulphate 6000 IU (Dexatrole eye drops, Egyptian Int. pharmaceutical Industries co. (E.I.P.I.CO.) - Egypt) 5 times daily together with antibiotic, corticosteroid eye ointment (Dexatrole eye ointment, Egyptian Int. pharmaceutical Industries co. (E.I.P.I.CO.) - Egypt) twice daily for 2 weeks were used. Tapering was done after corneal and conjunctival reepithelization. Tear substitute such as Dexpanthenol (corner gel, Minapharm. Under Licence of: Dr. MannPharma - Germany) was applied 5 times daily for 1 month.

Patients were followed up for 6 months after the surgery. Follow up visits were done after one day, one week, two weeks, one month and 6 months after surgery. All patients were subjected to a full ocular examination on each visit. Recurrence rates were assessed after 6 months of follow up.

Statistical analysis

Data were collected, reviewed, coded, and entered. The quantitative data were presented as mean, standard deviations and ranges. Independent t-test was used to compare between quantitative data of both groups. Comparison between groups regarding qualitative data was done by using Chi-square test and/or Fisher exact test. Spectrum of correlation coefficient was used to assess the correlation between two quantitative parameters in the same group. P-value > 0.05: Non-significant (NS) P-value (equals or less than) ≤ 0.05: Significant (S). P- Value < 0.01: Highly significant (HS).

RESULTS

This study includes 40 eyes with primary pterygium of 40 patients. In group (1) the age ranged between 21 and 65 years and in group (2) it ranged between 27 and 60. There was a male predominance of 30 cases (75%). According to the occupation of patients in both groups, in group (1) 11 patients (55%) were working outdoors, and 9 patients (45%) were working indoors. In group (2) 12 patients (60%) were working outdoors, and 8 patients (40%) were working indoors, so we found that most of them were working outdoors without statistical significant difference regarding age and sex between both groups (Table 1).

As regards the pterygium grading, we grade it according to the extent of corneal involvement. Statistically the difference between both groups was not significant as regards the pterygium grade distribution ($p > 0.05$) (Table 2).

Regarding duration of surgery according to the technique of surgical excision of pterygium, the mean duration of surgery in group (1) was (27.0 ± 5.12) which was significantly less in comparison to group (2) which was (41.0 ± 5.76) (Table 2).

Concerning recurrence: In group (1) it was reported in 2 cases (10%) within 6 months. In group (2) recurrence was reported in 1 case (5%) within 6 months, without statistically significant difference (Table 2).

Tears break up time have been measured before surgery. It was < 10 seconds in all patients of both groups. There were statistically significant differences in the mean TBUT that have been measured before surgery and that measured 6 months post operatively in both groups with not statistically difference between both groups (Table 3,4).

Postoperative evaluation: There was marked reduction of the duration of relieve of postoperative symptoms (pain, lacrimation, and foreign body sensation) in most of cases of group (2) in comparison to group (1) (Table 5).

There are also delayed corneal and conjunctival reepithelization in group 1 in comparison to group 2 where reepithelization of the donor site in group (2) was completed within 2 week. (Table 6).

There was one case (5%) in MMC group (Group 1) developed granuloma, and one case (5%) in conjunctival autograft group (Group 2) developed sutural granuloma. There was one case (5%) of graft dehiscence in group (2) (Table 7). Reepithelization of the donor site in group (2) was completed within 2 week.

Visual acuity: There was statistical non-significant difference between the two groups according to the best corrected visual acuity (BCVA) by decimal system preoperatively and 6 months postoperatively (Table 8)

Table (1): The demographic data of both groups

	Group 1	Group 2	P-value
Age:			
Range	21-65	27-60	0.626
Mean ± SD	41.20 ± 11.5	42.85 ± 9.65	
Sex			
M	16 (80.0%)	14 (70.0%)	0.465
F	4 (20.0%)	6 (30.0%)	
Occupation:			
Indoor	9 (45.0%)	8 (40.0%)	0.749
Outdoor	11(55.0%)	12(60.0%)	

Table (2): Comparison between the two groups according to the grade, duration of surgery and recurrence after 6 months

	Group 1	Group 2	P-value
Grade:			
G1	4 (20.0%)	4 (20.0%)	1.000
G2	10 (50.0%)	11(55.0%)	
G3	6 (30.0%)	5 (25.0%)	
Duration of surgery / min:			
Range	20-35	30-50	<0.001
Mean ± SD	27.0 ± 5.12	41.0 ± 5.76	
Recurrence after 6mon.:			
No	18 (90.0%)	19 (95.0%)	1.000
Yes	2 (10.0%)	1 (5.0%)	

Table (3): Comparison between the different studied periods according to TBUT/sec

TBUT/sec.	Pre	6 months	P
Group I			
Min. – Max.	4.0 – 10.0	5.0 – 13.0	<0.001*
Mean ± SD.	5.80 ± 1.58	9.15 ± 2.48	
Median (IQR)	6.0(4.5 – 7.0)	9.50(7.0 – 11.0)	
Group II			
Min. – Max.	4.0 – 10.0	5.0 – 13.0	<0.001*
Mean ± SD.	6.30 ± 1.69	9.55 ± 2.33	
Median (IQR)	6.0(5.0 – 7.5)	10.0(8.0 – 11.5)	

Table (4): Comparison between the two studied groups according to TBUT/sec. before and after 6 months postoperatively

TBUT/sec.	Group I (No. = 20)	Group II (No.= 20)	P
Pre			
Min. –Max.	4.0 – 10.0	4.0 – 10.0	0.339
Mean ± SD.	5.80 ± 1.58	6.30 ± 1.69	
6 months			
Min. –Max.	5.0 – 13.0	5.0 – 13.0	0.602
Mean ± SD.	9.15 ± 2.48	9.55 ± 2.33	

Table (5): Comparison between the two studied groups according to the duration of postoperative symptomatic relieve

Symptomatic relieve	Group I (n = 20) No. (%)	Group II (n = 20) No. (%)	χ^2	^{FE} p
2 weeks post-operative				
No (no relieve)	20 (10.00)	16 (80.0)	4.444	0.106
Yes (no symp.)	0 (0.0)	4 (20.0)		
1st month				
No	9 (45.0)	3 (15.0)	4.286*	0.038*
Yes	11 (55.0)	17 (85.0)		
6 months				
No	0 (0.0)	0 (0.0)	–	–
Yes	20 (100.0)	20 (100.0)		

Table (6): Comparison between the two studied groups as regards complete corneal and conjunctival re-epithelization

Complete reepthlization of cornea and conj.	Group I (No. = 20) No. (%)	Group II (No.= 20) No. (%)	^{FE} p
2 weeks postoperative			
No	7 (35.0)	0 (0.0)	0.008*
Yes	13 (65.0)	20 (100.0)	
1st month			
No	1 (5.0)	0 (0.0)	1.000
Yes	19 (95.0)	20 (100.0)	
6 months			
No	0 (0.0)	0 (0.0)	–
Yes	20 (100.0)	20 (100.0)	
Overall reepthlization			
No	7 (35.0)	0 (0.0)	0.008*
Yes	13 (65.0)	20 (100.0)	

Table (7): Comparison between the two studied groups according to complication

Complications	Group I (No.= 20)	Group II (No.= 20)	p
	No. (%)	No. (%)	
Granuloma formation	1 (5.0)	1 (5.0)	^{FE} p=1.000
Graft dehiscence	0 (0.0)	1 (5.0)	^{FE} p= 1.000

Table (8): Comparison between the two studied groups preoperatively and 6 months postoperatively as regards the BCVA by decimal system

BCVA	Group I (No.= 20)	Group II (No.= 20)	t	P
Preoperatively				
Range	0.70 – 1.0	0.70 – 1.0	0.524	0.603
Mean ± SD.	0.93 ± 0.09	0.95 ± 0.09		
Median (IQR)	1.0 (0.90 –1.0)	1.0 (0.90 –1.0)		
6 months Postoperatively				
Min. –Max.	0.70 – 1.0	0.80 – 1.0	0.932	0.357
Mean ± SD.	0.94 ± 0.09	0.97 ± 0.07		
Median (IQR)	1.0 (0.90 –1.0)	1.0 (1.0 –1.0)		

DISCUSSION

The effectiveness of pterygium surgery in prevention of the recurrence is the main interest of the surgeons. In the present study, the recurrence rate was insignificantly more 10% (2 cases) in group 1, and was 5% (1 case) in group 2 within 6 months of follow up, This finding is in agreement with ^[11,12] who found that conjunctival autograft is as effective as intraoperative Mitomycin C in reducing the recurrence of pterygium but the cosmetic results after conjunctival autograft were better. The main obstacle in conjunctival autograft is the prolonged duration of the surgery. Chan et al. ^[13] reported that the recurrence rate in conjunctival autograft group was (2.5%) while in the intraoperative mitomycin C group (15.4%), so that conjunctival autograft was more effective than intraoperative MMC in reducing the recurrence rate in a 10-year follow-up study of a randomized controlled trial. Another study revealed that, conjunctival autograft group had only (2%) recurrence as compared to (16%) recurrences in the MMC group that revealed a statistically significant difference ($p = 0.031$) ^[14]. The difference between the results of the previous two studies and the present study is due to the longer follow up period.

In the present study there were delayed conjunctival and corneal healing and delayed symptomatic relieve These findings are in agreement with Akinci and Zilelioglu ^[15] who found that complications such as pain, photophobia and lacrimation are more common in the group that was treated by mitomycin C than in the group that was treated by conjunctival autograft and Stephen et al. ^[12] who found that delayed epithelialization was noticed only with the usage of mitomycin C.

In the present work we use intraoperative MMC with a concentration of 0.02% for 3 minutes to decrease the post-operative complications. This agrees with Paracha et al. ^[11] who found that a single intraoperative use of mitomycin C (MMC) is effective and safer than preoperative and postoperative MMC. In their study they used a low dose of MMC for only a short duration i.e. 0.02% for only 2-3 minutes. This dose reduces the recurrence rate and the complications. Complications are associated with the usage of MMC for prolonged duration and high concentrations.

In the present study, one case (5%) in MMC group (Group 1) developed granuloma, and one case (5%) in conjunctival autograft group (Group 2) developed sutural granuloma. There was one case (5%) of graft dehiscence in group (2). Re-epithelialization of the donor site in group (2) was completed within 2week. Paracha et al. ^[11] found that in cases that treated with intraoperative MMC, conjunctival granuloma was noted in one case (4%) within 4 weeks. The granuloma was excised later. In patients treated with conjunctival autograft postoperative graft retraction was noted in 2 cases (8%) probably due

to the small size of the graft. The donor site healed spontaneously at its own. The difference between the results in this study and the present study is probably due to the larger sample then our study.

In the present study most of the cases showed no significant change in the BCVA before and 6 months after surgery this finding was in agreement with Koranyi et al. ^[16] who found that there was no considerable change in the postoperative best corrected visual acuity in groups treated by conjunctival autograft and intraoperative MMC. Surgery did not considerably change the BCVA or the average absolute astigmatism in either group and in agreement also with Chan et al. ^[13] who found that there was no statistical significant difference in the visual acuity postoperatively between intraoperative MMC and conjunctival autograft. However, Garg et al. ^[17] found that surgical excision of the pterygium results in a significant improvement of visual acuity by reducing the astigmatism. The difference between this previous study and ours most probably due to the difference in the grade of the excised pterygium and the duration of it.

We reported no other complications as graft necrosis, cyst formation, glaucoma, cataract, and scleral thinning, melting and necrosis. Also, no intraoperative complications as intraoperative hemorrhage was reported in our study. We recommend a longer follow up period and larger scale study to get more reliable results.

CONCLUSION

Both conjunctival autograft and intraoperative mitomycin C techniques are effective treatment modalities for primary pterygium and for the reduction of recurrence rate. Intraoperative MMC has a benefit over conjunctival autograft as regard the reduction of the duration of surgery, and the surgery was easier.

Conflict of interest

The authors declare that they had no conflict of interest.

Financial disclosure

Author declares that, the research completely financed by the author himself.

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الملخص العربي

مقارنة بين استخدام الترقيع الذاتي للملتحمة واستخدام مادة ميتوميسين أثناء العملية في علاج الظفرة الابتدائية جراحياً وذلك من حيث نسبة الإرتجاع بعد العملية

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ملخص البحث

الخلفية: إن الظفرة من الأمراض الشائعة التي تؤثر علي عدد كبير من البشر في العالم وخاصة في المناطق الإستوائية ومصر هي واحدة من أكثر البلاد تأثراً ومن أبرز التحديات التي تواجه الجراحين عند علاج الظفرة هو ارتفاع نسبة الإرتجاع بعد العملية.

الهدف: المقارنة بين الترقيع الذاتي للملتحمة واستخدام مادة ميتوميسين سي أثناء العملية لتحديد الأفضل بينهما من حيث تقليل نسبة ارتجاع الظفرة الإبتدائية بعد العملية.

الطرق: وقد اشتملت الدراسة علي 40 عين ل 40 مريضاً يعانون من ظفرة إبتدائية وقد تم تقسيمهم عشوائياً إلي مجموعتين كل مجموعة بها 20 حالة وذلك تبعاً للتقنية المستخدمة 1- المجموعة الأولى : تم استخدام مادة ميتوميسين سي أثناء العملية بتركيز 0.02% لمدة 3 دقائق. 2- المجموعة الثانية: تم استخدام تقنية الترقيع الذاتي للملتحمة وتمت متابعة الحالات لمدة 6 أشهر بعد العملية وذلك لمتابعة وتسجيل المضاعفات ونسبة الإرتجاع بعد العملية.

النتائج: وقد اسفرت نتائج الدراسة عن عدم وجود فروق ذات دلالة إحصائية بين المجموعتين في نسبة إرتجاع الظفرة بعد العملية، وقد تم تسجيل حالة واحدة 5% عانت من تورم حُببي بعد العملية في المجموعة الأولى وكذلك حالة واحدة 5% عانت كذلك من التورم الحُببي في المجموعة الثانية وكان ذلك التورم ناتج عن الخيط الجراحي كما سُجلت حالة واحدة 5% في المجموعة الثانية عانت من عدم إلتئام كامل للجرح وذلك نتيجة صغر حجم الرقعة المستخدمة.

الإستنتاجات: وخلصت نتائج الدراسة إلي أن الترقيع الذاتي للملتحمة واستخدام مادة ميتوميسين سي أثناء العملية كلاهما أثبتا فاعليته في علاج الظفرة الإبتدائية جراحياً وكذلك في تقليل نسبة الإرتجاع بعد العملية والفرق بين المجموعتين في نسبة الإرتجاع لم يكن ذا دلالة إحصائية.

الكلمات المفتاحية: الترقيع الذاتي للملتحمة، ميتوميسين سي، الظفرة، إرتجاع.

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