

EFFECT OF CONJUNCTIVA-LIMBUS TRANSPLANTATION WITH FIBRIN GLUE COMPARE TO SUTURE TECHNIQUE ON STABILITY OF THE GRAFT ATTACHMENT IN PTERYGIUM SURGERY

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Objective: Pterygium is a growth that develops on the conjunctiva or mucous membrane covers the white part of eye. It is a benign or noncancerous growth that is often shaped like a wedge. This study aims to assess the efficacy and safety attachment graft on conjunctiva-limbus autograft transplantation using fibrin glue compared with suture technique in pterygium patient. **Method:** Single-blind randomized clinical trials. The samples were all pterygium patients with grade two or more who underwent pterygium surgery at the eye clinic and central operating theatre Sanglah General Hospital Denpasar, Bali-Indonesia and met the eligibility criteria. Samples were divided into suture and fibrin glue groups based on permutation-block randomization. Mann-Whitney U test and repeated measurement of ANOVA Analyses were performed to determine the different between two treatments. **Results:** There were no significant differences in the stability of graft's attachment between the two groups either on the first day, first week and first month despite fibrin glue technique showed lower results in the first week and first month ($p = 0.787$, $p = 0.233$, and $p = 0.475$). The average time it takes the fibrin glue technique $21.80 \pm 2:37$ minutes, much shorter than 41.67 ± 6.99 min in the suture technique ($p = 0.001$). Postoperative comfort in the fibrin glue group showed lower scores on the first day, first week and first month compared with the suture group ($p = 0.000$, $p = 0.000$ and $p = 0.035$). During the follow-up period no complications were found. **Conclusion:** The stability of graft attachment between the fibrin glue and suture technique is not significantly different. Fibrin glue could be chosen as an alternative method in the conjunctiva-limbus autograft and helpful in shortening the operating time and improve comfort postoperatively.

Keywords: conjunctiva-limbal auto graft, fibrin glue, graft stability

INTRODUCTION

Pterygium is a disorder characterized by the proliferation of triangular or wing-shaped fibrovascular tissue toward the cornea, in the palpebral fissure.^{1,2,3} The exact cause of pterygium is still not known, but some studies found an association between the incidence of pterygium with the exposure to ultraviolet (UV) light.^{3,4,5} Management of pterygium can be divided into conservative and surgical management. Surgery is applied if the pterygium cause an visual impairment.⁶ Recurrence after surgery is still a problem in pterygium patients. Recurrence rate after simple surgery (bare sclera) ranged from 24% to 89%. Nowadays, surgical technique using conjunctive auto graft transplantation is a technique of choice. This technique was first introduced by Kenyon, et al in 1985. This technique reduce recurrence rate after pterygium surgery between 2% to 39% and also reduce the complications

after surgery.^{7,8,9} Conjunctive auto graft attachment technique is a type of suture technique. Recently, conjunctive auto graft attachment technique using fibrin glue become popular.^{2,10} Fibrin glue is an adhesive material that is widely used today, working as a biological fibrin glue mimics the final process of coagulation and is not influenced by the patient coagulation. During this time, fibrin glue is used in many countries for nearly 20 years in the field of neurosurgery, thoracic surgery and eye surgery. Until now there has never reported any transmission of disease in the use of it.^{11,12} This study compared the stability of attachment-limbal conjunctive auto graft with fibrin glue method compared to the suture techniques.

PATIENTS AND METHOD

This study applied a single-blind randomized clinical trial as a design and implemented at Eye Clinic Sanglah General Hospital/Faculty of Medicine Udayana University, Bali-Indonesia during period of February until July 2010. Samples were all patients with grade two or more pterygium that underwent pterygium surgery and met eligibility criteria. Institutional review board/ethics

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committee approval was obtained from Medical Ethic Commission Sanglah General Hospital and this study adhered to the tenets of the Declaration of Helsinki. Samples were divided into suture and fibrin glue groups based on permuted-block randomization as indicated in Figure 1.

To be eligible for the study the patients had to meet the following inclusion criteria: 1) Patient with primary pterygium; 2) Pterygium on one or both eyes (bilateral pterygium); 3) Pterygium stage two or more. Patients with nasal and temporal pterygium (pterygium duplex). Patients who have history of trauma to the eye were excluded from this study. Analyses were performed with Mann-

Whitney U test and repeated measurement ANOVA.

RESULTS

During the period of March 1 through June 31, 2010, there were 55 patients in the pterygium Eye Health Sciences Clinic Sanglah General Hospital Denpasar, Bali-Indonesia. Total of 29 patients (30 eyes) were participated in this study. A number of 36 eyes of the 60 eyes from 55 patients met inclusion criteria of the study. Six eyes refused to participate in this study and the remaining of 30 eyes was randomly allocated into two groups, i.e. suture group and fibrin glue group.

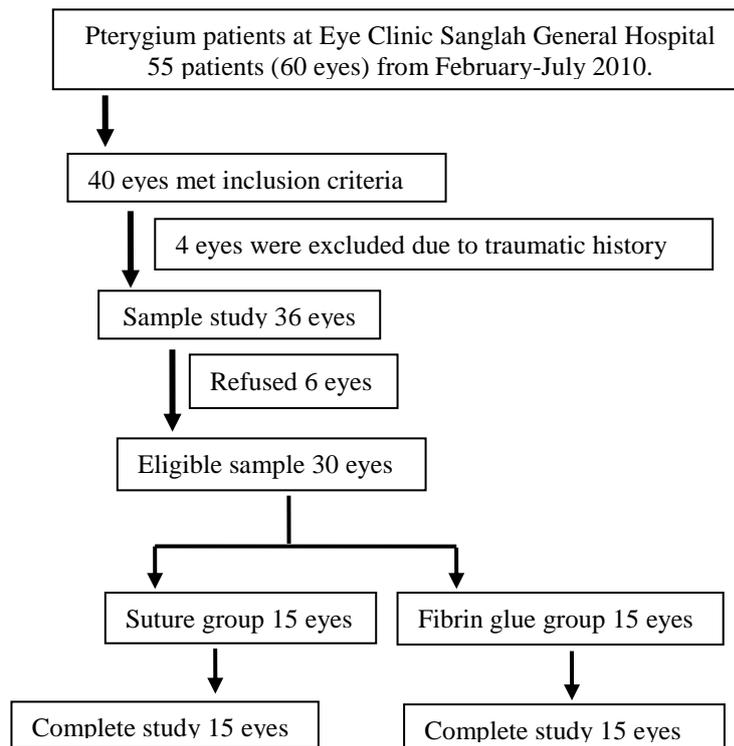


Figure 1

Derivation of Trials Study

All patients in each group completed the study within 1 month.

Table 1 shows the basic characteristics of the study subjects. Data characteristics of the two groups showed no difference in mean age, sex, location of pterygium, gradation and occupation.

Table 2 shows the comparison between the stability of the attachment graft using suture and fibrin glue technique. There was no significant difference in stability between the two groups either on the first day, first week and first month despite scores fibrin glue technique showed lower results in the first week and first month (consecutively $p = 0.787$, $p = 0.233$, and $p = 0.475$).

Table 3 shows the comparison of the operating time between suture and fibrin glue group. The average time in fibrin glue technique

was 21.80 ± 2.37 minutes, shorter than 41.67 ± 6.99 minutes on suture techniques. The difference in operating time between the two groups was statistically significant ($p = 0.001$).

Table 4 shows the comparison of postoperative comfortness between the sutures and fibrin glue group. Postoperative comfort in the fibrin glue group showed lower scores on the first day, first week and first month compared with the sutures. The difference in comfort scores during the postoperative follow-up period was statistically significant ($p = 0.001$, $p = 0.001$ and $p = 0.035$).

Comparison of stability in the sutures and fibrin glue groups on the first day the average were $1:00 \pm 0.65$ and 0.93 ± 0.79 , the first week of $1:00 \pm 0.53$ and 0.73 ± 0.79 , in the first month $0:33 \pm 0.61$ and $0:27 \pm 0.70$ ($F = 24.92$). The results showed that the average score of stability in each

group decreased significantly during the follow-up period but the overall the decrease of stability

between the two groups was not significant, $p = 0.055$ (Figure 2).

Table 1
Characteristics of Study Subjects

Variables	Group	
	Suture group (N = 15)	Fibrin glue group (N = 15)
Age	46,07±13,65	48,20±12,65
Sex		
Male	5 (33.3%)	8 (53.3%)
Female	10 (66.7%)	7 (46.7%)
Pterygium location		
Nasal	15 (100%)	13 (86.7%)
Temporal	0 (0%)	2 (13.3%)
Pterygium's grade		
Grade 2	12 (80%)	12 (80%)
Grade 3	2 (13.3%)	3 (20%)
Grade 4	1 (6.7%)	0 (0%)
Occupation		
Farmer	4 (26.7%)	7 (46.7%)
Fisherman	1 (6.7%)	0 (0%)
Government employee	4 (26.7%)	6 (40.0%)
Private	4 (26.7%)	1 (6.7%)
Merchant	1 (6.7%)	1 (6.7%)
Does not work	1 (6.7%)	0 (0%)

Table 2
Comparison of Attachment Score Stability Between the Sutures and Fibrin Glue Groups

Gradation stability score	Group		Z	p
	Suture technique (N = 15)	Fibrin glue technique (N = 15)		
Day I	15.90	15.10	-0.271	0.787
Week I	17.23	13.77	-1.193	0.233
Month I	16.30	14.70	-0.714	0.475

Mann Whitney U test

Table 3
Comparison of Operating Time Between the Suture and Fibrin Glue groups

Variable	Mean ± SD		p
	Suture technique (N = 15)	Fibrin glue technique (N = 15)	
Operating time (minute)	41.67±6.99	21.80±2.37	0.001

Independent-t test

Table 4
Comparison of Convenience Scores Postoperative Between Suture and Fibrin Glue groups

Convenience scale score	Group		Z	p
	Suture technique N = 15	Fibrin glue technique N = 15		
Day I	23.00	8.00	-5.109	0.001
Week I	23.00	8.00	-5.182	0.001
Month I	17.50	13.50	-2.107	0.035

Mann Whitney U test

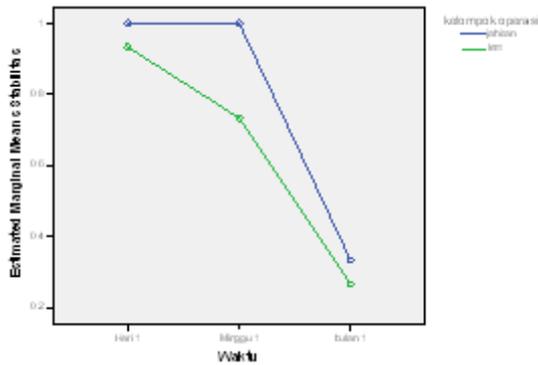


Figure 2

Comparison of Stability Between the Two Groups

Comparison of comfort postoperative between the suture and fibrin glue group on the first day was 2.07 ± 0.25 and 0.20 ± 0.41 , 1.20 ± 0.41 first week with $p = 0.001$, as well as the first month 0.40 ± 0.73 and 0.001 ($F = 77.45$). These results illustrate there were differences in postoperative comfort scores on each group and between the 2 groups in which the fibrin glue technique's scores is lower than the suture technique. The difference in comfort scores in the two groups was statistically significant ($p = 0.001$).

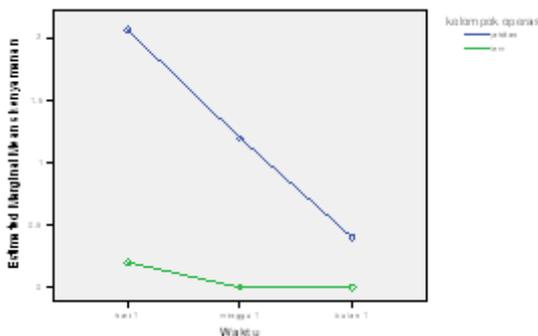


Figure 3

Comfort Between the Two Groups

Complications of surgery is one of the factors assessed in this study. No complications such as defects in the cornea, conjunctivitis giant papil, buttonhole and granuloma formation were found during pterygium surgery and three follow-up period. We found 2 cases of subconjunctival bleeding on the first day and first week of each group.

DISCUSSION

Option treatment for pterygium is surgical. However, the recurrence rate with surgery is still high. Currently, conjunctiva-limbal transplantation technique as a surgical method increased to reduce the recurrence rate after surgery and as a minimally invasive procedure. One of the factor that affect the success of the conjunctiva-limbal autograft in pterygium surgery is the stability of the graft

attachment to the base and surrounding tissue, especially in the limbal. Great stable of graft attachment allows optimal tissue vascularization, so that the graft can be grow in good quality at the donor area. Vascularization of the graft conjunctiva-limbal tissue is visible within one week after surgery. Complete reperfusion occurs in one until two months after surgery, indicating graft already grows well.^{13,14}

This study found that the stability of the graft attachment on sutures and fibrin glue groups were improved during the observation period. On the first day after the surgery, both group shows similar stability of the graft attachment. This is because of the ongoing inflammatory process, while the wound healing process just start to begin. In the first week after surgery, graft attachment stability in the fibrin glue group experienced a slight improvement compared to the suture technique although the difference is not too significant. This difference was probably due to the better wound healing in fibrin glue group. Histological study found that the wound gap on the use of fibrin glue is smaller, with faster epithelialization and angiogenesis process.¹⁵ Meanwhile, stability of graft attachment are equally good in both groups. This is because the wound healing process is over. Study by Srivasan et al¹⁶ found that the stability of graft attachment did not differ in the first week, first month and three months after surgery on the suture and fibrin glue groups. The only difference occurs in the inflammatory process in which the degree of inflammation in the fibrin glue group is smaller in the first week and first month post-surgery.

The average operation time required on methods conjunctiva-limbal graft with fibrin glue is faster than the suturing method. This study obtain the required operation time in the fibrin glue is faster than the suturing method. Size or gradation of pterygium may influence the timing of the operation but did not find a correlation between them.^{10,17} Koranyi¹⁰ found an average operating time with fibrin glue technique was 10 minutes compared to 17 minutes on the suturing method. Bahar et el¹⁶ also get almost the same results. Uy, et el¹⁸ also reported there is a significant time difference between sutures and fibrin glue method. This time difference is due to fibrin glue fixation takes 3-5 minutes to attach with the tissue.¹¹ Meanwhile, the sutures technique requiring several stitches to fix the graft to the surrounding tissue. Overall, this may illustrate that the use of fibrin glue is quite easy and can be done by anyone either beginner or experienced operators. By this technique, pterygium surgery can also be performed on more than one patient, especially in areas with a high incidence of pterygium.

Convenience after surgery has always been the hope of patients and operators. Post-operative

comfort in this study was measured with a scale to determine the degree of pain, watery or foreign body sensation. Assessment of pain is not easy because each patient may have a different experience or threshold to pain. At least, the use of a pain scale, we deem reasonably be used to identify postoperative comfort level. The results of post-operative comfort in this study which were assessed on the first day, first week and first month showed significant results. In the fibrin glue group showed better comfort from the first day until the first month post-surgery. While the other group shows better comfort felt after the first week. Research by Bahar et al¹⁶ find that comfort in the fibrin glue group is better, which is characterized by a lower score during the follow-up period. Kim et al¹⁷ found as much as 64% of patients using fibrin glue feel comfortable in the first week and 100% in the second week. Jiang et al¹² found a significant difference in comfort between the fibrin glue and suture groups (nylon 10.0) on the first day, the third day and the seventh day. No significant differences occurred after day 14 due to removal of the threads made on that day.

Suture group in this study using 8.0 vycril thread that is absorbable, where the absorption is complete after 60 days. During the process of absorption, absorbable threads can cause local inflammation causing discomfort. Follow up the first day and first week at the seams showed significant discomfort. This is because the pain caused by tissue trauma accompanied by a sewing thread which aggravate the trauma on the tissue. Unlike the fibrin glue group that does not require additional trauma, that pain and foreign body sensation felt is very minimal. Besides, the absorption of fibrin glue is complete on the seventh day. Comfort of the two groups was not different in the first month due to the healing process is complete and the degradation of absorbable thread is almost perfect. The process of attachment to the sclera graft tissue also occurs perfectly so that the inflammation has also been very minimal.

Conjunctiva-limbus autograft technique is a safe, effective, and rarely causing serious complications. Nevertheless, complications during and after operation were still evaluated. In this study, the whole graft can be completely attached to the end of the follow-up period. Found no serious complications in either group. There were two cases of subconjunctival bleeding in the seam and in the fibrin glue group. Subconjunctival bleeding in the study was due to additional trauma from the patient unconsciously rubbing the eyes during sleep. All cases improved after three weeks because of the subconjunctival bleeding already absorbed perfectly. Uy et al¹⁸ found one case with subconjunctival bleeding and spontaneous resolution occurred after 3 weeks without disturbing the stability of attachment graft.

In general, the use of fibrin glue in conjunctival-limbus autograft method gives good results. All grafts can be attached to the recipient area and found no graft dehiscence. Some factors must be consider that may affect the outcome of conjunctiva-limbus autograft surgery, among others, the level of pre-surgical inflammation and extensive excision of pterygium tissue that were not assessed in this study. High degree of pre-surgical inflammation will affect the proliferative activity of the stroma, so the level of graft attachment to the epithelium and stroma become unwell. The extent of graft in this study was adjusted to the size of the recipient area, but it is not differentiated by pterygium's gradation and morphology.

CONCLUSION

The stability of graft attachment between the fibrin glue and suture technique is not significantly different. Fibrin glue could be chosen as an alternative method in the conjunctiva-limbus autograft and helpful in shortening the operating time and improve comfort postoperatively.

REFERENCES

1. Krachmer, J. H., Mannis, M. J., and Holland, E. J. 2005. Pterygium In Cornea: Fundamentals, Diagnosis and Management. 2nd ed. St Louis: Mosby.1001-2.
2. Tan, T. D. 2002. Pterygium. In: Holland, E. J., Mannis, M. J., edition. Ocular Surface Disease. Medical and Surgical Management. New York: Springer-Verlag. 65-75.
3. Gazzard, G., Saw, M. S., Farook, M., Koh, D., Widjaya, D., Chia, S. E., et all. 2002. Pterygium in Indonesia: prevalence, severity and risk factor. Br J Ophthalmol. 86:1341-1346.
4. Nemesure, B., Wu, S., Hennis, A., and Leske, C. M. 2006. Nine-year incidence and risk factors for pterygium in the Barbados Eye Studies. Ophthalmology.113:29-35.
5. Nolan, M. T., DiGirolamo, N., Sachdev, H. N., Hampartzoumian, T., Coroneo, T. M., and Wakefield, D. 2003. The Role of Ultraviolet Irradiation and Heparin-Binding Epidermal Growth Factor-Like Growth Factor in the Pathogenesis of Pterygium. Am J Pathol.162: 567-574
6. Massaoutis, P., Khemka, S., and Ayliffe, W. 2006. Clinical outcome study of modified surgical technique for pterygium excision. Can J Ophthalmol. 41:704-8.
7. Varssano, D., Michaeli-Cohen, A., andLoewenstein, A. 2002. Excision of pterygium and conjunctival autograft. IMAJ. 4:1097-1100.
8. Sanchez-Thorin, J., Rocha, G., and Yelin, B. J. 1998. Meta-analysis on the recurrence rates after bare sclera resection with and without

- mitomycin C use and conjunctival autograft placement in surgery for primary pterygium. *Br J Ophthalmol.* 82:661-665.
9. Seid, A. And Bejiga, A. 2000. Free conjunctival autograft in the management of advanced primary and recurrent pterygia. *East African Journal.* 77:588-591.
 10. Koranyi, G., Seregard, S., and Kopp, D. E. 2004. Cut and paste: a no suture, small incision approach to pterygium surgery. *Br J Ophthalmol.* 88:911-914.
 11. Ramos-Esteban, C. J. and Tauber S. 2006. The Use of Tissue Glue in Corneal Surgery. *Techniques in Ophthalmology.* 4(1):30-34.
 12. Jiang, J., Yang, Y., Zhang, M., Fu, X., Bao, X., and Yao, K. 2008. Comparison of Fibrin Sealant and Sutures for Conjunctival Autograft Fixation in Pterygium Surgery: One-Year Follow-Up. *Ophthalmologica.* 222:105-111.
 13. Chan, C., Chew, P., Alsagoff, Z., Wong, J., and Tan, D. 2001. Vascular patterns in pterygium and conjunctival autographing: a pilot study using indocyanine green anterior segment angiography. *Br J Ophthalmol.* 85:350-353.
 14. Kucukerdonmez, C., Akova, Y. A., and Altinors, D. D. 2007. Vascularization is more delayed in amniotic membrane graft than conjunctival autograft after pterygium excision. *Am J Ophthalmol.* 143:245-249.
 15. Srinivasan, S., Dollin, M., McAllum, P., Berger, Y., Rootman, S. D., Slomovic, R. A. 2009. Fibrin glue versus sutures for attaching the conjunctival autograft in pterygium surgery: a prospective observer masked clinical trial. *Br J Ophthalmol.* 93:215-218.
 16. Bahar, I., Weinberger, D., Dan, G., and Avisar, R. 2006. Pterygium Surgery Fibrin Glue Versus Vicryl Sutures for Conjunctival Closure. *Cornea.* 25:1168-1172.
 17. Kim, H. H., Mun, J. H., Park, J. Y., Lee, W. K., and Shin, P. J. 2008. Conjunctivolimbal autograft using a fibrin adhesive in pterygium surgery. *Korean J Ophthalmol.* 22:147-154.
 18. Uy, H., Reyes, J. M. G., Flores, J. D. G., and Lim-Bon-Siong, R. 2005. Comparison of fibrin glue and sutures for attaching conjunctival autografts after pterygium excision. *Ophthalmol.* 112:667-671