

DISCRETION VALUES OF LIMBAL STEM CELL GRAFT WITH COMPARISON OF CONJUNCTIVAL AUTOGRAFT IN PTERYGIUM EXCISION

Hizbur Rahman¹, Tooba Rana², Samina Karim³, Nosheen Kanwal², Barjis Irum²

¹Department of Ophthalmology, Fatima Jinnah Medical University, Sir Ganga Ram Hospital, Lahore

²Trainee Medical Officers

³Department of Ophthalmology, Hayatabad Medical Complex, Khyber Girls Medical College

ABSTRACT

Objective: To determine the recurrence rate of pterygium in cases treated with limbal stem stem cell graft versus conjunctival autograft.

Materials and Methods: It was a randomized clinical trial conducted in Ophthalmology department of Hayatabad Medical Complex Peshawar from January 2018 to February 2019 i.e one year study duration. A total of 60 diagnosed cases of pterygium of both sexes and all ages were included in the study. The cases were randomized into two groups i.e 30 cases were treated with stem cell graft while the other 30 cases were treated with conjunctival autograft. The recurrence rate of pterygium was determined in both the groups by following them for 6 months i.e at 1st, 3rd and 6th month of excision. Recurrence rate was calculated for both the procedures. Mean and standard deviations were used for quantitative variables while frequency and percentages were used for qualitative data.

Results: A total of 60 diagnosed cases of pterygium were included in the study. Age of the study sample ranged from 22-55 years, with mean of 37 ± 9.3 SD. About 36 (60%) cases were males and 14 (40%) cases were females. Recurrence rate of pterygium was 3.3% in cases treated with limbal stem cell graft technique as compared to recurrence rate of 10% which was seen in cases treated with conjunctival autograft technique.

Conclusion: Recurrence rate of pterygium was more in cases treated with conjunctival autograft as compared to those treated with limbal stem cell graft. So, limbal stem cell graft is more effective as compared to conjunctival autograft in treating pterygium and should be preferred treatment option for pterygium in order to decrease the recurrence rate and hence morbidity of the patient.

Keywords: Pterygium, limbal stem cell graft, conjunctival autograft, randomized clinical trial.

INTRODUCTION

Pterygium is defined as overgrowth of fibrous and epithelial tissue on the cornea.¹ The exact mechanism for this condition is unclear.¹ Yet, it is proposed that it is caused because of abnormal proliferation of the epithelial cells and blood capillaries over the cornea.^{2,3,4} The etiological factors

that are believed to cause formation of the pterygium include the ultraviolet radiations from the sun light, eye infections, inflammatory processes in the eye, and dysregulation in the mediators of extracellular matrix regeneration.^{5,6,7,8,9,10,11} Recently, it is suggested that there may be a hereditary predisposition for the formation of pterygium in certain genetically predisposed individuals.¹²

The pterygium is a relatively common condition, and is seen throughout the world.¹³ However, it is seen more commonly in the areas that are at high altitude.¹⁴ This is so because there is high intensity

Correspondence:

Dr. Hizbur Rahman

Senior Registrar Ophthalmology Department, Fatima Jinnah Medical University, Sir Ganga Ram Hospital, Lahore.

Email: hrahman@live.com

Contact: +923219603673

of ultraviolet radiations in these hilly areas, which is a known risk factor for the development of pterygium.^{13,14} The prevalence of pterygium is reported to be 10.2% worldwide.^{4,15,16} In South East Asian region, the prevalence of pterygium ranges from 9.5% to 13%.⁴ The condition is more common in male population.⁴

The surgical removal of pterygium is currently the treatment of choice.¹ However, the surgical removal is associated with the high rate of recurrence depending on the techniques used.^{1,4} Therefore, certain surgical techniques have been developed in order to decrease the recurrence rate of pterygium after surgery.¹⁵ The various surgical techniques used for the excision of pterygium include bare sclera technique, conjunctival autograft technique and limbal stem cell transplant technique.¹⁷ The bare sclera technique had the highest rate of recurrence.⁴ In order to reduce the recurrence rate, it was suggested to cover the area with the graft.⁴ So, the conjunctival autograft technique was introduced.⁴ Later on, limbal stem cell graft was used to cover the bare area of sclera and this led to introduction of limbal stem cell graft technique. The recurrence rate of pterygium after its surgical removal may be as high as 89% (in bare sclera technique) or as low as 0% (in limbal stem cell graft technique).¹ It is not clear which factor determine the recurrence of pterygium.^{1,4} Other therapies used for treatment of pterygium include irradiation therapy, use of anti mitotic agents and anti angiogenic growth factors like bevacizumab.^{4,18} However, these techniques are associated with complications.⁴ So, these techniques have lost their popularity.⁴

Conjunctival autograft technique was first introduced by Kenyon in 1985.^{1,19} In this technique, the conjunctival graft is taken from bulbar conjunctiva and then placed on the area of sclera from where the pterygium tissue is removed.¹ The recurrence rate for this procedure ranges from 3- 12%.^{1,20} It was later discovered that the stem cells in limbal area of conjunctiva act as a barrier for the migration of the conjunctival cells over the cornea.^{19,21} This helps in preventing the recurrence of pterygium.²¹ Also, it was suggested that the limbal stem cells promote healing.¹³ So, limbal stem cell graft technique was introduced in which limbal tissue is included in the transplant graft.¹³ Limbal stem cell graft technique is more effective than conjunctival autograft technique

in terms of decreased rate of recurrence of pterygium.¹³ The recurrence rate of limbal stem cell graft may be as low as 3% to as high as 11%.²¹

The present study was done with the rationale to compare the recurrence rate of pterygium in cases treated with limbal stem cell graft technique versus conjunctival autograft technique, and hence the efficiency of these techniques.

MATERIALS AND METHODS

It was a randomized clinical trial. It was conducted in Ophthalmology department of Hayatabad Medical Complex, Peshawar. The study was done from January 2018 to February 2019. The study duration was one year. A total of 60 diagnosed cases of pterygium of both the sexes and all ages were included in the study. Cases who were having pseudopterygium, infection of the eye, and recurrent pterygium were excluded from the study. Sampling was done through non probability purposive technique. The cases were randomized into two groups i.e 30 cases were treated with stem cell graft technique, while the remaining 30 cases were treated with conjunctival autograft technique. The outcome of the study was the recurrence rate of pterygium after the operation. Recurrence was defined as the growth of fibrous tissue over the cornea across the corneoscleral limbus.¹⁵ The recurrence rate of pterygium was determined in both the groups by following them for 6 months i.e at 1st, 3rd and 6th month of excision. Mean and standard deviations were used for quantitative variables while frequency and percentages were used for qualitative data.

The procedure was performed under topical anaesthesia by Ophthalmologist. The area was exposed by using solid lid speculum. Pterygium was excised. In case of conjunctival autograft technique, the conjunctival graft was obtained from the bulbar conjunctiva and placed in bare area from where pterygium was excised. In cases where limbal stem cell graft technique was used, conjunctival limbal stem cell graft was taken from limbus and stitched on excised area. Follow up examination was done at 1st, 3rd and 6th month after surgery in order to detect recurrence of the pterygium.

RESULTS

A total of 60 diagnosed cases of pterygium were included in the study. Age of the study population

ranged from 22-55 years, with mean of 37 ± 9.3 years.

About 36(60%) cases were males and 14(40%) cases were females. Male to female ratio was 1.5: 1.

Demographic data of the study sample is shown in table 1.

The recurrence rate for each of the 30 cases who underwent conjunctival autograft and limbal stem cell graft is shown in table 2.

Table: 1 Demographic characteristics of the study population (n=60)

Demographic variables	n (%)
Gender distribution	
Males	36(60%)
Females	14(40%)
	Range (Mean $\pm$ SD) years
Age	22- 55 (37 ± 9.3)

Table: 2 Recurrence rate of pterygium in cases undergoing limbal stem cell graft versus conjunctival autograft

Surgical technique performed	Total number of cases (n)	Recurrence rate n (%)
Limbal stem cell graft technique	30	1(3.3%)
Conjunctival autograft technique	30	3(10%)

DISCUSSION

Pterygium is disorder of sclera that is commonly seen in tropical countries where there is high exposure of public to ultraviolet radiations, heat, dust and sunlight.⁴ It causes cosmetic disfigurement, repeated inflammation of the eye, and visual abnormalities like astigmatism or total impairment of visual axis.⁴ The surgical excision of pterygium is associated with high rate of recurrence.⁴

The earliest surgical procedure introduced for the treatment of pterygium was the Bare sclera technique.⁴ In this technique, the sclera is left bare after excision of the pterygium.⁴ But, it is associated with a higher recurrence rate.⁴ Therefore, it is no longer used nowadays.⁴ Later on, the conjunctival autograft technique was introduced.⁴ In this technique, area left after removal of pterygium was covered with conjunctival flap that was taken from the bulbar conjunctiva.⁴ Finally, limbal stem cell graft transplantation was introduced, which was associated

with a lower recurrence rate as compared to the previous methods.⁴

In the present study, the mean age of the study sample was 37 ± 9.3 years. In study done by Shirjeel M in Lahore in 2016, mean age of patients with pterygium was 41.18 years.²¹ In another study done by Mejia LF, the mean age of patients with pterygium was 42 years.²² However, Fayeze MF suggested the age of 33 years in patients of pterygium which is quite close to that reported in our study.²³ In our study, male to female ratio was 1.5: 1. So, the pterygium was common in male patients as compared to the female patient. Similarly male predominance was observed in the study by Shirjeel from Lahore, Mahdy MS from Oman and Satish K from India.^{19,21,24} The male predominance of pterygium in our study is same as reported by literature.^{25,26,27} The male predominance in pterygium is due to the reason that men mostly work outdoors and are exposed to sunlight and dust more as compared to the females.

In the present study, it was observed that recurrence rate in cases undergoing limbal stem cell graft was lower as compared to those who underwent conjunctival autograft (i.e 3.3% versus 10% respectively). This shows that limbal stem cell graft technique is associated with lesser rate of recurrence and hence more efficient outcome. Similarly lower rate of recurrence for stem cell graft as compared to conjunctival autografts for pterygium are reported by a meta analysis done by Zheng K, who analyzed data of 13 randomized controlled trials in his study.²⁸ Similar findings are suggested by another meta analysis, done by Medical Advisory Secretariat in Canada, where it was reported that stem cell graft was associated with lower recurrence rate than other techniques in treatment of pterygium.²⁹ Similar findings are reported by Othman FM from Egypt.³⁰ Similar findings are suggested by Fayeze MF, Rao SK and Abdall WM in their studies.^{23,31,32} Mahdy MS from Oman suggested that limbal stem cell graft is a very effective technique to prevent recurrence of pterygium post operatively.²⁴ However in a study done by Satish K from India suggested equal recurrence rate in both the techniques, suggesting both the techniques are equally effective.¹⁹

LIMITATIONS

The main limitation of the study was that it was conducted in a single tertiary care center. There is

a need to conduct similar study involving patients from multiple health centers so that a bigger data may be generated which may be true projection of the whole community.

CONCLUSION

Limbal stem cell graft is more effective surgical technique to treat pterygium as compared to conjunctival autograft as it is associated with lower rates of recurrence and hence lower morbidity of the patient.

ACKNOWLEDGMENTS

All glories be to Allah for enabling me to complete this research work.

REFERENCES

1. Nuzzi R, Tridico F. How to minimize pterygium recurrence rates: clinical perspectives. *Clin Ophthalmol*. 2018; 12: 2347–62.
2. Tsai YY, Chiang CC, Yeh KT, Lee H, Cheng YW. Effect of TIMP-1 and MMP in pterygium invasion. *Invest Ophthalmol Vis Sci*. 2010;51(7):3462–7.
3. Liang K, Jiang Z, Ding BQ, Cheng P, Huang DK, Tao LM. Expression of cell proliferation and apoptosis biomarkers in pterygia and normal conjunctiva. *Mol Vis*. 2011;17:1687–93
4. Chowdhury S, Sneha, Priti. New Surgical Technique for Pterygium:Conjunctival In situ Autograft. *J Univer Surg*.2018;6 (3):1-4. DOI: 10.21767/2254-6758.100106
5. Marchetti C, Adrar SN, Collin F, Jore D, Albert GM, Rousselot BD.Melatonin protects PLPC liposomes and LDL towards radical-induced oxidation. *J Pineal Res*.2011;51(3):286–96
6. Balci M, Sahin S, Mutlu FM, Yağci R, Karanci P, Yildiz M. Investigation of oxidative stress in pterygium tissue. *Mol Vis*. 2011;17:443–7
7. Girolamo DN. Association of human papilloma virus with pterygia and ocular-surface squamous neoplasia. *Eye*. 2012;26(2):202–11
8. Cantú CE, Zavala J, Valenzuela J, García JE. Molecular basis of pterygium development. *Semin Ophthalmol*. 2016;31(6):567–83.
9. Siak JK, Ng SL, Seet LF, Beuerman RW, Tong L. The nuclear-factor κ B pathway is activated in pterygium. *Invest Ophthalmol Vis Sci*. 2011;52(1):230–36.
10. Ling S, Liang L, Lin H, Li W, Xu J. Increasing lymphatic microvessel density in primary pterygia. *Arch Ophthalmol*. 2012;130(6):735–42.
11. Riau AK, Wong TT, Lan W. Aberrant DNA methylation of matrix remodeling and cell adhesion related genes in pterygium. *PLoS One*. 2011;6(2):e14687.
12. Anguria P, Kitinya J, Ntuli S, Carmichael T. The role of heredity in pterygium development. *Int J Ophthalmol*. 2014;7(3):563–73.
13. Fuest M, Mehta JS, Coroneo MT. New treatment options for pterygium. *Exp Rev Ophth*. 2017;12(3), 193-6
14. Chui J, Coroneo MT, Tat LT. Ophthalmic pterygium: a stem cell disorder with premalignant features. *Am J Pathol*. 2011;178:817–27.
15. Hwang HS, Cho KJ, Rand G, Chuck RS, Kwon JW. Optimal size of pterygium excision for limbal conjunctival autograft using fibrin glue in primary pterygia. *BMC Ophthalmol*. 2018; 18: 135
16. Liu L, Wu J, Geng J. Geographical prevalence and risk factors for pterygium: a systematic review and meta-analysis. *BMJ Open*. 2013;3(11):e003787. doi: 10.1136/bmjopen-2013-003787.
17. Fonseca EC, Rocha EM, Arruda GV. Comparison among adjuvant treatments for primary pterygium: a network metaanalysis. *B J Ophthal*. 2018 :102: 748-56
18. Karalezli A, Kucukerdonmez C, Akova YA, Koktekir BE. Does topical bevacizumab prevent postoperative recurrence after pterygium surgery with conjunctival autografting? *Int J Ophthalmol*. 2014; 7: 512-6
19. Satish K, Prakash DN, Tanwar M, Gopal M, Patil S, Acharya AA et al. A Comparative Study of Free Conjunctival Autograft Versus Conjunctival Autograft with Stem Cell Transfer in Primary Pterygium. *J Evol Med and Dent Sci*. 2013; 2(45):8805-12. .
20. Bilge AD. Comparison of conjunctival autograft and conjunctival transposition flap techniques in primary pterygium surgery. *Saudi J Ophthalmol*. 2018;32(2):110–3
21. Sharjeel M, Ali F, Malik IQ. Frequency of Pterygium Recurrence with Limbal Stem Cell Autograft. *Pak J Ophthalmol* 2016.32(4):210-5.
22. Mejia LF, Sanchez JG, Escobar H. Management of Primary Pterygia Using Free Conjunctival and Limbal- Conjunctival Autografts without Antimetabolites. *Cornea*. 2005; 24: 972–5.
23. Fayez MF. Limbal versus conjunctival autograft transplantation for advanced and recurrent pterygium. *Ophthalmology*. 2002;109(9):1752-5.
24. Mahdy MS, Bhatia J. Treatment of primary pterygium: Role of limbal stem cells and conjunctival autograft transplantation. *Oman J Ophthalmol*. 2009 ; 2(1): 23–6.
25. Khan N, Ahmad M, Baseer A, Kundi NA. To compare the recurrence rate of pterygium excision with bare sclera, free conjunctival autograft and amniotic membrane grafts. *Pak J of Ophthal* 2010; 26: 138-42.
26. Hussain Z, Rehman HU, Bilal M. Comparison of preoperative injection vs intraoperative application of

- mitomycin c in recurrent pterygium. *Ophthalmology Update*. 2013; 11: 21-4.
27. Kanski JJ, Bowling B. *Clinical Ophthalmology – A systemic approach* 7th ed. Philadelphia Butterworth-Heinemann; 2011; 5: 163.
 28. Zheng K , Cai J, Jhanji V, Chen H. Comparison of pterygium recurrence rates after limbal conjunctival autograft transplantation and other techniques: meta-analysis. *Cornea*. 2012 Dec;31(12):1422-7.
 29. Medical Advisory Secretariat. Limbal stem cell transplantation: an evidence-based analysis. *Ont Health Technol Assess Ser*. 2008;8(7):1-58.
 30. Othman FM. Inferior limbal conjunctival autografting in primary pterygium. *J Egypt Ophthalmol Soc* 2015;108:43-6.
 31. Rao SK, Lekha T, Mukesh BN, Sitalakshmi G, Padmanabhan P. Conjunctival-Limbal autografts for primary and recurrent Pterygia: Technique and results. *Indian J Ophthalmol* 1998;46:203-9.
 32. Walid M Abdalla. Efficacy of Limbal-conjunctival Autograft Surgery with Stem Cells in Pterygium Treatment. *Middle East Afr J Ophthalmol*. 2009 ; 16(4): 260–2. doi: 10.4103/0974-9233.58417