

# Amniotic Membrane Transplantation in Primary Pterygium Compared with Bare Sclera Technique

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## ABSTRACT

**Objective:** To compare the excision of primary pterygium by bare sclera technique and excision combined with amniotic membrane transplantation (AMT).

**Study Design:** An experimental study.

**Place and Duration of Study:** Eye Department, Military Hospital, Rawalpindi, presently known as Armed Forces Institute of Ophthalmology, Rawalpindi, from May 2007 to July 2008.

**Methodology:** A pilot study of 70 patients was conducted. Patients were divided in two groups. In group I, pterygium excision was done by bare sclera technique while in group II, AMT was done after excision. Patients were followed for 6 months. Proportion of recurrence of pterygium was noted in each group and compared with chi-square test with significance at  $p < 0.05$ .

**Results:** Number of patients who presented with recurrence of pterygium in group-I were 12 (37.5%) and in group-II were 4 (12.9%). Chi-square tests showed that there was a statistically significant difference in frequency of recurrence between the two groups ( $p = 0.025$ ).

**Conclusion:** AMT after excision of pterygium appeared to be safe and effective way of treating primary pterygium as compared to bare sclera technique due to lesser recurrence at 6 months.

**Key words:** Amniotic membrane transplantation (AMT). Pterygium. Recurrence. Bare sclera technique.

## INTRODUCTION

Pterygium is a wing shaped conjunctival growth onto the cornea which is generally situated on the nasal side. Pterygium is more frequently seen in areas with more ultraviolet radiation, hot, dry and smoky environments.<sup>1</sup> Presently, pterygium is recognized as an ocular surface growth disorder, secondary to solar radiations-induced p53 mutations in limbal epithelial stem cells.<sup>2</sup> It is more common in patients with outdoor occupations like farmers, labourers, and soldiers and less common in patients with indoor activity like housewives and teachers.<sup>3</sup> The prevalence of pterygium is more common in countries within the peri-equatorial (pterygium-belt) latitude of 37 degree north and south of the equator.<sup>4,5</sup>

Recurrence of pterygium is the major and most common complication after surgery which is described as the development of fibro-vascular tissue on to the excision site.<sup>6,7</sup> Different modalities of treatment like buccal mucous membrane graft, lamellar keratoplasty, penetrating keratoplasty, sclerokeratoplasty and Yttrium-

aluminium-garnet (YAG) laser treatment have been tried but the results were not encouraging.<sup>8</sup> The mainstay of surgery remains the bare sclera excision, followed by either adjunctive therapy by application of antifibrotic agents such as mitomycin-C or by covering the defect with conjunctival autograft.<sup>2</sup>

Human amniotic membrane is rich in basement membrane components such as laminin and type-IV collagen. It lacks immunogenicity, has anti-bacterial, anti-inflammatory, and anti-scarring effects.<sup>9</sup> The membrane produces various growth factors including basic fibroblast growth factor, hepatocyte growth factor, keratinocyte growth factor and epidermal growth factor which can stimulate epithelization and act as promoters of epithelization.<sup>10</sup> In comparison with conjunctival autograft and topical mitomycin-C treatment, amniotic membrane transplantation (AMT) is as effective as the other two methods and is safe and easier with no major complications. Ma suggested that "amniotic membrane graft may be a preferred procedure for primary pterygium, and is especially suited for pterygium with diffuse conjunctival involvement or glaucoma patients waiting for filtering operations".<sup>11</sup> The amniotic membrane is prepared under sterile conditions and preserved at  $-80^{\circ}\text{C}$  by the method outlined by Tseng *et al.*<sup>12</sup>

The rationale of this study was to evaluate the role of AMT in treatment of primary pterygium so that if the

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recurrence rate is less than bare sclera technique, AMT could be used as an alternative cost effective method. This will also benefit Ophthalmologists especially in those cases of pterygium where conjunctiva is to be spared like patients waiting for their filtration surgery for glaucoma and large pterygium with diffuse conjunctival involvement.

The objective of the study was therefore, to compare the excision of primary pterygium in terms of frequency of recurrence in 6 months follow-up by the bare sclera technique versus AMT.

## METHODOLOGY

The study was conducted at Eye Department, Military Hospital, Rawalpindi, presently known as Armed Forces Institute of Ophthalmology, Rawalpindi, from May 2007 to July 2008.

The patients were included in the study from outpatient department. Random allocation was done by random sampling number chart and each patient was placed in either of the two groups. Group-I underwent excision of pterygium by using bare sclera technique while group-II underwent pterygium excision combined with AMT.

Recurrence of pterygium was defined as the development of fibro-vascular tissue with radially oriented blood vessels encroaching on the excision site and extending 1 mm or more onto the cornea.<sup>7</sup>

Inclusion criteria included all diagnosed cases of primary pterygium on the basis of history and clinical examination, age 20 years or more with redness, discomfort, foreign body sensation, cosmetic problem and gross astigmatism. Exclusion criteria were asymptomatic cases, recurrent pterygium, dry eye, infection of cornea or lacrimal apparatus, patient who had already undergone squint, cataract or vitreoretinal surgery.

Pre-operatively detailed history was taken. Complete ocular examination included visual acuity, refraction, complete anterior segment examination including intraocular pressure, extra-ocular movements and fundoscopy was done in all patients. An informed written consent was taken from the included patients.

Amniotic membrane was obtained under sterile conditions after elective caesarean delivery from donor mothers. Consent for donation, subsequent use, and screening for infections was also obtained. Approval from hospital ethical committee was taken after discussing all ethical issues of use of amniotic membrane in eye surgery. Serum samples from all donors were tested for anti-HIV, hepatitis B surface antigen (HBsAg), anti-hepatitis C virus (anti-HCV) and syphilis (VDRL).

The placenta was collected under clean and aseptic conditions in a container containing one liter of Ringers lactate. The container was immediately transferred to an

ice box and brought to eye operation theatre. Under strict aseptic conditions, the placenta was first washed free of blood clots with balanced saline solution containing 50 ug/ml of ampicillin, 50 ug/ml of streptomycin, 80 ug/ml of gentamycin, and 2.5 ug/ml of amphotericin B. The inner amniotic membrane was separated from the rest of the chorion by blunt dissection through the potential spaces between these two tissues. Amniotic membrane was then again washed with the antibiotic containing saline solution. The membrane was then flattened onto a sterile nitrocellulose filter paper (Millipore), with the epithelium surface up and cut according to the size of paper. The membrane with the paper was sutured with 4/0 silk to identify epithelial side. The membrane was then placed in a sterile plastic container containing Dulbecco's modified Eagle's medium and glycerol at a ratio of 1:1 (vol/vol) which was prepared under strict aseptic measures as described by Tseng *et al.*<sup>12</sup> at Virology Department, Armed Forces Institute of Pathology, Rawalpindi. The plastic containers were frozen at -80°C in a special refrigerator at Armed Forces Bone Marrow Transplantation Centre, Rawalpindi. The membranes were thawed immediately before use by warming the container to room temperature for 10 - 15 minutes.<sup>13</sup> The membranes were washed with 100 ml of balance saline solution and then transplanted.

All surgeries were performed by same surgeon. In cases of group-I, surgery was performed under microscope set at low magnification and intensity. Head of pterygium was grasped with toothed forceps at the limbus and a little pull was applied to make the dissection easy. Dissection was done using number 15 blade to free the head from the cornea. Conjunctival epithelium was bluntly dissected away from sub-epithelial tissue. Sub-conjunctival tissue was then excised with Westcott scissors. At the end, 3 - 4 mm of sclera was left bare. The blade was then used to clear any remnant adherent to the cornea. The aim was to leave the corneal surface as smooth as possible to have minimum postoperative astigmatism. In cases of group-II, after removing the pterygium by the bare sclera technique, a rectangular conjunctival defect of approximately 5 x 7 mm or larger was created. This bare sclera was then covered with amniotic membrane, which was oriented with epithelial side up. The amniotic membrane was sutured through the episcleral tissue to the edge of conjunctiva along the bare sclera border with 7 - 8 interrupted stitches of 8/0 Vicryl sutures.<sup>11</sup> The eye was padded after instillation of antibiotic ointment (chloramphenicol 1%). The patients were advised to take oral diclofenac sodium 50 mg tablets and oral ciprofloxacin 500 mg tablets twice daily postoperatively for 3 days. Patients were examined a day after surgery and topical prednisolone acetate 1% and chloramphenicol 0.5% eye drops were given four times daily for 4 weeks. They were advised monthly follow-up for 6 months. On every follow-up visit, recurrence of pterygium was noted.

Data was analyzed using Statistical Package for Social Sciences (SPSS) version 15.0. Mean age of patients in both groups were expressed as mean ± SD and compared among two groups using t-test. Male-to-female ratio was calculated in each group. Chi-square test was applied to compare gender distribution and frequency of recurrence of pterygium between two groups. P-value of < 0.05 was taken as significant.

### RESULTS

There were a total of 63 patients among which group-I had 32 patients and group-II had 31 patients. Using t-test, insignificant difference was observed between age distribution of both the groups (p = 0.279). Male to female ratio in group-I was approximately 4:1 while in group-II it was approximately 3:1. Using chi-square test, it was found that both groups were comparable with respect to gender (p = 0.501).

In group-I and II, the frequency of recurrence of pterygium were found to be 37.5% and 12.9% respectively which was statistically significant difference (p = 0.025). The results are summarized in Table I.

**Table I:** Comparison of group I and II in terms of age, gender and frequency of recurrence of Pterygium.

Variables	Group I (n=32)	Group II (n=31)	p-value
Age (years) ± SD	47.16 ± 12.75	43.68 ± 12.51	0.279
Male (frequency)	26 (81.3%)	23 (74.2%)	0.501
Female (frequency)	6 (18.8%)	8 (25.8%)	
Recurrence (frequency)	12 (37.5%)	4 (12.9%)	0.025

### DISCUSSION

The reported recurrence rate of 12.9% after excision of primary pterygium with AMT is comparable with work done by other researchers. Prabhasawat *et al.* reported the result of AMT following pterygium excision and found a higher rate of recurrence when compared with conjunctival autograft (10.9% and 37.5% vs. 2.6% and 9.1% for primary and recurrent pterygium, respectively).<sup>14</sup> The present study included primary pterygium only and the results (12.9%) were comparable.

Ma *et al.* compared the recurrence rates after excision of primary pterygium combined with AMT, conjunctival autograft, and topical mitomycin-C.<sup>11</sup> Recurrence was low and comparable among all 3 groups (3.8%, 5.4%, and 3.7%, respectively). The recurrence rate was significantly higher in this study (12.9%) as compared to Ma *et al.*'s. This was probably due to their technique of removing more conjunctival tissue, especially adjacent to pterygium at limbus. Moreover, this study was non-randomized, which was its major drawback.

Küçükerdönmez *et al.* reported recurrence rate of 10.5% and 3.5% of primary pterygium excision and AMT which was comparable with study.<sup>15,16</sup> Ozkurt *et al.* and Katircioglu *et al.* carried out AMT on 12 patients of primary

pterygium and reported recurrence rate of 41% and 25% which is quite high as compared to this study, but their smaller sample size (n = 12) was probably the major reason for such a high recurrence rate.<sup>17,18</sup>

Essex *et al.* reported a high recurrence rate (64%) after AMT for pterygium.<sup>7</sup> He argued that a number of factors might have contributed for his failure. Firstly, he was working in a tertiary care centre and the cases referred might be more aggressive. Secondly, they were of lower socioeconomic status. Thirdly, UV light and surgical techniques were discussed in relation to other researchers, but no satisfactory reason was found out for such a higher recurrence rate. It was a non-randomized and non-comparative study. In the present study the recurrence rate was quite less (12.9%).

Ozer *et al.* reported recurrence rate of pterygium in his long-term follow-up study of almost 5 years as 39.58%, 14.29% and 23% after bare sclera, limbal conjunctival autograft and AMT respectively.<sup>19</sup> This study revealed 37.50% recurrence rate after bare sclera technique which is comparable to his work but as follow-up was only of 6 months we expect higher recurrence at 5 years. This study revealed lesser recurrence in AMT group and again it is because of shorter follow-up time. Moreover, the present study is a pilot study with smaller sample size. A larger randomized control trial with longer follow-up time is recommended to get more reliable and comparable results.

Khan *et al.* reported 36.6% recurrence rate after excision of pterygium by bare sclera technique and only 7.4% recurrence when excision was combined with AMT.<sup>20</sup> The results of this study augment his results by showing lesser recurrence rate when excision is combined with AMT. Rehman *et al.* revealed 41.33% recurrence of pterygium with bare sclera technique as compared to 33.33% when 5-Fluorouracil was used.<sup>21</sup> Similarly, Saleem *et al.* also reported higher recurrence rate of 30% with bare sclera technique.<sup>22</sup> Kamil *et al.* studied the effect of AMT alone and AMT combined with mitomycin-C in reducing the recurrence rate of pterygium and reported recurrence rate of 16.6% versus 6.6% in both groups respectively.<sup>23</sup> Shakir *et al.* in the same institute studied the effect of AMT in non-healing corneal ulcer and reported a success rate of 69.56% in maintaining corneal integrity.<sup>24</sup> Results of this study support the previous local work.

The results between the two groups were comparable with regard to age having similar age-wise distribution. Patients younger than the age of 15 rarely develop a pterygium. The prevalence of lesion increases with age but studies have revealed a mean age varying from 47 to 52 years.<sup>25,26</sup> Total male to female ratio in both groups was 7:2, males being more than females. Pterygium is found to be more common in males than females because of their outdoor activities and thus more

exposure not only to the ultraviolet lights but also other irritants as well. In few studies, the male to female ratio was reported as 2:1 which is comparable to the present study.<sup>25,27</sup>

## CONCLUSION

AMT after excision of pterygium appeared to be safe and effective method. It is a superior procedure than bare sclera excision technique alone due to lesser recurrence rate and it can be used as a preferred procedure for excision of primary pterygium.

**Disclosure:** This is a dissertation-based article.

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