Original article

Safety profile and complications of autologous limbal conjunctival transplantation for primary pterygium

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Abstract

Purpose: Primary pterygium is a fibrovascular proliferation over the nasal cornea, probably resulting from the limbal stem cell deficiency. Intraoperative mitomycin-C application seems to associate with reduced recurrences, however produced ocular surface problems and vision threatening complications. The present clinical study investigated the safety profile of autologous limbal conjunctival transplantation in terms of recurrence rate, as the main outcome measure and complications as the secondary outcome.

Methods: The present study was randomised, interventional and prospective clinical study conducted from a tertiary Hospital. Pterygium excision was performed with limbal conjunctival autograft availed from the affected eye. Secondary pterygia resulting from inflammation, trauma and other diseases were excluded. Patients were followed up for 18 months for recurrence and other complications. Microsoft Office Excel 2007 was used for statistical analysis.

Results: A total of 71 eyes of sixty-eight patients with primary pterygia included between November 2007 and October 2010. The study recruited 35 (51%) males and 33 (49%) females with mean age of 36.9 with ±12.82 years standard deviation (mean, SD) ranging from 19 to 75 years. Age grouped by range intervals categorised into six groups. Pterygium was diagnosed in 32 (45%) right eyes and 39 (55%) left eyes. There were 65 (91.55%) nasal and 4 (5.63%) temporal pterygium and no case of double head pterygia found. Average horizontal extension of the pterygium measured was 1.67 mm (±4.23) from the apex to the corneal limbus. Graft oedema in 1 (0.71%) patient, graft bleed in 2 (1.42%) cases and 1 (0.72%) case of granuloma observed. No recurrences encountered during 18 months follow up.

Conclusions: Pterygium occurred predominantly in the younger population group 36.9 mm (±12.82) probably due to the increased outdoor activity with high exposure to sunlight and dusty atmosphere. Absence of recurrences was probably attributable to the smaller pterygium size of 1.67 mm (±4.23), use of the autologous limbal conjunctival graft and treatable intra and post operative complications successfully.

Keywords: Limbal stem cells (LSC), Conjunctival autograft (CG), Limbal conjunctival autograft (LCAG)

Introduction

Proprioception from the ocular surface is not normally perceived, firstly because of lack of proprioceptors and secondly due to the smooth and regular surface pattern. Blinking reflex helps in the lubrication of the ocular surface with precorneal tear film. Therefore any irregularities that alter the corneocconjunctival surface produce foreign body sensation. The exact pathophysiology of primary pterygium remains elusive in spite of its characteristic clinical appearance and florid recurrence after simple excision. It is proposed that normally the limbal stem cells provide anatomical and physiological

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http://dx.doi.org/10.1016/j.sjopt.2014.03.006
barrier to the growth of conjunctiva blood vessels over the cornea. Hence, local or diffuse limbal stem cell deficiency is probably the accepted hypothesis for primary pterygium evolution.

Simple excision by ‘bare sclera’ technique alone resulted in increased incidence rates of recurrent pterygium.\(^1\) Meta-analytical study following bare sclera method revealed, a sixfold increase in recurrence if no conjunctiva grafting was performed and twenty-five times higher incidence was reported without intraoperative/postoperative mitomycin-C use.\(^2\) Although mitomycin-C proved to be an excellent adjuvant in terms of decreasing the incidence of recurrent pterygium, unfortunately caused ocular surface problems namely dry eye, persistent photophobia and chronic irritation. Bare sclera technique without the use of adjuvant carried a high risk of pterygium recurrences and sight threatening complications, commonly surgically induced necrotising scleritis.\(^3\)

Conjunctival autografting yielded acceptable limits of recurrences with no reports of long term vision threatening complications.\(^4,5\) Limbal conjunctiva contains stem cells demarcated externally by palisade of Vogt’s that normally visualised as longitudinal wavy brownish striations running perpendicular to the corneal surface at the superior and inferior limbus.\(^6\) This prospective study was undertaken to investigate the anatomical, physiological and cosmetically acceptable ocular surface reconstruction by autologous limbal epithelium/stem cell transplantation in terms of its safety profile and post operative complications.

### Patients and methods

Data collection included patient demographics of age, sex and laterality of the primary pterygium. Patients of all age groups with true progressive primary pterygium who attended outpatient Department of Ophthalmology from a tertiary hospital were enrolled in the present prospective and interventional randomised clinical study from 2007 to 2010. The data collection and sampling method done by identifying the patients with the primary pterygium after obtaining informed consent from the patients with the permission granted from the Institutional ethics committee board. Seventy-one eyes of 68 patients were enrolled in the study who presented with classical primary pterygium.

The patients with the primary pterygium were classified into unilateral and bilateral pterygium. Pterygium present in the nasal and temporal side of the limbus was categorised into nasal and temporal pterygium respectively. When the pterygium was seen on both the sides of the limbus (nasal or temporal) in the same eye, then it was classified as double headed pterygia. The inclusion criteria consisted of all patients with primary pterygium and the secondary pterygium due to trauma, inflammation, chemical burns; thermal and autoimmune conditions were excluded.

Primary pterygium was diagnosed by the presence of thick reddish fibrovascular growth encroaching upon the cornea, either on the nasal (in most of the cases) or on the temporal bulbar aspect of the conjunctiva present in the interpalpebral area, characterised by the wing shaped configuration consisting of the superior and inferior margins with rounded apex and the body. Bowman’s probe test was helpful in differentiating the true pterygium from the pseudopterygium by the inability of the probe to insinuate freely underneath the body of the primary pterygium, due to its adherence to underlying episclera and the sclera throughout the extent of the growth. The morphological features of the pterygium were studied under the slit lamp microscopy with photographic documentation and by measuring the horizontal growth extension by means of a simple transparent scale graduated in millimetres from the apex of the pterygium to the corneal limbus.

Regarding the history of pterygium presence, primary pterygium was seen most commonly in the agriculturists and the teachers who regularly travelled in dusty and hot climates throughout the year. There was history of constant exposure to sunlight in the male patients although the female patients remained indoors. Patients were unaware of pterygium probably due to the negligence or the lack of education in the initial stages of the natural course of the condition and to the benign nature of the growth. Younger patients complained of increase in the size of the growth and presented after 6 months to 1 year when the pterygium started invading the cornea and sought surgical treatment for the restoration of the cosmetic appearance. In older patients surgical excision was indicated due to the recurrent inflammation, infection and pain.

Ocular examination included the best corrected visual acuity recordings performed by the Snellen vision chart and the refractive state of the eyes with the pterygium was assessed by the TOPCON AR RM-8000B autorefractor made in Japan. Preoperative and intraoperative photography of the pterygium was taken in the operation theatre through the eye piece of the surgical microscope by placing 10 pixels resolution Sony camera.

### Procedure

All the patients were admitted to the hospital and operated by single surgeon. Pre operative measures included eyelash trimming and topical gatifloxin and dexamethasone to decrease the pre operative inflammation. All the patients were operated under the peribulbar anaesthesia using 3 ml of 2% Lignocaine hydrochloride with adrenaline 1:10,000 and 2 ml of 0.5% Sensocain. By using 26 Gauge insulin needle, a nick was made to enter the subtenons space near the upper and lower borders at the centre of the body of the pterygium.\(^7\) Underlying scleral adhesions were released by passing the Tooke’s knife through and through the nicks. Using conjunctival scissors, the main mass of the pterygium was designed in a semicircular fashion about 5 mm from the limbus to avoid injuring the medial rectus insertion. The dissected part of the pterygium was reflected over the cornea for further advancement. The dissection was continued tangentially towards the limbus by using the 15 number Bard Parker’s knife until the limbus is free of any pterygial tissue. At this time no cauterisation was done and the dissection was further extended towards the apex of the pterygium. Excision was completed by forming a smooth and transparent area at its site of corneal encroachment. Any residual remnants are shaved by means of the Tooke’s knife parallel to the corneal surface.

The excised raw area of the bare sclera was measured by Castrovejo’s callipers and the approximate size of the conjunctival graft was demarcated by gentle markings made by the points of the callipers on the superolateral bulbar aspect of the same eye. The eye ball was rotated downwards by the
use of corneal stay suture at 6 o clock by 8-0 Ethicon suture for free dissection of the superior conjunctiva. The superficial part of the conjunctiva was lifted by the smooth forceps without injecting the conjunctiva with Ringers Lactate and a small nick was made in the demarcation area that was always away from the limbus. The nick was extended and meticulous and gentle dissection carried forward up to its insertion into the cornea without the tenons capsule inclusion. Dissection carried out from the fornix towards the limbus and lastly the conjunctiva carrying the limbal portion was closely disinserted at its attachment by Vannus scissors. The limbal border was identified by its brownish colour that was tough and firm, somewhat characterised by wavy margin. The epithelial surface was recognised from the stromal side by its smooth and shiny surface, and slippery in nature without adherence to the wicks. By maintaining the limbus to limbus polarity, the graft was rotated on the excised area, initially anchoring and fixing the graft at the limbal margin and then proceeding towards the other sides by suturing to the normal healthy conjunctival margin with 8-0 Ethicon silk sutures (6–8 sutures). The corneal stay suture was removed and Tobramycin-dexamethosone eye ointment was instilled into the conjunctival sac and the eye was patched.

Post operative regimen included topical installation of Tobramycin-dexamethosone 4 times a day for four weeks and the same mixture was used as ointment at bed time for one week. The sutures were removed by the 10th day of surgery. The patients were reviewed subsequently in the first, third, sixth, twelfth and eighteenth month for any recurrences and other complications.

Results

A total of 71 eyes of sixty-eight patients with the primary pterygium were investigated in the present study with 35 (51%) males and 33 (49%) females. Microsoft Office Excel 2007 was used for statistical analysis. The mean age of the sample was 36.9 years (±12.8) (mean, standard deviation) ranging from 19 to 75 years with a median age value of 35 years (Fig. 1). The age grouped by range intervals were categorised into 6 divisions shown in the bar diagram. Between 19 and 29 year interval category there were 25 (36.76%) patients, there were 20 (29.41%) patients in 30–40 year group, between 41 and 51 year intervals there were 12 (17.65%) cases, between 52 and 62 range intervals there were 9 (13.24%) patients and one (1.47%) each between 52–62 years and 74–84 years category respectively. Predilection observed more frequently for the left eyes 39 (55%) than the right eyes 32 (45%). There were 65 (91.54%) nasal pterygium cases and 4 (5.63%) temporal pterygium patients and no case of double head pterygium found. The horizontal extension of the pterygium was measured by an average of 1.67 mm (±4.23) from the apex to the corneal limbus (Fig. 2). There were no recurrences observed in the present study, although one patient had graft oedema (0.71%), one case presented with granuloma (0.71%) and graft bleeding was noticed in two patients (1.42%) (Fig. 3).

Discussion

The present prospective study included a total of seventy-one eyes of 68 patients composed of 35 (51%) males and 33 (49%) females with a mean age of 36.9 (±12.8) years characterised into 65 (91.54%) nasal pterygium and 4 (5.63%) temporal pterygium patients and no case of double head pterygium found. The horizontal extension of the pterygium was measured by an average of 1.67 mm (±4.23) from the apex to the corneal limbus (Fig. 2). There were no recurrences observed in the present study, although one patient had graft oedema (0.71%), one case presented with granuloma (0.71%) and graft bleeding was noticed in two patients (1.42%) (Fig. 3).
procedure was heralded by the sight threatening complications and ocular surface disruption in the long run. In a previous comparative study, a recurrence rate of 15.9% with the mitomycin-C group and 1.9% in the limbal conjunctival group suggested that the latter procedure showed acceptable recurrence rate. The present study investigated the efficacy and safety of the autologous limbal stem cell conjunctival transplantation for the ocular surface reconstruction in primary pterygium. The age of onset observed in this study ranged from 19 to 75 years suggesting that the tendency of pterygium development seen in all the age groups. The mean age of the patients observed in the present study was 36.9 years (±12.8) that included the younger population compared to the previous studies on the pterygium surgery that showed higher mean age groups. Another retrospective review study reported no specific predisposing factors like environmental or familial were detected that contributed to pterygium development in children less than 16 years of age suggesting the idiopathic nature of the disease. Surprisingly most of the cases were amenable for conservative management without resorting to pterygium excision and grafting procedures. The younger to middle age seem to be vulnerable for the development of pterygium, probably because of their increased outdoor occupations for prolonged time. There was almost equal preponderance noticed between the males and the females in the present study, since both the sexes were agriculturists and teachers. In comparison to the other studies the left eye showed more predilections for the pterygium than the right eye, the reason was not known. The mean horizontal extension of the pterygium measured 1.67 mm (±4.23) compared to the previous report of the study of the factors influencing the success of pterygium surgery that reported pterygium less than 5 mm of base width had weak positive correlation with the recurrence rates and reported 8 recurrences out of 36 patients during one year follow up. They concluded that the male gender and continuous exposure to the sunlight were strongly and independently associated with the pterygium surgery success rates which were closely associated with the present study results. The previously reported method differed from the present study in that trephination demarcation was used to include the apex of the pterygium and the body. The author used hydro dissection for the conjunctival graft preparation, however a smooth conjunctival forceps with its tips slightly opened, secure only the conjunctiva sparing the tenons capsule inclusion. In another study pterygium was dissected from the body towards the corneal side to find out the cleavage plane that was correlated with the methods followed in the present investigation. The same study reported 100% success rate with follow up for 19 months similar to the results of the current study with no recurrences observed in 18 months follow up.

A study on pterygium excision with conjunctival graft was investigated for long term survival rate in a retrospective cohort study that invited patients for interrogation about the pterygium recurrence 10 years after the surgical procedure. There were 20 (11.4%) recurrences out of 176 patients during a mean follow up time of 34.4 years and concluded that worse prognosis could be expected for younger patients with the use of thicker sutures and probably in lesser invading pterygium. The present study found no recurrences during the 18 months follow up possibly due to the use of limbal conjunctival graft and thin sutures. In the present study 8-0 Ethicon-silk suture was used to minimise the post operative ocular irritation that might be more pronounced with

![Figure 4. Preoperative image of the left eye pterygium.](image)

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of eyes</th>
<th>Mean age (range)</th>
<th>Sex</th>
<th>Laterality</th>
<th>Follow up in months</th>
<th>Recurrence rates (percentage)</th>
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<td>Abdalla WM</td>
<td>40</td>
<td>Range 21–51</td>
<td>M 22 F 18</td>
<td>RE 19 LE 20</td>
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<td>Young AL</td>
<td>52</td>
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<td>M 19 F 33</td>
<td>RE 31 LE 21</td>
<td>16.73</td>
<td>1.9</td>
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<tr>
<td>G. Mery</td>
<td>16</td>
<td>56 (31–81)</td>
<td>M 11 (69%) F 5 (31%)</td>
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<td>19</td>
<td>0</td>
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<tr>
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<td>42</td>
<td>43.4 (21–66)</td>
<td>M 30 (71%) F 12 (29%)</td>
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<td>4.75</td>
</tr>
<tr>
<td>Present study</td>
<td>71</td>
<td>36.9 (19–75)</td>
<td>M 35 F 39</td>
<td>RE 32 LE 39</td>
<td>18</td>
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</tr>
</tbody>
</table>

![Figure 5. Postoperative appearance of graft integration to globe with sutures (10th day).](image)
in this study that correlated with a 0% recurrence rate reported by Mery et al. Previous prospective study on recurrence and complications after 1000 extended conjunctival transplants that was followed up for 1 year showed only one pterygium recurrence (0.1%), nevertheless with some postoperative complications unlike the present study that had a small sample size, however no sight threatening complications observed during the follow up of the patients. Young et al. observed three conjunctival cysts, three symblephara, one granuloma and one dellen as post operative complications. In this study two cases had graft bleeding that subsided in three weeks and the delay in suture removal incited granuloma formation in another patient that settled after its excision. One patient had graft oedema that resolved with the conservative management. The donor site observation revealed conjunctival epithelialisation with no signs of limbal stem cell deficiency. All the patients had comfortable ocular surface reconstruction with the absence of irritation, dry eye and photophobia during eighteen months supervision with satisfactory postoperative vision.

Primary pterygium was observed in the younger patients more often than seen in the old aged population, mostly attributable to their increased outdoor activity due to their occupational liabilities in their most active productive period of life. The risk factors in the present study were younger age group, high constant continuous exposure to sunlight and dusty field atmosphere. No other specific risk factors were found. The pterygium was more fleshy and reddish with more prominent vascular component than the fibrous component in the younger patients compared to thin and membrane like appearance with decreased vascular component that was more commonly observed in elderly patients. The mean age found was higher than 45 years in most of the published literature compared to the present study that found a lower mean age sample (36.9 ± 12.8, mean ± SD) found in the present study might be taken into account of the preventive aspects of the primary pterygium which may include the use of the umbrellas and the brimmed hats that may not be practical when the patients compliance is concerned.

**Conclusion**

In conclusion, the present study revealed a lower mean age sample of 36.9 ± 12.8 years compared to the higher mean age found in most of the published literature. The contributing factors may be multifactorial in the development of pterygium with only known risk factor as prolonged sunlight exposure and dusty atmosphere. The plausible factors attributable to no recurrence in the present study might be pterygium extension less than 1.67 mm and meticulous surgical methods followed with the use of autologous limbal conjunctival autograft that contained stem cells and thin suture material for graft anchorage.

**Sources of support**

J.S.S. Medical College & Hospital, Mysore 570004, Karnataka, India.

**Conflict of interest**

The authors declared that there is no conflict of interest.

**Acknowledgements**

We profusely thank the Head of the Institution and the Department of Ophthalmology for the cooperation extended in pursuing the clinical data for the completion of the study.

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