

Original Article

Experience of Sutured Limbal Stem Cell Conjunctival Autograft after Pterygium Excision

Eddyanto, Ismi Z, Fazarramah, Windi IR

Department of Ophthalmology, Faculty of Medicine, Airlangga University
Soetomo Hospital, Surabaya, East Java

ABSTRACT

Background: To know the effectiveness of sutured limbal stem cell conjunctival autograft after pterygium excision in order to avoid recurrences.

Method: This is a prospective study of limbal stem cell conjunctival autograft after pterygium excision during December 2011 until April 2012. Type of operation were pterygium excision followed by conjunctival limbal stem cell autograft. Follow up be conducted at day 1, 1 week, 1 and 3 month post operatively. The recurrence rate was evaluated using Portable PASW statistics 18 software.

Result: Twenty cases of pterygium had been operated. Ten cases could be evaluated 3 months. Three males and 7 females, average age was 50.2 ± 10.55 year, range 38-72. 2 cases were pre existing recurrence pterygium. BCVA pre operation range 1.00 - 0.1. BCVA post operation range 1.00 - 0.20. One of 10 cases was recurrence after this study, the BCVA decrease and need repeated excision and limbal stem cell conjunctival autograft. There is no statistically significant correlation of the type of pterygium pre and recurrence post operatively. Moderate association was noted between BCVA pre operation and recurrence rate post operatively. Very strong association was noted between age of these patient and recurrence post operatively. There is a significantly difference of BCVA before and after operations.

Conclusion: Sutured limbal stem cell conjunctival autograft after pterygium excision in order to avoid recurrences was effective 3 months after operation. The recurrence rate is 10%. This study need more samples and comparing group with other technique in order to know this technique is better than other or not.

Keywords: Ocular surface disorder; corneal conjunctivalisation, pterygium excision, limbal stem cell transplantation

Pterygium is a fibrovascular overgrowth of bulbar conjunctiva, which grows over the limbus and encroaches over the cornea. The pterygium represents a pathologic condition more frequently seen in certain populations, and its incidence varies greatly in different geographic zones. Typically become clinical evident between the age of 20 and 50 years. Pterygium is thought to be caused by increased light exposure, dust, dryness, heat, ultraviolet (UV) light, and wind.¹

The goal of surgical treatment in pterygium is directed at excision, prevention of recurrence, and restoration of ocular surface integrity. A myriad of techniques, some combined with others, have been described for achieving these goals. These include bare sclera excision, excision with simple conjunctival closure, excision with administration of antimetabolite adjuvants such as mitomycin C, excision with conjunctival autograft, and excision followed by amniotic

membrane transplantation. Treatments such as radiation therapy and the use of antimetabolite agents have succeeded in diminishing the number of recurrences from between 5% and 12%. The ideal and perfect method, one that is easy to perform, results in a good cosmetic outcome, and is risk free and recurrence free, has yet to be established.^{1,2}

A recurrent pterygium is one that develops after removal of a true pterygium. It is often more adherent to the underlying limbus and anterior stroma. The majority of recurrences develop within 6 months of the primary surgery and are more common in young patients, individuals who have had a high level of sunlight or ultraviolet exposure and those who have had an aggressive inflammatory growth pattern. Recurrence after pterygium excision remains a major challenge, as evidenced by the existence of multiple surgical methods that have evolved over the years to deal with this problem. Adjunctive therapies designed to reduce recurrences include application of antimetabolites, radiotherapy, conjunctival or limbal conjunctival autograft, and amniotic membrane graft, but there is no established effective technique without significant side effects.^{2,3}

In 1985, Kenyon and collaborators⁴ introduced the conjunctival autograft for the treatment of recurrent or advanced pterygium. Although this surgical technique is time-consuming, it has reduced the number of recurrences with the same efficacy as the previously described treatments without the risk of potentially serious complications. Recently some works have emphasized the importance of limbal stem cells as the cause of pterygia⁵ and the role that a healthy limbus plays as a barrier to conjunctival overgrowth⁶. Conceptually, one could possibly reduce the number of pterygium recurrences by including the limbus in the conjunctival autograft. Besides, one should not expect a greater number of ocular surface complications because of only moving a limited area of limbus without losing a significant amount of stem cells.⁴

The corneal epithelium renews itself within approximately 5-7 days, with the superficial cells being constantly shed into the tear pool. Terminal differentiation of cells, coupled with cell death by apoptosis, prompts the cell loss by

desquamation, which is aided by blinking. The maintenance of the corneal epithelium is thought to be achieved by the unipotent stem cells, the basal epithelium of the corneoscleral limbus (= Limbal stem LSC).^{1,2}

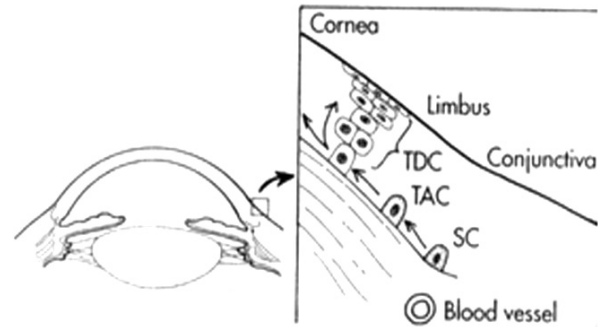


Fig 1. Schematic representation of limbal stem cells (SC). These cells are located in the basal epithelium of the limbus and give rise to transient amplifying cells (TAC) of the basal corneal epithelium and to terminally differentiated cells (TDC), which compose the suprabasal corneal epithelium.²

LSC or Corneal epithelial stem cell (CESC): is cell group with high capacity of error-free cell renewal, unlimited slow cycling (slow mitotic activities), poor differentiation primitive cytoplasm, and activation to proliferate by wounding or replacement in culture.² LSC can mitosis to generate transient amplifying cells (= TAC) that are short lived and function primarily to amplify cell numbers and has limited renewing activity. The TAC finally differentiates into limited post mitotic cells that are committed to cellular differentiation. Once this differentiation starts is irreversible.^{1,2} Similarly, limbal stem cell deficiency may lead to the invasion of the cornea by conjunctival cells including goblet cells, a process termed conjunctivalization of the cornea¹. Circumferential damage of the limbus or damage of apposition of the limbus, produce a varying extent of conjunctival epithelial ingrowth. These changes are known to result from limbal stem cell deficiency, and together constitute the hallmark clinical features used to identify stem cell insufficiency.⁷

Approximately 25%-33% of the limbus must be intact in order to ensure normal ocular resurfacing. The normal limbus acts as a barrier against corneal vascularization from the conjunctiva and invasion of conjunctival

cells from the bulbar surface. When LSCs are congenitally absent, injured or destroyed, conjunctival cells migrate onto the ocular surface, often accompanied by superficial neovascularization. The absent of LSC reduces the effectiveness of wound healing, as evidence by compromised ocular surface integrity with irregular ocular surface and recurrent epithelial breakdown.² Replacement of stem cell by limbal transplantation seems to be logical choice for ocular surface reconstruction in diseases associated with LSC deficiency. When the limbus is focal affected in one eye, as with pterygium, a limbal or conjunctival autograft can be harvested from the ipsilateral eye.^{2,7,8,9}

The limbal stem cell hypothesis of pterygium formation implies that the conjunctiva grows on to the cornea due to the loss of limbal stem cell barrier function. Armed with the above observations and limbal stem cell hypothesis we perform a novel approach to pterygium surgery which preserves Tenon capsule, minimizes conjunctival excision, and employs a small conjunctival autograft. We performed a prospective study the conjunctival autografting technique.³

MATERIAL AND METHODS

The bare sclera technique, removing the head of the pterygium by blunt dissection (without conjunctival autograft to cover the epithelial defect), keeping the adjacent Tenon capsule intact, and performing a limbal stem cell (LSC) conjunctival autograft to cover the bare sclera and 0.5 mm periferal corneal defect.

All patients underwent pterygium excision during December 2011 until April 2012 by several surgeons (ed¹, im²).

Type of operation were pterygium excision followed by conjunctival limbal stem cell autograft with 10.0 nylon buried sutured. Follow up be conducted at day 1, 1 week and 1 month post operatively. The recurrence rate was evaluated by using Portable PASW statistics 18 software.

RESULT

Twenty cases of pterygium had been operated. Ten cases could be evaluated 3 month. 3 males and 7 females, average age was 50.2 ± 10.55

year, range 38-72. Two cases were pre existing recurrence pterygium.

BCVA pre operation: 1.00 in 3 cases, 0.90 in 2 cases, 0.80 in 1 case, 0.50 in 2 cases and 0.16 in 1 case, 0.1 in 1 case. BCVA post operation: 1.00 in 4 cases, 0.9 in 2 cases, 0.8 in 1 case, 0.63 in 1 case, 0.32 in 1 case, 0.20 in 1 case. The characteristic of patients showed in table 1.

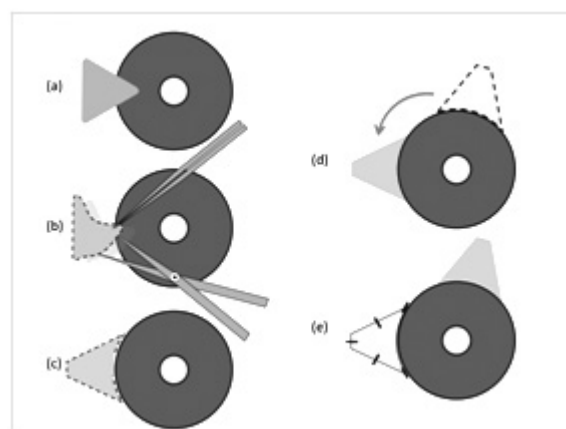


Fig 2. Pterygium excision followed by conjunctival limbal stem cell autograft.

Table 1. Demographic data of patients undergoing pterygium surgery

Characteristic		SD
Number of patients	10	
Diagnosis		
Primary pterygium	8	
Recurrence pterygium	2	
Age, y, mean \pm SD (year)	50.2	± 10.55
Range (year)	38-72	
Sex, n (%)		
Male	3	
Female	7	
Pre operative VA, mean \pm SD range	0.68	± 0.35
Post operative VA, mean \pm SD range	0.77	
Follow up period, month	3	± 0.29
Recurrence 1 month after op (%)	1 (10%)	

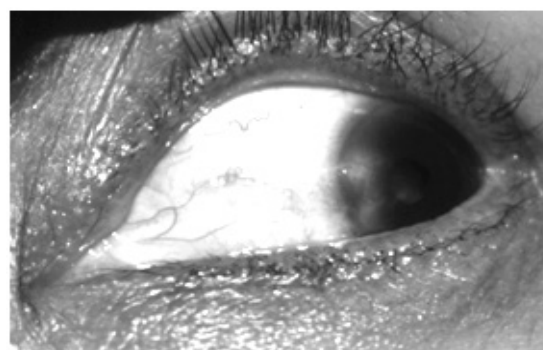


Fig 3. Limbal stem cell grafting after pterygium excision 2 months after surgery with no recurrent

DISCUSSION

The current study by Mahdi and Bhatia¹ included 42 patients with pterygia surgically treated with conjunctival and limbal stem cells autograft. The results showed that after a period of followup that ranged from 10 to 28 months, 95.25% of cases were successfully treated without recurrence of pterygial growth or significant complications. Success was defined as absence of pterygial growth beyond the edge of the limbus. Only 4.75% of cases showed recurrence of pterygial growth.

Multiple previously described types of surgical procedures for treatment of pterygium with high postoperative recurrence rates reflects that there is no definitive treatment. The ideal surgical technique should be one that effectively prevents recurrence without development of complications. These procedures used most often to treat recurrent or advanced pterygium, the one that comes closest to achieving this goal is, probably, the conjunctival autograft described by Kenyon and collaborators⁶. This procedure reduces recurrence with minimal complications when compared with the use of β -radiation or mitomycin C. However, recurrence was not eliminated, specially in those patients who live in areas where they are frequently exposed to high levels of UV light.

Considering the importance of the limbus and its stem cells in the pathogenesis of pterygium, a new technique has been developed that includes, in addition to the conjunctival autograft, a part of the limbal stem cells, which aids in the complete anatomic and physiologic reconstruction of the excised pterygial area. This limbal reconstruction may theoretically reduce the recurrence rate. The complication rate of this method should not be greater than that described by Kenyon and Tseng¹⁰. The surgical procedure used in the current study differs only in the fact that a small portion of limbus is included in the graft. Other researchers used larger areas of limbal resection for grafts in the opposite eye that have not caused complications. Complications related to conjunctival autograft transplantation have been described. These complications include transient graft edema, corneoscleral dellen, graft retraction, epithelial cysts, and Tenon granuloma. A more significant complication such as graft necrosis may occur if

the graft was not properly oriented or placed on a completely avascular zone. However, none of these complications developed in our study.

Shimazaki et al¹¹ had used a more or less similar technique to treat two groups of patients, 16 of them with primary pterygium. After an average follow-up period of 10.5 months, only 7.4% showed slight recurrence, with only 1 mm of extension beyond the limbus and no need for additional surgery. The average age of these study patients was 61 years as compared to 50.2 years in our study.

Gris et al¹², in a small group of patients with recurrent pterygium (7 patients), used a similar technique closer to the one used in our study. They reported no recurrence or significant complications.

A study by another group in which 2 groups of patients were operated has been conducted. The group with limbal conjunctival autograft with amniotic membrane transplantation showed no recurrence of pterygium; the group with mitomycin C and amniotic membrane transplant reported a recurrence rate of 20%.¹³ Minimal limbal conjunctival autograft was used but the authors reported a recurrence rate in 9.2% of cases after a follow-up period of 6–29 months. The recurrence rate in our study is 10%, which could be nearly same result.¹⁴

We consider the relatively young age of the patient operated on and the geographic area in which these patients are living (windy and sandy with high and prolonged exposure to UV light, as they are living and working in the Arabian Gulf region), this rate of recurrence is excellent.¹

CONCLUSION

Sutured limbal stem cell conjunctival autograft after pterygium excision in order to avoid recurrences was effective one month after operation. The recurrence rate is 10%. This study need more samples and comparing group with other technique in order to know this technique is better than other or not.

REFERENCES

1. Mohamed A.E, Soliman Mahdy, Jagadish Bhatia, Treatment of primary pterygium: role of limbal stem cells and conjunctival autograft transplantation, *European Journal of Ophthalmology*, vol. 19 no. 5, pp. 729-732, 2009.

2. Brightbill FS, Mc Donnell PJ, Mc Ghee CNJ, Farjo AA, Serdarevic ON, 2009. Corneal Surgery, Theory, Technique and Tissue. IVth ed, Mosby Elsevier inc, pp 25-29, 53, 187-197, 241-251, 605-615
3. Bozkir N, Yilmaz S, Maden A, Minimally invasive pterygium surgery: A new approach for prevention of recurrence, *European Journal of Ophthalmology*, vol. 18 no. 1, pp. 27-31, 2008
4. Kenyon KR, Wagoner MD, Hettinger ME. Conjunctival autograft transplantation for advanced and recurrent pterygium. *Ophthalmology* 1985; 92: 1461-70.
5. Kwok LS, Coroneo MT. A model for pterygium formation. *Cornea* 1994; 13: 219-24.
6. Coroneo MT, Girolamo ND, Wakefield D. The pathogenesis of pterygium. *Curr Opin Ophthalmol* 1999; 10: 282-8.
7. Daya SM, Holland EJ, Mannis MJ, 2002. Living-Related Conjunctival Limbal Allograft. In (Edward JH, Mark JM, eds) *Ocular Surface Disease: Medical and Surgical Management*. New York: Springer-Verlag, pp 201-207.
8. Schwartz GS et al, 2002. Preoperative Staging of Disease Severity. In (Edward JH, Mark JM, eds) *Ocular Surface Disease: Medical and Surgical Management*. New York: Springer-Verlag, pp 158-166.
9. Tabin GC et al, 2002. Limbal Stem Cell Transplantation. In *Corneal Transplantation*. New Delhi: Jaypee, pp 235-244.
10. Kenyon KR, Tseng SCG. Limbal autograft transplantation for ocular surface disorders. *Ophthalmology* 1989; 96: 709-23.
11. Shimazaki J, Yang HY, Tsubota K. Limbal autograft transplantation for recurrent and advanced pterygia. *Ophthalmic Surg Lasers* 1996; 27: 917-23.
12. Gris O, Guell JL, del Campo Z. Limbal-conjunctival autograft transplantation for the treatment of recurrent pterygium. *Ophthalmology* 2000; 107: 270-3.
13. Fallah MR, Golabdar MR, Amozadeh J, Zare MA, Moghimi S, Fakhraee G. Transplantation of conjunctival limbal autograft and amniotic membrane vs mitomycin C and amniotic membrane in treatment of recurrent pterygium. *Eye* 2008; 22: 420-4
14. Oguz H, Kilitcioglu A, Yasar M. Limbal conjunctival mini-autografting for preventing recurrence after pterygium surgery. *Eur J Ophthalmol* 2006; 16: 209-13.