EFFICACY OF MITOMYCIN - C 0.02% VERSUS CONJUNCTIVAL AUTOGRAFT IN PREVENTING RECURRENCE FOLLOWING PTERYGIUM EXCISION: A COMPARATIVE STUDY

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ABSTRACT: BACKGROUND: Pterygium is an elevated, triangular, fibrovascular encroachment of bulbar conjunctiva on to the cornea. Prevalence of pterygium is high in the tropical belt of the world, especially in India where hot, sunny and dusty weather favors its growth. The recurrence rate of traditional Bare Sclera technique ranges from 24% - 89%. To tackle the problem of recurrence, many adjuvant therapies have been tried among which Intraoperative application of Mitomycin-C (MMC) and Conjunctival autograft (CAG) have stood the test of time. Hence this study is undertaken to compare the efficacy of these two standard techniques in preventing recurrence following excision of pterygium. **AIMS:** To compare the effectiveness of 0.02% Intraoperative Mitomycin-C application for two minutes versus Conjunctival Autografting in preventing recurrence following excision of pterygium. **METHODS AND MATERIALS:** The present prospective randomized clinical trial was conducted over a period of two years. In the study, 80 eyes of 80 patients were included after detailed preoperative evaluation. They were randomized into two groups to receive either conjunctival autograft or Intraoperative application of 0.02% Mitomycin C for 2 minutes, following excision of pterygium. 80 cases completed the study with follow up of one year. **STATISTICAL METHOD:** prospective clinical randomized study **RESULTS:** Of the 80 cases, there were 7 recurrences, out of which 3 cases belonged to CAG Group (7.5%) and 4 cases were from MMC Group (10%). This difference was not statistically significant ($p>0.05$). 75% of the recurrent cases were Progressive Pterygium and 25% were regressive. The average time of recurrence was 6 months. The average age of recurrence was 41 years. The overall rate of complication was 11.25%, with the rate in CAG Group being 10% and 12.5% in MMC Group. The difference is not statistically significant ($p>0.05$). **CONCLUSION:** From our study, we conclude that both Conjunctival Autograft technique and Intraoperative application of 0.02% Mitomycin C for two minutes is equally effective in preventing or reducing recurrence following excision of Pterygium. Both the methods appear to be safe and acceptable in pterygium surgery.

KEYWORDS: Pterygium; recurrence; randomized; Conjunctival Autograft; Mitomycin C; progressive; complications.

INTRODUCTION: Pterygium, considered an ophthalmic enigma, is an elevated, triangular, fibrovascular encroachment of bulbar conjunctiva on to the cornea.

Prevalence of pterygium is high in the tropical belt of the world, especially in India where hot, sunny and dusty weather favors its growth.

A small pterygium usually gives rise to no symptoms. But large pterygia can be cosmetically unacceptable, induce astigmatism or impair vision-when intervention is necessary.

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Surgical removal remains the mainstay of treatment, basic procedure being complete excision leaving a bare area of sclera.¹The recurrence rate of this traditional Bare Sclera technique ranges from 24% - 89%.²

So the use of adjunctive treatment is only justified to tackle this problem. Among the various modalities in use are β -irradiation, intraoperative application of Mitomycin-C and Conjunctival autograft.

Conjunctival auto grafting has been a novel method to reduce recurrence following pterygium excision and gives a satisfactory post-operative cosmesis.

A prospective study is needed to compare these two standard treatment modalities. Hence this study is undertaken to compare the safety and efficacy of intraoperative application of 0.02% Mitomycin-C for 2 minutes versus Conjunctival Autograft in preventing recurrence following Bare Sclera excision of the pterygium.

METHODOLOGY:

Source of Data: All the cases undergoing pterygium excision surgery at Basaveshwar Teaching & General Hospital attached to M. R. Medical College, Gulbarga.

Study Design: Prospective randomized clinical trial.

Sample Size: 80 Cases this study included 80 eyes of 80 patients who visited the Department of Ophthalmology with significant complaints related to pterygium. The total sample size was 80.

Duration: Two years; → for data collection; and for the follow up of the last case.

Inclusion Criteria:

- All patients with progressive pterygium who are willing for pterygium excision surgery for cosmetic purpose.
- Patients with progressive pterygium who want to undergo excision surgery for inflamed condition leading to irritation, congestion, watering and blurring of vision.

Exclusion Criteria:

- Patients with history of autoimmune diseases, uncontrolled diabetes mellitus, conditions with poor wound healing, pregnant, lactating women and other systemic diseases.
- Patients with uveitis, corneal ulcer, scleritis, episcleritis.
- Patient's with pseudopterygium.

Preoperative Evaluation:

- History
- Visual Acuity recording
- Refraction
- Slit Lamp Examination
- Staining
- Tear film tests – (1) Schirmer's test and (2) Tear film breakup time (BUT)
- Anterior segment photography (for selected cases)
- Fundus examination
- Keratometry

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The anterior segment was examined with special attention to the assessment of tear film to rule out dry eye states. Lid abnormalities and other conditions predisposing to poor wound healing. Evaluation of lens and thereafter fundus examination was done to rule out any posterior segment pathology responsible for diminution of vision. The radial and circumferential extent of pterygium was measured from limbus to corneal encroachment and at the limbus respectively by using slit lamp beam directed horizontally and vertically and the vascularity of the pterygium was noted.

INVESTIGATIONS:

- CBC
- Urine routine
- ESR
- RBS
- HIV
- HBsAg

METHOD: After taking informed written consent, selected cases will be randomly allotted into groups A and B, 40 each, based on computer generated randomization table.

Group A, where conjunctival autografting after bare sclera excision; Group B, where application of 0.02% mitomycin-c following bare sclera excision of pterygium.

Preoperative Preparation:

- Anesthesia-Peribulbar anesthesia given.
- Cleaning and draping of the surgical field: Preparation included using 10% povidone-iodine to clean the skin area. 5% povidine-iodine was applied into the conjunctival cul de sac with subsequent saline wash to cleanse the area followed by adequate draping.
- All surgeries were performed using an operating microscope.
- A wire speculum was used to separate the lids. A superior rectus bridle suture put using 4-0 black silk.

Conjunctival Autograft Technique:

The first step is the Bare Sclera method of Excision.

The bridle suture was used to rotate the globe downwards exposing the superior limbus and conjunctival surface. A tree of conjunctival graft required to resurface the exposed scleral surface was excised from superior bulbar conjunctiva.

The limbus was smoothened using crescent. Using a Pierse-Hoskins forceps and Westcott's scissors the graft was excised. Care was taken to obtain a graft as thin as possible without button holing.

After excision, the conjunctival autograft was slid and moved onto the bare sclera with non-toothed forceps and sutured with 10-0 nylon interrupted sutures. The graft was smoothened out in its bed. The four corners of the graft were anchored with episcleral bites to maintain position. The medial edge of the graft was sutured with 2-4 additional sutures, preferably including episclera.

At the end of the surgery, the eye was patched firmly after application of antibiotic ointment.

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Intra Operative Mitomycin C: Again the basic procedure is the bare sclera method of pterygium excision.

Preparation of Mitomycin C Solution: Mitomycin C is available as Crystalline Mitomycin C for injection. The vial contains 2mg of crystalline Mitomycin C and 9.8mg of Na Cl. When 1 vial of 2mg preparation is dissolved in 10ml of distilled water the concentration of Mitomycin C 0.02%(0.2mg/ml) was attained. Once the preparation was ready, it could be used for a maximum period of 1week, with storage in refrigeration, avoiding exposure to light.

Intraoperative Application: After the Bare sclera excision of the pterygium, the patient received Mitomycin C 0.02%. A sterile sponge 5 X 5mm soaked in 0.02% (0.2 mg/ml) solution of Mitomycin C was placed on the bare sclera for 2 minutes. Care was taken so that the pledget did not come in contact with cornea. After removal of sponge, the application site was thoroughly irrigated with 20-30 ml of BSS solution.

Eyes were patched with antibiotic ointment application.

Postoperative Advice: In both the groups, postoperatively topical antibiotic-steroid eye drops (Ofloxacin & Dexamethasone) were used every 2hours for the first postoperative week and then tapered over the next 4 weeks. Lubricant ointment – Lacrigel (1% HPMC) was applied twice a day. Sutures were removed after one week.

Postoperative Follow Up: Patients will be followed up post operatively on Day 1, 1 week, 1 month, 3 months, 6 months and one year to evaluate the results. At every follow up patients will be assessed and the following parameters recorded-symptomatic improvement, visual acuity, any adverse effect of the drug, any surgical complications, cosmetic appearance and finally post-operative recurrence.

At the end of one year, patients were asked to grade their satisfaction as 'Good', 'Fair' or 'Poor'.

Criteria for Recurrence: Recurrence was diagnosed when a fibrovascular growth occurred in the area of the previously excised pterygium crossing the limbus and extending on to the cornea for at least a distance of 0.5mm.

Statistical analysis was done with the Chi Square test and Student's paired t test was used to calculate 'p' value, if less than 0.05 was considered significant.

RESULTS: 80 patients were included in our study. They were randomly assigned to either Group A or Group B. 40 patients in Group A underwent Bare Sclera Excision technique followed by Conjunctival Autograft. 40 patients in Group B underwent Bare Sclera Excision followed by Intraoperative Application of 0.02% Mitomycin-C for two minutes.

Groups	No. of Patients	Percentage
Group A	40	50%
Group B	40	50%

Table 1: Randomization

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Age (Yr.)	Group A	Group B	Total	Percentage
20-29	1	5	6	7.5%
30-39	4	5	9	11.25%
40-49	16	14	30	37.5%
50-59	8	8	15	20%
60-69	9	7	16	20%
70-79	2	1	5	3.75%

Table 2: Age Incidence

Z=1.45, p value >0.05(not significant)

Gender	Group A	Group B	Total	Percentage
Males	21	20	41	51.25%
Females	19	20	39	48.75%

Table 3: Sex Incidence

χ^2 -0.041, p value >0.05 Not significant

	Group A		Group B		Total Outdoors	%
Occupation	Outdoors	Indoors	Outdoors	Indoors		
Primary	21	17	20	18	41	51.9%
Recurrent	2	0	1	1	3	3.75%
Total	23	17	21	19	44	55%

Table 4: Relation of Pterygium to The Occupation of Individual

χ^2 = 1. 516 p value >0.05

Type	Group A	Group B	Total	%
Primary	38	38	76	95%
Recurrent	2	2	4	5 %

Table 5: Type of Pterygium

χ^2 = 0.001 p>0.05.

Recurrence	Group A	Group B
No. of recurrences	3(7.5%)	5(12.5%)
Mean age of recurrence (Years)	44.37	43.85
Mean time of recurrence (months)	6	6

Table 6: Recurrence Characteristics

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Complications	Group A		Group B		Total	%
	(n)	%	(n)	%		
Limbal/Scleral avascularity			1	2.5%	1	1.25%
Granuloma	3	7.5%			3	3.75%
Scleral Thinning/ Necrosis			2	5%	2	2.5%
Loose sutures	1	2.5%			1	1.25%
Superficial Punctate Keratitis			2	5%	2	2.5%
Total	4	10%	5	12.5%	9	11.25%

Table 7: Complications

$\chi^2 = 2.7$ p value >0.05 Not significant.

Figure 12: Operative & Clinical Photographs

Grade II: Pterygium

Grade III: Pterygium

Excision of Head of Pterygium

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Blunt dissection with crescent

**After excision of head
and body of pterygium**

Bare Sclera

Application of mitomycin- C 0.02%

Application of mitomycin-C 0.02%

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Excision of superior bulbar conjunctival graft

Placement of graft on bare sclera

Sutured graft

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Intra-operative profuse bleeding

Scleral bleaching

Loose sutures

Granuloma

Inflamed pinguecula

Pseudo-ptyerygium

Recurrent pterygium

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DISCUSSION: This study is an attempt to compare the efficacy and also evaluate the safety of the two standard techniques of Conjunctival Autograft and Intraoperative application of Mitomycin-C 0.02% for 2 minutes, for preventing recurrence.

80 patients included in our study completed it. They were randomly assigned to either Group A or Group B. 40 patients in Group A underwent Bare Sclera Excision technique followed by Auto-conjunctival graft. 40 patients in Group B underwent Bare Sclera Excision followed by Intraoperative Application of 0.02% Mitomycin-C for two minutes.

1. AGE DISTRIBUTION:

- In our study ages of patients ranged from 20-75 years. The highest number of patients was in the Age group 40-49 years (37.5%). Lowest number of cases was in the age group 70-79 years (3.75%).
- In another study, ages of the patients ranged from 23-79 years. Mean age in that study was 47 years.³ This correlates with the present study.

2. SEX DISTRIBUTION:

- In our study, number of males included is 41(51.25%) and females were 39 in number (48.75%). However the dominance of male sex is not statistically significant (p value >0.05).
- In a study published in literature, of the total of 108 patients, 66(61%) were male and 42(39%) were female.³

3. LATERALITY: Of the 80 patients in our study, 45 (56.25%) patients had Bilateral pterygium and 35 (43.75%) cases were unilateral

4. LOCATION:

- In our study pterygium was located nasally in 79 cases and in 1 case both temporally and nasally located with a mean pre-operative encroachment of 3.2mm.
- In a study done under similar conditions, 61 cases (95.31%) was nasally located, 2 cases(3.12%) were temporal and 1 case (1.56%) were both nasal and temporal with a mean corneal encroachment of 3x3.6mm.⁴

5. TYPE OF PTERYGIUM:

- Of the 80 cases, 76(95%) were primary pterygium and 4(5%) cases were recurrent pterygium. However this distribution of primary and recurrent pterygia is not statistically significant (p>0.05).
- In a similar study published in Literature, 123 cases(78.34%) were primary pterygium and 34cases (21.66%) were recurrent pterygia.⁵

6. EFFECT OF OCCUPATION OF INDIVIDUAL ON PTERYGIUM:

- In our study, 41 patients with primary pterygium (51.9%)were engaged in occupations involving predominantly outdoor activity. 35 patients with primary pterygium (43.75%) were involved in indoor work, the influence of outdoor activity was not considered statistically significant (p value>0.05).

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- In an Indonesian study to assess the risk factors for pterygium in tropical conditions, a history of more than 5 hours per day of outdoor activity 10 years earlier was associated with almost twice the rate of those without such a history (12.3% v 6.5%).⁶

7. COMPLAINTS: In our study the most frequent complaint given by the patient was fleshy growth, dry eye symptoms like ocular irritation and watering followed by redness and defective vision.

8. COMPLICATIONS: In the present study we encountered 1 intra-operative complication during surgery. Profuse bleeding after excision of neck and body of pterygium and was managed immediately by cauterization. The post-operative complications that we came across in 40 cases of Group A were:

- 1(2.5%) case of loose suture and 3(7.5%) cases of conjunctival granuloma .
- The postoperative complications noted in 40 cases of Group B were-
- 2 cases of scleral thinning, were noted and were due to an adverse effect of the drug Mitomycin C.
- One case of Limbal avascularity documented was due to excessive reaction to the drug Mitomycin C.
- 2 cases of Super ficial punctate keratitis were noted.
- In our study the overall rate of complication was 11.25%, with the rate in Group A being 10% and Group B 12.5% .The difference is not statistically significant (p value >0.05).
- In a recent review, the complications documented were 4 cases of Granuloma at donor conjunctival site(2.88%), 3 cases had conjunctival cyst (2.16%), 1 case developed scleral thinning (0.72%).⁷
- In a study published, to compare Intraoperative Mitomycin-C (MMC) with Limbal Conjunctival Autograft (LCAU), there were three conjunctival cysts (two MMC, one LCAU), three symblephara (two MMC, one LCAU), one granuloma (MMC), and one dellen (MMC). No scleral thinning, necrosis, or any other visually significant complications were encountered in either groups.⁸

9. RECURRENCE:

- In the present study, there were 7 cases of recurrence on the whole (8.75%) that was encountered. Among them 3 cases belonged to Group A (7.5%) and 4 cases in Group B(10%). This difference in recurrence rate is not statistically significant (p value >0.05).
- The average age of recurrence was 41 years. In a similar study patients younger than 37 years showed a higher risk of pterygium recurrence.⁹
- In another Indian study, all cases of recurrences occurred in patients below 40 years of age.¹⁰
- The average time of recurrence noted in Group A and Group B was 6months.
- 4 recurrent cases were male and 2 were female.
- 5 cases were primary with nasal pterygium and one was primary case with both temporal and nasal pterygium and 1 was recurrent case.

The average post-operative corneal encroachment of recurrent pterygium was 2.5mm x 2mm. The mean corneal encroachment in tropical studies of recurrent pterygia was noted to be 3mm x 3.7mm.⁴

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In study done under similar conditions, the mean age of recurrence was 24 and the mean time of recurrence was 3.5months.¹¹

In a recent review on comparison between Intraoperative Mitomycin C (MMC) and Limbal Conjunctival Autograft (LCAU), there were 10 recurrences (15.9%) in the MMC group – one at 3 months, four at 6 months, two at 9 months, and three at 12 months. There was only one recurrence (1.9%) in the LCAU group identified at 3 months and the difference in recurrence rates was statistically significant ($p=0.04$).⁸

Recurrence rates of Conjunctival autograft and Postoperative Mitomycin C were similar in another Chinese study (38% and 39% respectively).¹²

- Among the 11 cases of recurrences seen in our study (including those seen after inclusion in our study and those who already presented with recurrence), 9 cases were of the category Progressive Pterygium, 2 cases were of Regressive type. It has been shown in population based studies that "fleshier," higher grade lesions are more likely to recur after surgery.⁶
- The vascularity of pterygium tissue may have significance in terms of pterygium severity and progression. It is proved that fleshiness of the body of the pterygium, denoted by obscuration of underlying episcleral vessels by the fibrovascular pterygium tissue, was a risk factor for recurrence rate after bare sclera excision, while the morphology of pterygium recurrence inevitably reflects a high degree of vascularity.⁵
- From the above observations, younger age and progressive pterygium appears to be a risk factor for recurrence and hence these patients should be treated aggressively and with more caution.
- Majority of the recurrences were noted in male patients probably due to more exposure to irritating agents. Hence a definite predilection for sex cannot be commented.

The Tables below enumerates the recurrence rates of Conjunctival autograft and Mitomycin C, when compared with each other or with Bare Sclera technique.

Sl. No.	Study (Year of Publication)	Type of Study	No. of Eyes	Type of Pterygium	Follow-up	Recurrent Rate
1.	Chen et al (1995)	Double masked clinical trial	64	Primary	9.3 months	Placebo-88% Mitomycin – C – 38% Conjunctival Autograft- 39%
2.	Tan DH et al (1997)	Prospective	157	Primary/ Recurrent	15.1 months	Bare Sclera Excision – 38% Conjunctival Autograft - 2%
3.	Kammoun et al (2001)	Prospective	167	Primary/ Recurrent	3 years	Bare Sclera Excision – 55.9% Conjunctival Autograft -

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						10.3% Mitomycin -C- 11.1%
4.	Present study	Randomize d Clinical Trial	80	Primary/ Recurrent	One year	Conjunctival Autograft- 7.5% Mitomycin C- 10%

Table 15: Comparative Study

CONCLUSION: From our study and the analysis of our results, we conclude that both Conjunctival Autograft and Intraoperative application of 0.02% Mitomycin C for two minutes are equally effective in preventing or reducing recurrence following Bare sclera excision of Pterygium. Both the methods appear to be safe and acceptable as adjuvants in pterygium surgery, as no major complications have been noted in the present study.

Conjunctival autograft technique following pterygium excision appears to be essential to ensure low recurrence rate. The complications in Autograft technique can be avoided by use of meticulous dissection and skillful transplantation of graft to the recipient bed. This technique is safe and inexpensive, most suited for Indian population, presenting with primary or recurrent pterygium, although it is technically more difficult.

With the use of 0.02% Intraoperative Mitomycin C for two minutes, taking due precautions, recurrent pterygium can be successfully tackled. With-out any sight threatening complications, a number of cases of scleral thinning and avascularity have been reported

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