

A Clinical Study of Efficacy of Limbal Stem Cell Transplantation in the Management of Pterygium.

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Abstract:

Aim: To study the efficacy of the limbal stem cell transplantation in the management of pterygium.

Methods: In an interventional case series, 50 patients with pterygium underwent surgical excision with limbal stem cell transplantation on to bare sclera at Rajiv Gandhi Institute of Medical Sciences, kadapa .Patients were followed for 6 months and results were evaluated in terms of recurrent growth and other postoperative complications.

Results: 50 eyes of 50 patients including 32 females and 18 males of mean age of 40 ± 8 years were operated on the pterygia extended onto cornea for more than 2mm. Only two eye with limbal stem cell transplantation(4%) demonstrated recurrent pterygium growth.

Conclusion: Short term results suggest that pterygium excision with limbal stem cell transplantation is safe and effective method. Recurrent growth is less and cosmetic appearance also better with limbal stem cell transplantation. A larger randomized clinical trial with longer follow up period is however recommended.

Keywords: Pterygium, Limbal stem cell transplantation, Recurrence.

I. Introduction

Pterygium is a benign condition characterized by a wedge like fibro vascular growth of actinically damaged conjunctiva encroaching across limbus and invading the cornea. It is a common external eye condition, affecting different populations especially in tropical and subtropical regions .The primary indication for surgical removal of pterygium is decreased visual acuity, which can be the result of encroachment of the lesion onto the visual axis, induced irregular astigmatism, or breakup of precorneal tear film. Other indications for surgical intervention include discomfort and irritation unresponsive to conservative therapy, restricted ocular motility, difficulty with contact lens wear, anticipated keratorefractive surgery and for cosmetic reason.

Major adjuncts for prevention of pterygium recurrence are conjunctival or limbal auto grafts, amniotic membrane grafts, application of Mitomycin C, post operative beta irradiation, postoperative Thiotepe application, buccal mucus membrane grafting etc. .Although many other therapeutic modalities have been proposed, further studies on their efficacy and safety are required. The purpose of the current study is to find out the efficacy and outcome of pterygium excision with limbal stem cell transplantation in terms of recurrence and complications.

II. Materials and Methods

This interventional case series was conducted from December 2015 to November 2016 at Rajiv Gandhi Institute of Medical sciences, Kadapa and included a consecutive series 50 eyes of 50 patients with pterygium extending at least 2mm on to cornea. Data was collected in standardized proformas from all the patients who are willing to participate in study including taking history, physical and ocular examination and relevant investigations both preoperative and postoperative like visual acuity, slit lamp bio microscopy, Intraocular pressure measurement. Patients were followed for 6 months postoperatively.

Inclusion Criteria:

- 1) All patients > 18 years age with pterygium, willing to participate in the study and given informed consent.
- 2) Ability to attend follow ups.
- 3) Pterygium 2mm or more than 2mm encroaching onto cornea.

Exclusion Criteria:

- 1) Age < 18 years.
- 2) Pseudo pterygium.
- 3) Pterygium less than 2mm.
- 4) Lid abnormalities, trichiasis, entropion, ectropion., coloboma of lids
- 5) Sac infection, Chronic conjunctivitis.

- 6) Bell's palsy, Dry eye syndrome.
- 7) Patients with recurrent epithelial erosions.

III. Surgical Procedure

Anesthesia: Two point Peribulbar Infiltration anesthesia.

Under aseptic conditions, eye is draped & speculum is inserted. Head of pterygium was first separated at limbus and dissected towards central cornea. After excising head, most of body and subconjunctival fibrovascular tissue is separated from overlying conjunctiva and excised. While excising medially, be caution not to damage Medial rectus. Residual fibro vascular tissue over cornea was detached using toothed forceps or by gentle scraping with # 15 surgical blade. Conjunctiva above and below was trimmed to create a rectangular area of bare sclera.

Now the eye is turned down to approach the superior bulbar conjunctiva. The area of corresponding size is measured with calipers and exact dimensions marked with marker pen. These marks are included with in the graft tissue margins, during the excision of the donor tissue to facilitate its reorientation in the recipient site. The graft is thinly dissected, avoiding Tenon's tissue and episclera and stem cells gently separated at the limbus. After freeing, the graft is transferred to the recipient bed and secured to adjacent conjunctiva and episclera with blood clot. Antibiotic eye ointment applied in lower fornix and pad and bandage applied for 24 hours.



Postoperatively, Ciprofloxacin-Dexamethasone eye drops were given 6 times/day for 1 week. Later Dexamethasone eye drops 4 times/day for one month, 2 times/day for 10 days.

Post op follow up was done at 1st postoperative day, 1 week, 4 week, 6 week, 12 week, 6 Month post operatively. At each visit, complaints are enquired, looked for any complications. Slit lamp examination to monitor graft bed integrity and development of other complications.



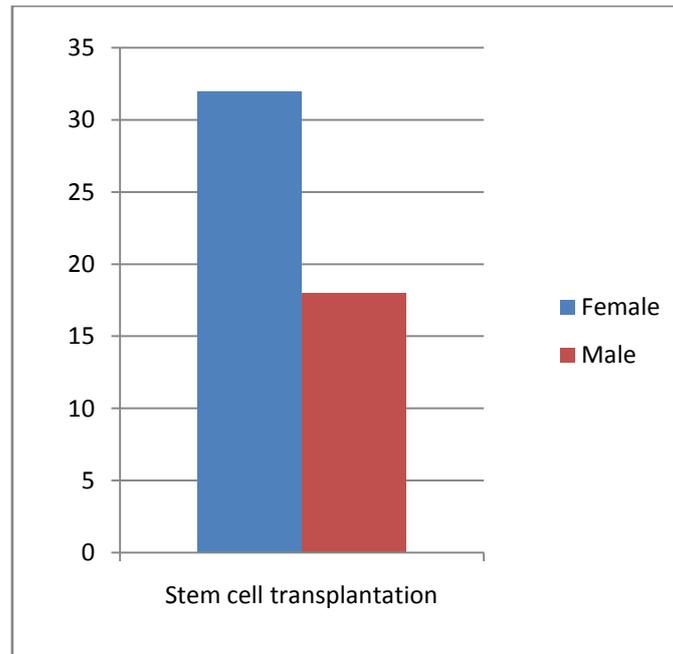
Pre op(R.E)

Intra op

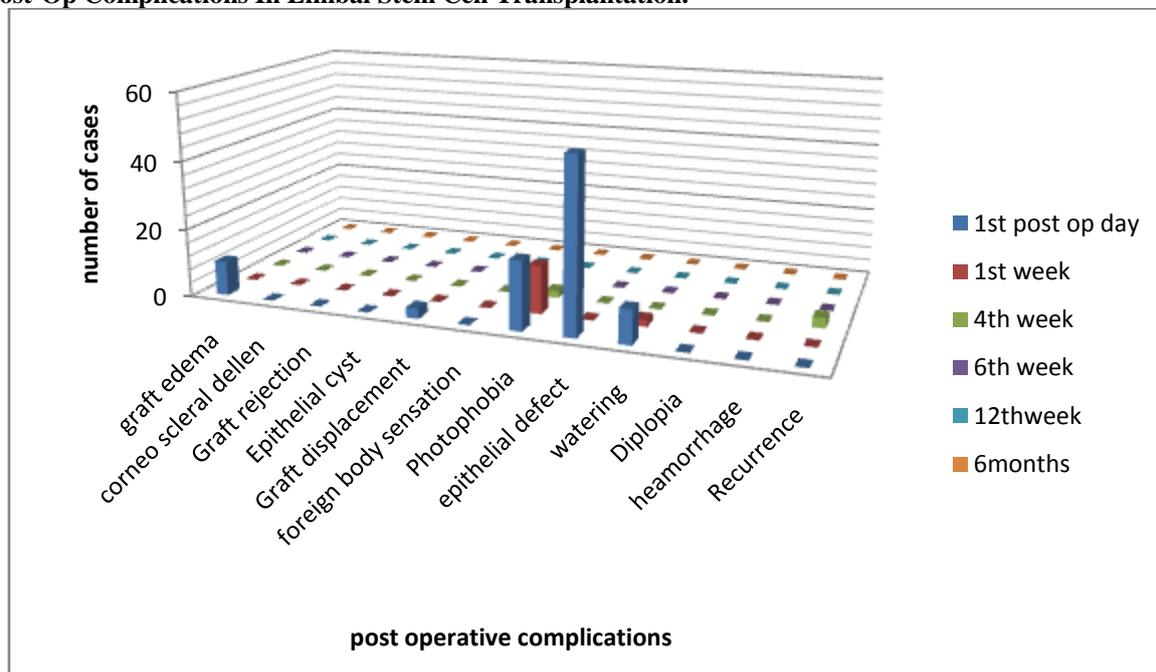
Post op(R.E)

IV. Results

50 eyes with pterygia of 50 patients including 32 females and 18 males with mean age of 40 ± 8 years were operated. The extent of pterygium invasion beyond 2mm from limbus. On the first postoperative day, all patients had corneal epithelial defects. By one week, all epithelial defects healed completely and there was no corneal staining with fluorescein. Minor post operative complaints like watering noted in few people. Four patients out of 50 with stem cell transplantation developed graft edema (8%). One patient developed hemorrhage (2%). In two patients (2 out of 50) pterygium recurrence was noted (4%). Recurrence may be due to use of very thin stem cell graft devoid of tenons tissue. No other adverse effects or complications occurs throughout the study period. Commonest complaints are watering. No significant change in visual acuity or intraocular pressure is noted postoperatively.



Post-Op Complications In Limbal Stem Cell Transplantation.



V. Discussion

A pterygium is a multifactorial degenerative disorder. Different procedures have been proposed for treatment of Pterygium. However, the main complication common to all is recurrent disease which is more difficult to control. The mechanism of pterygium recurrence has been attributed to surgical trauma, post-operative inflammation, proliferation of fibroblasts and deposition of extracellular matrix.

Recurrence rates are as high as 40% and 16.7% have been observed in the bare sclera and primary closure techniques, respectively. To reduce this recurrence rate, adjunctive limbal stem cell transplantation or Amniotic membrane graft or topical Mitomycin C could be used. Following pterygium excision with limbal stem cell transplantation recurrence rate of 7% have been reported. Topical mitomycin C has been used as a method of reducing recurrence. However, it has a recurrence rate of 38% which is comparatively high. Moreover, some vision threatening side effects such as scleral ulceration, cataract formation and glaucoma have been reported.

Ocular surface describes the entire epithelial surface of the external eye encompassing the corneal epithelium as well as the bulbar and palpebral conjunctival epithelium. Initially considered as only an anatomic classification that organized the physical continuity of stratified non keratinizing epithelium of the conjunctiva, limbus, and cornea, the clinical and research insights of Friedenwald, Thoft and colleagues, and many others have offered compelling evidence of important functional relationships within this anatomic continuum. Crucial notion of the ocular surface as the functional unit has stimulated a complete reorganization of our approaches to the pathogenetic concept and the clinical management of ocular surface disease. Although the conjunctiva and especially the limbus perform several functions, their contributions to the proper maintenance and integrity of the corneal epithelium are critical.

Because corneal epithelium is highly differentiated cell type with rapid self renewal abilities, its stem cells should be readily available. Davanger and Evensen were possibly the first to postulate that limbal papillary structure serves as the generative organ for corneal epithelial cells. Kenyon and Tseng ultimately postulated that the stem cells are the most qualified cell to differentiate into normal corneal epithelium.

This stem cell hypothesis also has been extended to a pathogenetic concept of pterygium, where by the pterygium can be considered the consequence of "local stem cell deficiency". In particular, where as normal limbal tissue acts as a barrier between conjunctiva and cornea and thus prevents the invasion of subconjunctival tissue onto cornea. When this barrier function damaged by various insults like UV radiation or mechanical injuries, sub conjunctival cells are allowed to stream onto adjacent cornea, resulting in pterygium formation. Reestablishing normal barrier function by transplanting healthy limbal tissue may prevent this process. Based on this concept limbal autograft transplantation has recently been performed in cases with recurrent and advanced pterygia.

In this study, a recurrence rate of 4% was recorded. This is lower than the findings in other studies done by Kucukerdonmez et al., and Luanratanakorn et al^(10,12) which reported recurrence rates of 7.9% and 28.1% respectively. Even though similar in that these cohorts comprised both primary and recurrent pterygia these studies differed in study design, sample size and follow up period. While this study evaluated 50 eyes with primary pterygia who had pterygium excision with conjunctival autograft, Kucukerdonmez et al and Luanratanakorn et al studied 38 and 287 eyes respectively. Kucukerdonmez et al followed up their patients for 13.4 months (mean period) while follow- up period of this study was for 6 months.

Nakamura et al⁽¹³⁾ recorded no recurrence in their series. However this study had a longer mean follow- up period of 13.9±6 months.

In the present study, only the minor post- operative Complications like transient graft edema, hemorrhage were reported. No significant sight- threatening complications were recorded. The low recurrence rate and favourable safety profile of pterygium excision with limbal stem cell transplantation in the current study attest to the efficacy of this treatment modality and It's results are superior to that of amniotic membrane graft and bare sclera.

VI. Conclusion

No major post- operative complications following limbal stem cell transplantation in the present study agree with other reports that this procedure is effective and safe. The recurrence rate with limbal stem cell transplantation is much lower than fresh amniotic membrane graft. Based on results of our study we agree that limbal stem cell transplantation will give less recurrence and better cosmetic appearance than amniotic membrane graft. And complications like foreign body sensation and watering are absent due to sutureless surgery with the help of blood clot to adhere graft to underlying sclera. But, due to the study's small sample size and a short period of follow- up, the findings should be interpreted with caution. A larger randomized controlled study will be required to confirm our findings.

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