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## Original Research Article

## Evaluation of outcome of primary pterygium excision combined with different techniques

Manjunath BH<sup>1</sup>, Raksha V<sup>1,\*</sup><sup>1</sup>Dept. of Ophthalmology, JJM Medical College, Davanagere, Karnataka, India

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## ABSTRACT

**Objectives:** To compare different techniques combined with excision in treatment of primary pterygium: Amniotic membrane transplant [AMG], Limbal-conjunctival autograft [CLAG], and mitomycin c with limbal-conjunctival autograft.[MMC+CLAG]

**Materials and Methods:** A prospective comparative study was performed in tertiary hospital on 105 patients satisfying the inclusion and exclusion criteria. Combined with excision, 35 eyes each were treated with AMG transplantation [Group 1] and CLAG [Group 2] for closure of defect. In 35 eyes low-dose mitomycin -C [0.02%] was applied on bare sclera for 1 minute and a CLAG was applied thereafter [Group 3]. Patients were followed up for 9 months.

**Results:** Study was conducted from June 2018 to April 2020 on patients of age 26 to 72 years with mean age of  $46.3 \pm 10$  years with 42[40%] male and 63[60%] female. A statistically significant change [paired t test,  $p < 0.001$ ] was noted in K-horizontal value pre- and post- pterygium surgery. Change in K-vertical pre- and post- surgery was not statistically significant [paired t test,  $p < 0.58$ ]. Pterygium recurred in 3 patients [8.6%] in group 1, 1 patient [2.9%] each in group 2 and 3. Other postoperative complications include graft displacement [5.7%], graft oedema [6.7%] and congestion [9.5%]. A minor case of scleral melting was noted in one patient [2.9%] in group 3.

**Conclusion:** Pterygium excision followed by CLAG and MMC+CLAG are an effective way of reducing recurrence. However close monitoring is required for use of adjuvant MMC.AMG can be reserved in patients with bilateral pterygium, severe limbal stem cell loss and in need of glaucoma surgery.

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## 1. Introduction

Pterygium is a triangular 'wing-like' growth consisting of conjunctival epithelium and hypertrophied subconjunctival connective tissue that occurs nasally and/or temporally in the palpebral fissure, and encroaching onto the cornea.<sup>1</sup>

UV radiations play an important role in inducing damage to the limbal stem cells. It results in chronic inflammation and fibrovascular changes along with migration of conjunctiva over the cornea.<sup>2</sup> Other contributing factors include dry eye, smoking, prolonged outdoor activities and

high altitude.

Decrease in visual acuity, discomfort and irritation, restricted ocular movements, and unacceptable appearance are some of the indications for surgical removal.

Surgical trauma and subsequent postoperative inflammation contribute to recurrence of pterygium, which is a main drawback of pterygium surgery. Bare sclera excision has the highest recurrence rate ranging from 24% to 89%, simple closure or a superior rotational flap similarly show high recurrence rates of 37% and 29%, respectively.<sup>1</sup> Conjunctival autografts recur at a rate of 5–25% and amniotic membrane grafts at 10–35%.<sup>3</sup>

\* Corresponding author.

E-mail address: [rvr1893@gmail.com](mailto:rvr1893@gmail.com) (Raksha V).

MMC is an antibiotic-antineoplastic agent that selectively inhibits the synthesis of DNA, cellular RNA, and protein.<sup>4</sup> Use of Mitomycin-C in pterygium surgery was first described by Kunimoto and Mori of Japan. MMC is now being used in two ways: The postoperative use of topical mitomycin C as eyedrops,<sup>5</sup> [Recurrence rates - 0% to 38%.], and the intraoperative application of surgical sponges soaked in MMC solution directly to the scleral bed after pterygium excision.<sup>6</sup> [Recurrence rate- 3% to 43%]. More recently subconjunctival injection of MMC preoperatively directly into the pterygium tissue was described.<sup>7</sup> Few studies have been conducted combining CLAG with MMC with a recurrence rate of 2% to 9%.<sup>8,9</sup>

Studies on amniotic membrane [AMG] transplantation for pterygium surgery have shown that it facilitates epithelialization, inhibits pathological neovascularisation, scar formation and inflammation thus yielding better results in reducing pterygium recurrence.<sup>10–12</sup>

In the present study we report the surgical outcomes of amniotic membrane grafting, limbal-conjunctival autograft and MMC+CLAG in terms of safety, efficacy and recurrence rate.

## 2. Materials and Methods

The study was conducted in the department of ophthalmology of a tertiary care centre obtaining ethical permission from the institutional ethical committee. The methods adhere to the tenets of the declaration of Helsinki.

105 Patients of all ages and sex, and with primary pterygium tissue extending more than 2 mm beyond the limbus attending the outpatient department of ophthalmology between December 2018 to April 2020 were considered for this study.

### 2.1. Exclusion criteria

Included patients with other ocular surface disorders, glaucoma, vitreoretinal diseases, collagen vascular diseases, dry eye and cicatricial pemphigoid.

After an informed consent a detailed history including demographics and preoperative assessment including visual acuity using Snellen's chart, refraction, keratometry, IOP using Goldman applanation tonometry and slit lamp examination was done.

Pterygium was staged based on its encroachment on to cornea:<sup>13</sup> Stage 1- just beyond the limbus, stage 2- encroaching up to point between limbus and pupillary margin, stage 3 -pterygium extending up to pupillary margin. Stage 4- pterygium i.e. pterygium crossing the pupillary margin.

Pterygium was also graded based on Tan grading<sup>14</sup> T 1 – Atrophic type, T2 – Intermediate type and T 3 – Fleshy and opaque type of pterygium.

Patients were segregated randomly into AMG [n=35, group1], CLAG [n=35, group 2] and MMC+CLAG [n=35, group 3]. All surgeries were done by a single surgeon and patient's auto serum was used to secure the graft over the bare sclera.

### 2.2. Procedure

Peribulbar block, 4ml, was given to the operating eye using 2% lignocaine and 0.5% bupivacaine. After taking all aseptic precautions, operating eye was exposed. The pterygium was separated from the underlying structure and incised at the limbus separating the body from the head of pterygium. The pterygium head was dissected from the cornea using reverse peeling technique. The body of the pterygium, including the adjacent Tenon's capsule, was dissected and excised from the underlying sclera. The area of recipient bed was measured.

#### 2.2.1. After excision of pterygium one of the three procedures was performed

Amniotic membrane graft: a desired size of commercially available pre-processed dry AMG was excised and carefully placed on the bare sclera. Patient's auto serum was used as adhesive to secure graft in place.

#### 2.3. Limbal-conjunctival autograft

The desired size of the conjunctiva in the supero-temporal region was marked, which included part of limbus. The donor graft was excised making sure there is no adherent tenon's on the graft and placed on the bare sclera with epithelium facing up and with limbus to limbus approximation of graft and recipient bed. Patient's autologous serum was used as adhesive to secure the graft.

#### 2.4. Combined MMC+CLAG

After achieving haemostasis, a merocele sponge soaked in 0.02% MMC was placed over the bare sclera for 1 minute and irrigated with normal saline of 30 ml. Care was taken not to touch the cornea with MMC. This was followed by excising a limbal-conjunctival autograft of desired size from the supero-temporal bulbar conjunctiva, and the donor graft was secured over bare sclera using patient's auto serum.

Topical antibiotics and corticosteroids were instilled and followed by eye pressure patching.

Postoperatively, comprehensive slit-lamp examinations of the anterior segment were done on day 1, week 1, 1 month, 3 months, 6 months and 9 months after surgery in order to determine recurrence and the presence of inflammatory events such as hyperaemia, haemorrhage, graft contraction, and pyogenic granuloma. Recurrence was graded based on Prabhasawat classification.<sup>10</sup>

Grade 1- The appearance of the operated site is not different from the normal appearance.

Grade 2- Some fine episcleral vessels in the excised area extending up to but not beyond the limbus and without fibrous tissue.

Grade 3- Additional fibrous tissue in the excised area that does not invade the cornea.

Grade 4- Fibrovascular tissue invading the cornea

### 2.5. Statistical analysis

Results are presented as Mean $\pm$ SD and range values for continuous data and frequencies as number and percentages. Categorical data was analysed by Chi-square test. A P value of 0.05 or less was considered to be statistically significant. SPSS (Version 22, IBM) software was used for data analysis.

### 3. Results

A total of 105 eyes with the primary pterygium were investigated in the present study with 42 (40%) males and 63 (60%) females. The mean age of the sample was 46.3  $\pm$  10 (mean, standard deviation) ranging from 26 to 72 years. Between 26 and 35 year category there were 14 (13.3%) patients, there were 40 (38.1%) patients in 36–45 year group, between 46 and 55 year intervals there were 32 (30.5%) cases, between 56 and 65 range intervals there were 14(13.3%) patients and 5 (4.87%) between >65 years category.

53[50.5%] worked indoors and 52[49.5%] were outdoor workers. Predilection observed more frequently for the right eyes 55 (52.4%) than the left eyes 50 (47.6%). Out of 105 patients, 33 [31.4%] patients presented with Tan 1, 43 [41%] patients had intermediate type [TAN 2] and 29 [27.6%] patients presented with fleshy type [TAN 3] of pterygium.

87[82.8%] suffered with WTR astigmatism, 15[14.3%] had ATR astigmatism and 3[2.95] had no astigmatism. Change in keratometry values pre and 1-month post pterygium surgery was compared using paired t test. The k-vertical value was 43.85 $\pm$ 1.83 D. After surgery, the mean astigmatic values decreased to 43.80  $\pm$ 1.80 D. The decrease was not statistically significant (P =0.58, paired t test). The k-horizontal value preoperatively was 43.05 $\pm$ 2.02 D. After surgery, the mean astigmatic values decreased to 43.51  $\pm$ 1.93 D. The decrease was statistically significant (P <0.0001, paired t test).

Postoperatively, in our study we had 10[9.5%] cases of congestion in immediate post-operative day 1. 1 [2.9%] case each of graft displacement was noted in group 2 and 3, while 4 [11.4%] cases in group 1. This is attributed to the thin and delicate nature of dry AMG. Graft oedema was observed in 1<sup>st</sup> week follow-up in 2 [5.7%] patients each in group 1 and 2, and 3[8.5%] in group 3. This was attributed to inadequate debridement of graft. The pterygium recurred in 3 patients (8.6%) in group 1, in 1 patients (2.9%) in group 2, and in 1 patient (2.9%) in group 3.

In group 3, 1 case of mild scleral melting was noted after 2 weeks of surgery the process was controlled by using a systemic corticosteroids and judicious use of topical lubricants.

### 4. Discussion

A pterygium is characterised by chronic inflammation and excessive fibrovascular proliferation of conjunctiva on exposure to climatic factors and aggravated by microtrauma.<sup>15</sup>

Pterygium is a common occurrence in males than females. However, in our study 42 [40%] were male and 63 [60%] were female. The synergistic effect of UV rays and dust on the interpalpebral conjunctival tissue is among the probable causes for increased incidence in rural women who are also outdoor workers.

Pterygium causes deterioration of vision by distorting the corneal smooth surface, and so inducing astigmatism usually with the rule type. Out of the 105 patients preoperatively, majority [82.8%] suffered with WTR astigmatism. A statistically significant steepening of the horizontal meridian post pterygium surgery was noted in all the techniques. The K-horizontal value preoperatively was 43.05 $\pm$ 2.02 D. After surgery, the mean astigmatic values decreased to 43.51  $\pm$ 1.93 D. Similar changes in the keratometry values were also noted by Meitei et al<sup>16</sup> Maheshwari S,<sup>13</sup> Lindsay et al,<sup>17</sup> Deepakar U P et al.<sup>18</sup>

The successful treatment of pterygium remains a challenge for the clinician. To prevent recurrence, various techniques for closure of the defect and a number of adjunctive techniques have been developed.

Many ophthalmologists still prefer conjunctival autografting after pterygium excision in order to avoid complications of MMC. This procedure is time-consuming, requires a significant learning curve, and has greater postoperative recurrence rates as compared with MMC.<sup>19,20</sup>

MMC acts as an antifibrotic agent and alkylating agent, thus preventing pterygium recurrence. However, the safest dosage of MMC which caused no complications but can prevent recurrence of pterygium is still to be evaluated. Single intraoperative use of MMC is safer than postoperative topical daily application, as multiple use of MMC may lead to complications such as scleromalacia, corneal perforation, glaucoma, iritis, pain and punctate Keratopathy.<sup>21,22</sup>

Human amniotic membrane has anti-scarring, anti-angiogenic and anti-inflammatory properties. The basement membrane acts as a substrate to allow healing and epithelization. It also suppresses TGF beta signalling in conjunctival and pterygium fibroblasts, thus effective in reducing scarring and fibrosis in ocular surface surgery.<sup>1,10</sup>

Few studies have shown that CLAG is better than AMG in terms of recurrence rate.<sup>23,24</sup> However, some other studies reported that using only AMT could also present

**Table 1:** comparison of demographics, staging of pterygium and complications in AMT, CALG and CLAG+MMC.

Parameters	AMG	CLAG	MMC+CLAG	Total	Statistics
<b>Stage of pterygium</b>					
Stage 2	25 [71.4]	26 [74.3]	27 [77.1]	78 [74.3]	X <sup>2</sup> =0.30 P=0.86, NS
Stage 3	10 [28.6]	9 [25.7]	8 [22.9]	27 [25.7]	
<b>Tan grading</b>					
T1	9 [25.7]	12 [34.3]	12 [34.3]	33 [31.4]	X <sup>2</sup> =1.21 P=0.88, NS
T2	15 [42.9]	15 [24.9]	13 [37.1]	43 [41.0]	
T3	11 [31.4]	8 [22.9]	10 [28.6]	29 [27.6]	
<b>Pre-operative VA</b>					
6/6-6/9	12 [34.3]	11 [31.4]	13 [37.1]	36 [34.3]	X <sup>2</sup> =0.25 P=0.88, NS
6/12-6/24	23 [65.7]	24 [68.6]	22 [62.9]	69 [65.5]	
<b>Pre-operative AST</b>					
WTR	30 [85.7]	29 [82.8]	28 [80.0]	87 [82.8]	X <sup>2</sup> =0.47 P=0.98, NS
ATR	4 [11.4]	5 [14.3]	6 [17.1]	15 [14.3]	
NIL	1 [2.9]	1 [2.9]	1 [2.9]	3 [2.9]	
<b>Post-op complications</b>					
Graft displacement	4 [11.4]	1 [2.9]	1 [2.9]	6 [5.7]	P=0.597 NS
Graft oedema	2 [5.7]	2 [5.7]	3 [8.5]	7 [6.7]	
Congestion	4 [11.4]	4 [11.4]	2 [5.7]	10 [9.5]	
Recurrence	3 [8.6]	1 [2.9]	1 [2.9]	5 [4.8]	
Scleral melting	0 [0.0]	0 [0.0]	1 [2.9]	1 [1.0]	
Uneventful	22 [62.9]	27 [27.1]	22 [77.1]	76 [72.3]	

AMG: amniotic membrane graft; CLAG: conjunctival limbal autograft; MMC: mitomycin-c; WTR: with the rule; ATR: against the rule.

**Table 2:** Pre- and Post operative keratometry values

Total		Mean	Std. Deviation	Paired t test
K-V	Pre OP	43.85	1.84	P<0.589, Not Sig
	Post OP	43.85	1.82	
K-H	Pre OP	43.05	2.02	P<0.000, Highly Sig
	Post OP	43.51	1.93	

K-V: keratometry vertical; K-H: keratometry horizontal; OP: operative

good results.<sup>25</sup> AMT is an alternative choice, especially in patients who might need glaucoma surgery later, patients with bilateral pterygium or those with severe limbal stem loss.

In this study, we also observed recurrence in 3 patients (8.6%) in group 1, in 1 patient (2.9%) in group 2, and in 1 patient (2.9%) in group 3.

Similarly, Frucht -pery et al<sup>9</sup> in his study using 0.02% MMC for 1 minute showed no [0%] recurrence in MMC+CLAG group. He inferred that there was significant improvement in the outcome due to additive effect of 1 minute of use of MMC. In similar study by Claudia et al<sup>26</sup> on 69 patients 13 cases of CLAG showed recurrence and no patient of MMC+CLAG group had recurrence.

In our study one case of mild scleral melting was observed in the 2<sup>nd</sup> week follow-up. The permanent inhibition of fibroblast proliferation coupled with the delay in wound healing results in vascular compromise to the surgical site thus exposing the sclera to avascular necrosis. Another reason being excessive cauterization. A similar case was encountered by Frucht-pery et al<sup>9</sup> with use of 0.02% MMC for 1 min intraoperatively on 10<sup>th</sup> day post

operatively. This was attributed as a result of conjunctival swelling over the flap with formation of dellen.

## 5. Conclusion

Adjunctive use of AMT reduces the recurrence rate after pterygium surgery. It is a faster and less tedious surgery with a faster recovery time. It also helps to save the conjunctiva for future surgeries.

MMC in small doses for shorter exposure time can reduce recurrence of pterygium with minimal complications. The combined effect of the antiproliferative property of MMC and the contact inhibition effect of the conjunctival limbal transplantation may be beneficial in pterygium surgery.

Further long-term controlled studies are needed to support our findings.

## 6. Conflict of Interest

The authors declare that there are no conflicts of interest in this paper.

## 7. Source of Funding

None.

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## Author biography

**Manjunath BH**, Professor

**Raksha V**, Junior Resident

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