

Comparative Evaluation of Conjunctival Autograft and Mitomycin-C in Preventing Recurrence of Pterygium

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ABSTRACT

Introduction: Pterygium recurrence is a common complication. To prevent this various methods including conjunctival autografting and Mitomycin-c have been tried with different success rates. In this study it was proposed to study the role of conjunctival autograft and a Mitomycin-C, an antineoplastic drug in preventing recurrence of pterygium.

Material and Methods: 60 cases of pterygium were included in this study. Study was done over a period of two years. Case control study was done with each patient followed up for minimum six months. Group – I. In this area of sclera left uncovered after excision of the pterygium. Group –II Free autograft was harvested from the same eye. The donor site heals without covering under the protection of lid. Group – III A surgical sponge soaked with Mitomycin-C solution 0.02% was placed in contact with exposed sclera surface with the conjunctival layer draped over the sponge for 3 minutes followed by irrigation of 100 ml ringer lactate solution to prevent further contact of drug with eye tissue. Standard surgical technique as described earlier was used.

Results: Excision leaving bare sclera is the least effective of all techniques with high rate of recurrence. Conjunctival autografting is the safest procedure. No vision threatening complications were observed with conjunctival autografting. Conjunctival autografting and Mitomycin-C both are effective in reducing the recurrence rate of pterygium, with comparable results of surgery.

Conclusion: Conjunctival autografting and intraoperative Mitomycin- C 0.02% for three minutes are safe and effective methods in management of pterygium.

Keywords: Pterygium, Conjunctival Autograft, Mitomycin C, Bare Sclera, Recurrence rate

INTRODUCTION

Pterygium is essentially a triangular encroachment of bulbar conjunctiva onto the cornea.¹ It is an elastotic degenerative condition of subconjunctival tissue which proliferates as a vascularised granulation tissue to invade the cornea, destroying, as it does so, the superficial layer of stroma and bowmans membrane, the whole being covered by conjunctival epithelium.

It is found in sunny, hot, dry, dusty regions of the world. Aetiology of pterygium is unknown but ultraviolet light is most significant environmental factor. Incidence varies with exposure to these factors. It is more common in outdoor workers and in males. It usually occurs on nasal side. It may be unilateral or bilateral. It usually follows pinguecula.

A fully developed pterygium consists of three parts.

Head - Apical part present on cornea.

Neck – Limbal part

Body - Scleral part

Pterygium can be classified into -

- Progressive pterygium

- Regressive pterygium

(a) Progressive pterygium is thick, fleshy and vascular with infiltrates in the cornea in front of pterygium.

(b) Regressive pterygium is thin atrophic attenuated with little vascularity. Ultimately it becomes membranous but never disappears.

Prevention of pterygium recurrence is a difficult clinical problem inspite of tremendous advancements in ophthalmology. Various surgical procedures like excision, avulsion, transplantation and plastic repair were tried but recurrence rate was still very high. When pterygium reoccurs it assumes a very vascular and angry look. It may encroach more on the cornea then it was prior to operation, even crossing the midline.

Various methods have been devised to reduce the recurrence rate of pterygium. In this study it was proposed to study the role of conjunctival autograft and a Mitomycin-C, an antineoplastic drug in preventing recurrence of pterygium.

MATERIAL AND METHODS

60 cases of pterygium were included in this study from out patients departments of Command Hospital, Lucknow and Command Hospital, Kolkata. Study was done over a period of two years. Case control study was done with each patient followed up for minimum six months. Recurrent pterygium were excluded. Patients with ocular pathology like glaucoma

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How to cite this article: Vivek Sharma, Sudheer Verma, Avinash Mishra, Maneesh Jha, Sandeep Gupta, S K Singh. Comparative evaluation of conjunctival autograft and mitomycin-c in preventing recurrence of pterygium. International Journal of Contemporary Medical Research 2018;5(12):L10-L14.

DOI: <http://dx.doi.org/10.21276/ijcmr.2018.5.12.14>

were excluded. Patients data collected included age, sex, past ocular, medical and surgical history, indication for surgery, surgical technique and complications, post operative medications, complications and recurrence and final cosmesis. Characteristic of pterygium including location, size, and extent across cornea, inflammation, growth and previous treatment were also recorded.

Cases were randomly assigned to three groups:-

Group 1 – Bare sclera technique

Group 2 - Conjunctival autograft technique

Group 3 - Intra operative Mitomycin-C in 0.02% for three minutes

Standard surgical technique was used.

Outcome was recorded and compiled as:

1. Recurrence - Any re-growth beyond the limbus
2. No recurrence

Surgical technique

1. Preoperative topical antibiotics ciprofloxacin 0.3% was given 6 hourly one day before surgery.
2. General surgical asepsis of cleaning the periocular skin with 5% povidine – iodine solution was used.
3. For anesthesia topical lignocaine 4% was used. Sub conjunctival lignocaine 2% mixed with epinephrine 1: 1,00,000 was given with 26 G needle under the body of pterygium so that injection balloons the pterygium away from sclera thus establishing dissection plane.
4. For conjunctival autograft and un-cooperative patients peribulbar anaesthesia was given with 2% lignocaine and 0.5% bupivacaine.
5. Wire speculum was used to separate the lids after draping the area with sterile towels
6. Eye was washed with isotonic saline
7. Pterygium was infiltrated by lignocaine with adrenaline
8. Two radial incisions were made with scissors in the bulbar conjunctiva one just above the upper border and the other just below the lower border of the pterygium, from limbus nasally for about 3 mm. This incision ensured the creation of perilimbal strip of bare of conjunctiva.
9. Blunt dissection of pterygium done to separate it from the conjunctiva and sclera, avoiding injury to insertion of medial rectus.
10. Pterygium excised closed to medial rectus insertion and reflected forwards.
11. Apex dissected either from the limbal end or corneal head end using Bard Parker 15 no's Blade. From limbal side the bleeding was less and it was easier to preserve separation plane. In case of corneal head the epithelium ahead of pterygium was scraped with minimum damage to bowmans layer and stroma. Use of sufficient tension while grasping and elevating the pterygium can literally avulse the pterygium from the underlying stroma, resulting in a relatively smooth surface.
12. Once bulk of pterygium was removed any abnormal tissue on the cornea was scraped and polished.
13. Limbus and sclera was cleaned of residual tenons

capsule and sub conjunctival tissue.

14. Hemostasis achieved by use of cautery. Use of cautery kept to minimum to avoid excessive scar formation and scleral shrinkage.
15. Pad and bandage applied after:-
 - (a) Subconjunctival injection of gentamycin – 20 mg and dexamethasone – 2 mg
 - (b) Antibiotic steroid ointment

Group – I

In this area of sclera left uncovered after excision of the pterygium. If excised pterygium and sub conjunctival tissue extend as far as insertion of medial rectus muscle then conjunctiva approximated over the exposed muscle

Group – II

Free autograft was harvested from the same eye. Superotemporal bulbar conjunctiva was used in case of nasal pterygium as superior bulbar conjunctiva is extensive and protected from the upper lid.

The globe was rotated infero medially by the superior and inferior rectus birdle suture of 4.0 silk. The size of graft required was determined by measuring the hosts bed with calipers. These dimensions were marked on the donor site with cautery spots. These marks were included in the graft margins to facilitate proper orientation in the recipient bed. The graft was dissected as thinly as possible avoiding tenons capsule and episclera. Two radial incisions were created along the graft margins and the conjunctiva was separated with spring action scissors introduced through one of incisions and exiting through the second. Once the graft tissue was undermined the superior circumferential incision was performed. The graft was then elevated and inverted, epithelial side down, over the cornea to expose tenons capsule remnants, which should be removed until the remaining tissue becomes translucent. This lessens postoperative oedema. Final step is freeing the limbal edge of the graft with scissors. A margin of 2 – 3 mm was left to avoid damage to the corneal limbal stem cells. The donor site heals without covering under the protection of lid.

The graft was then transferred to recipient bed. Extreme caution exercised to avoid suturing the graft into place epithelial side down or the graft will become necrotic and slough off. Proper tissue orientation is assured by retention of initial cautery localization marks within the graft. The four corners of the graft were anchored to recipient conjunctiva and episclera with four interrupted 10-0 nylon sutures. Additional interrupted sutures complete the procedure. A margin of 2 mm of bare sclera is left between the edge of the graft and the limbus to avoid formation of dellen due to early postoperative oedema of the graft.

Group – III

A surgical sponge soaked with Mitomycin-C solution 0.02% was placed in contact with exposed sclera surface with the conjunctival layer draped over the sponge for 3 minutes followed by irrigation of 100 ml ringer lactate solution to prevent further contact of drug with eye tissue. Standard surgical technique as described earlier was used.

Post operative care

Wound was inspected on day one post operatively followed by pad and bandage

1. After day three patient advised dark sunglasses for period of three months.
2. Topical dexamethasone 0.1% with chloramphenicol 1% was used four times daily and tapered over six to eight weeks
3. Ciprofloxacin 0.3% drops used 6 hourly for 2 weeks
4. Sutures removed after six weeks
5. Follow of visits scheduled daily for 2 weeks, weekly for 8 weeks and monthly for 6 months

STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS software version 17 (SPSS, Inc., Chicago, IL). To compare the results between the groups, the Mann-Whitney U test was performed.

RESULTS

The results of pterygium excision for primary pterygium were analyzed in 60 cases.

Cases were randomly distributed to three groups: -

Group – I - Bare sclera technique

Group –II - Conjunctival autografting

Group – III - Intraoperative Mitomycin-C 0.02% for 3 min

The Sex distribution 60 patients 33 (55%) were male and 27 (45%) were female.

The mean age was 41.66 yrs with range of 20-70 yrs. The pterygium was nasal in 53 (88.3%) and temporal in 7 (11.7%). 47 (78%) cases were progressive pterygium and only 13 (22%) were regressive pterygium. The extent of pterygium across cornea was average of 3.3 mm (range of 0.5 to 4 mm). Indication for surgery in 21 (35%) was cosmetic, 5 (8.3%) was visual impairment, 6 (10%) was pain, 28 (47%)

Group	No of case	Without recurrence	With recurrence	%
I	20	14	6	30%
II	20	14	1	5%, P< 0.01
III	20	19	1	5%, P< 0.01
Total	60	52	8	13%

Table-1: Post operative recurrence

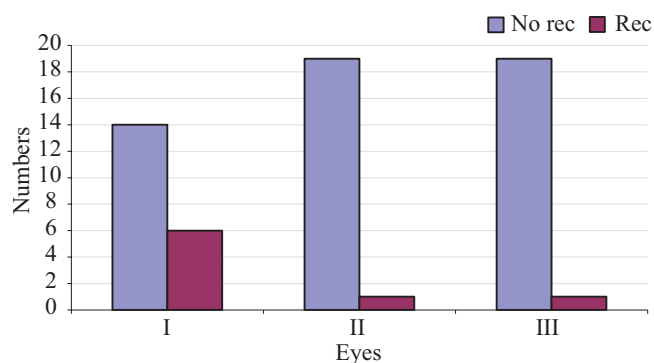


Figure-1:

	With recurrence (%)	Without recurrence (%)
No of eyes	8	52
Age- < 40 years	6	23
Age > 40 years	2	29
Chi-square=2.689, DF=1, P<0.10		
	With recurrence (%)	Without recurrence (%)
No of eyes	8	52
Site Nasal	7	46
Site Nasal + Temporal	1	6
Chi-square=0.05, DF=1, P<0.50		
	With recurrence (%)	Without recurrence (%)
No of eyes	8	52
Size 0—2 mm	2	21
Size >2 mm	6	31
Chi-square=0.64, DF=1, P<0.50		
	With recurrence (%)	Without recurrence (%)
No of eyes	8	52
Type --Progressive	7	40
Type -Regressive	1	12
Chi-square=0.43, DF=1, P<0.50		
Table-2: Comparison of eyes with recurrence and those without recurrence		

S No	Group I	No of eyes
1	Conjunctival granuloma	3
2	Dellen	2
3	Delayed wound healing	1
S No	Group II	No of eyes
1	Graft Oedema	3
2	Dellen	1
3	Graft slippage	2
4	Button holing	2
S No	Group III	No of eyes
1	Limbal avascularization	2
2	Superficial punctate keratitis	1
3	Delayed wound healing	3
Table-3: Post operative complications		

had other symptoms like irritation, watering and redness). None of the cases had field effects or diplopia as symptoms. Postoperative cosmetic appearance was graded as excellent in 16 (26.7%), good in 26 (43.3%), fair in 9 (15%) and poor in 9 (15%) eyes.

Table 1 shows rate of recurrence with 8 eyes showing recurrence over a follow up period of 6 months. Bare sclera technique highest recurrence of 6 (30%) eyes. Conjunctival autograft had recurrence in 1 (5%) eye. Mitomycin-C group also had recurrence in 1 (5%) eye.

Table 2 compares eyes with recurrences and those without recurrences. 6 cases were younger than 40 yrs and 7 cases had nasal pterygium in the recurrence cohort. Extent of pterygium was comparable in both groups. Most of recurrences were in progressive pterygium eyes (7 eyes).

None of the patients had any significant intra operative

Author s	Location	No of eyes	Recurrence	Follow up mths
Dowlut ¹⁴ , 1981	Canada	15	7.7% (1)	NA
Kenyon ¹⁵ , 1985	Boston	57	5.3% (3)	24
Sing ¹⁶ , 1990	Los Angeles	15	6.6% (1)	1.5
Allen ¹⁸ , 1993	Perth	93	6.5% (6)	20
Guler ¹⁷ , 1994	Turkey	31	13.3% (4)	10
Chen ²¹ , 1995	Los Angeles	23	39% (9)	13.5
Tan ¹⁹ , 1997	Singapore	61	2% (1)	15.1
Rao ²⁰ , 1998	India	53	3.8% (2)	18

Table-4:

Authors	Therapy	Nos of eyes	Recurrence
Hayaska ⁸ , 1988	Post op	29	7% (2)
Chen ²¹ , 1995	Post op	24	38% (9)
Panda ²⁴ , 1998	Intra op	25	12% (3)
Cano-Parra ²² , 1995	Intra op	30	33.3%(10)
Mastropasqua ²³ , 1996	Intra op	45	12.5% (5)
This study 2017	Intra op	20	5% (1)

Table-5:

complication. Postoperative complications were minor in nature and easily rectified (Table 3).

DISCUSSION

One of the main problems with surgical excision of pterygium is the recurrence, which can be as high as 30-70%. Over the past decade the technique of conjunctival autograft and intraoperative Mitomycin-C have been found effective in reducing the recurrence rate of pterygium.

The results of pterygium excision with bare sclera technique, conjunctival auto graft and intra operative 0.02% Mitomycin-C done on 60 eyes in our institution between March 2016 to Dec 2017 were analyzed the sex and age distribution is in accordance with published data² and shows higher prevalence in younger age group and males. This is possibly due to exposure of this age group to UV energy, which may be responsible for inducing alternations in the limbal basal stem cells and pterygium formation^{3,4,5}

The increased occurrence of nasal pterygium in this study correlates well with predilection of pterygium for nasal limbus.⁵

This may be due to increase UV exposure to nasal limbus

The pre-operative pterygium extended on average of 3.3 mm past the cornea scleral limbus on to the cornea. 47(78) were progressive and 13 (22%) were regressive.

In this study the indications for surgery were cosmetic 21 (35%), symptomatic 28 (47%), pain 6 (10%) and visual 5 (8%) The increase nos. of cosmetic reasons signifies the blemish caused by this benign condition.

None of the cases had significant intra-operative complications. The postoperative complications were minor and not vision threatening. The conjunctival auto graft complications were minor and comparable to other studies^{7,8,9}

Graft oedema resolved within 2 to 4 weeks. The possible causes of oedema could be excessive surgical manipulation, retention of tenons capsule or poor graft orientation. Dellen observed in one case resolved on conservative treatment of

lubrication and patching. Graft slippage observed in two cases and managed conservatively. This could have been due to graft of inadequate size or due to poor quality of graft.

The complications seen with use of Mitomycin-C were delayed wound healing and limbal avascularization. These were less compared to post operative use of Mitomycin-C, which causes large cumulative dose.^{10,11,12} These were comparable to other intra operative studies.¹³ Minimizing exposure of epithelium to Mitomycin-C is critical for rapid wound healing after surgery.

The postoperative cosmetic appearances were comparable to other studies. With best cosmeses with conjunctival autograft followed by Mitomycin-C used group and lastly bare sclera group.

The recurrence rate in this study was compared to historical data of other procedures available. This data shows that excision alone has resulted in high rates of recurrence. Though use of adjuvant treatment like beta irradiation and thio-tepa help to decrease the incidence of recurrence, it was associated with significant intraoperative or postoperative complications sometimes even sight threatening. Only one study has reported the use of argon laser and unless long-term studies are available regarding its safety and efficacy it cannot be routinely advised for all patients.

Conjunctival autografting because of its lack of significant complication, simplicity and efficacy is today a good technique for pterygium surgery.

The recurrence rate of conjunctival autografting was compared with those of other authors following the same technique (Table 4).

Mitomycin-C used as an adjuvant reduces the recurrence rate of pterygium surgery. But the initial reports of high dose of Mitomycin-C used postoperative cost severe complications.

To reduce the cumulative dose of Mitomycin-C the trend shifted towards using intra operative Mitomycin-C. The comparative studies are following (Table 5).

Variations in the results of a given technique may be influence by a number of factors:-

Variations within technique e.g., in some studies limbal tissue were included in conjunctival autograft. Limbal stem cells are effective in reducing recurrences rate as alter limbal basal cells invading advancing edge of pterygium have been demonstrated by immunohistological technique

The proportion of recurrent case, more recurrent cases worse the result. Let alone the case with associated complications like symblepharon, ectropion, entropion etc.

The age, location and occupation of the population studies. Difference in postoperative medication and compliance of patient group studied. Postoperative Mitomycin-C caused more severe complications. Less concentration of Mitomycin-C. Caused fewer complications.

The length of follow up and definition of recurrence employed. Although later recurrence may occur, prospective observations indicate that majority will be apparent within first three to four months. A minimum follow up of six months should avoid a significant under estimate of recurrence rate.

CONCLUSION

Excision leaving bare sclera is the least effective of all techniques with high rate of recurrence. Conjunctival autografting is the safest procedure. No vision threatening complications were observed with conjunctival autografting. Conjunctival autografting and Mitomycin-C both are effective in reducing the recurrence rate of pterygium, with comparable results of surgery. Single intraoperative application of Mitomycin-C 0.02% for three minutes is effective and safe to use in pterygium excision as it is controlled and less likely to induce significant side effects than in postoperative topical application by patients.

To conclude it can be said that conjunctival autografting and intraoperative Mitomycin- C 0.02% for three minutes are safe and effective methods in management of pterygium.

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Source of Support: Nil; **Conflict of Interest:** None

Submitted: 22-10-2018; **Accepted:** 09-11-2018; **Published:** 11-12-2018