Use of fibrin glue in the management of recurrent pterygium by conjunctival autograft

Virendra K. Malik, MBBS, MS, *Sandeep Kumar,* MBBS, MS.

ABSTRACT

الأهداف: تقييم مدى أهمية استخدام صمغ الفبرين (fibrin glue) بدلاً من الخيوط الجراحية في عملية استئصال الظفرة (pterygium) وترقيع مكانها بجزء من الملتحمة (conjunctival auto-graft) وذلك من أجل تقليل نسبة ظهور الظفرة مرة أخرى.

الطريقة: أُجريت هذه الدراسة الاستطلاعية المفتوحة التسمية في قسم العيادات الخارجية التابعة لجامعة سبهاري الطبية، ميروت، شمال الهند وذلك خلال الفترة من يناير 2009م إلى يوليو 2010م. شملت هذه الدراسة 50 عيناً (50 مريضاً) مصابة بمرض الظفرة المتكرر الظهور وقد تم تقسيم المرضى عشوائياً إلى مجموعتين وهي كالتالي: المجموعة (ج1) التي ستخضع لعملية استئصال الظفرة واستخدام صمغ الفبرين لترقيع مكانها بجزء من الملتحمة، و(ج2) التي ستخضع لنفس العملية ولكن باستخدام 6 غرز متقاطعة من الخيوط الجراحية من أجل ترقيع مكان الظفرة بجزء من الملتحمة. وقد كان عدد المرضى في كل مجموعة 25 مريضاً، وتم عمل مقارنة فيما بينهما على أساس الوقت الذي استغرقته العملية، ونسبة ظهور المرض مرة أخرى، وأعراض ما بعد العملية الجراحية (تهيج العين، ورطوبتها، واحمرارها)، بالإضافة إلى مضاعفات العملية.

النتائج: لقد كانت نسبة ظهور الظفرة مرة أخرى في (ج1) 4% (عيناً واحدة)، فيما كانت هذه النسبة (12%) (3 أعين) في (ج2) وذلك بعد العملية الجراحية بحوالي 9-13 شهراً. وكانت الاختلافات بين المجموعتين غير كبيرة من الناحية الإحصائية، غير أن الوقت الذي استغرقته العلمية الجراحية، والتهابات ومضاعفات العلمية الجراحية كانت أقل في (ج1)، في حين كانت أعراض ما بعد العملية أكثر في (ج2).

خاتمة: أشارت الدراسة إلى أن استخدام الخيوط الجراحية لتثبيت الملتحمة في جراحة استئصال الظفرة قد تكون وسيلة علاجية آمنة وسهلة، إلا أنه عند التحدث عن سهولة العملية الجراحية، وتقليل الوقت الذي تستغرقه، بالإضافة إلى تقليل مضاعفات العملية ونسبة ظهور الظفرة مرة أخرى فإن اللجوء إلى صمغ الفبرين بدلاً من الخيوط قد يكون خياراً أفضل.

Objectives: To evaluate whether use of fibrin glue instead of sutures for the treatment of recurrent pterygium with conjunctival auto-graft (CAG) further decreases its recurrence.

Methods: A prospective, clinical open trial of 50 eyes of 50 patients with recurrent pterygium, who were randomly assigned to either, pterygium excision and CAG with fibrin glue (Group 1) or with 6 interrupted sutures (Group 2), was carried out from January 2009 to July 2010 at the outpatient department of Subharti Medical College, Meerut, North India. Both groups had 25 patients each. The groups were compared with regards to the surgical time taken, development of recurrence, postoperative symptoms (irritation, watering, and redness), and complications.

Results: Recurrence was seen in one (4%) eye in group I, and 3 (12%) eyes in group II after 9-13 months of follow up. The difference between the 2 groups was not statistically significant. The surgical time was significantly reduced, and postoperative inflammation and complications were less in group I. Postoperative symptoms were significantly more in group II patients.

Conclusion: While conjunctival autograft with sutures for management of recurrent pterygium appears to be a safe and feasible modality, fibrin glue fixation of the autograft is a more viable option in terms of surgical ease, less time consuming, less postoperative complications, and less recurrence.

Saudi Med J 2010; Vol. 31 (12): 1326-1330

From the Department of Ophthalmology, Subharti Medical College, Meerut Uttar Pradesh, India.

Received 21st August 2010. Accepted 18th October 2010.

Address correspondence and reprint request to: Dr. Virendra K. Malik, Department of Ophthalmology, Subharti Institute of Medical Sciences Meerut Uttar Pradesh, India. Tel/Fax. +91 (121) 2668080. E-mail: vkmalik55@yahoo.com

Although a number of surgical adjunct therapies have been advocated for management of pterygium, ophthalmic surgeons are still in search of an ideal procedure to reduce the postoperative recurrence rate. In the recent past, major adjuvant therapies like anti-metabolite application,[1,2] amniotic membrane graft,[3-8] and conjunctival autograft[9-13] are recommended for primary as well as recurrent pterygium. More recently, use of conjunctival autograft with fibrin glue application is gaining popularity with varied outcomes.[14-27] Due to the limited number of studies on this topic, this prospective study was conducted to assess the efficacy of fibrin glue (Tisseel Duo Quick, Baxter, Vienna, Austria) in decreasing recurrence rate following recurrent pterygium excision with conjunctival autograft (CAG).

Methods. Fifty eyes of 50 patients with recurrent pterygium who attended the outpatient department of Subharti Medical College, Meerut, North India, a tertiary eye care center, were enrolled in the study between January 2009 and July 2010. Due to the qualitative nature of the study, a randomized clinical trial was carried out for 50 patients. Ethical clearance was obtained from the Institutional Ethics Committee. The eyes were randomly divided into 2 groups as per the surgical procedure performed: Group I (25 eyes) underwent CAG with fibrin glue application, and group II (25 eyes) underwent CAG with sutures. Surgery was performed by 2 surgeons, both from the same department and institute. The same surgical procedure, as mentioned in the text, was followed by both surgeons. The groups were compared with regards to the surgical time taken, development of recurrence, and superficial punctate keratitis (SPKs) by an independent observer, also an ophthalmologist. The patients were given a questionnaire postoperatively for grading of postoperative discomfort using the Wong-Bakers FACES Pain Rating Scale.[28] They were asked to mark the scale from 0-5 based on the severity of discomfort. The mean values were compared in both the groups. All patients were stratified according to tissue thickness as atrophic/grade one, intermediate/grade 2, and fleshy/grade 3, but not according to age. Detailed history was taken regarding any exiting systemic diseases. With suspected history, the patients were evaluated for existing collagen vascular disease and diabetes mellitus. Patients with any such disease were excluded from the study. Informed written consent was obtained from all the patients after explaining the safety/potential risk of using fibrin glue, even if negligible. Complete ophthalmic examination included best-corrected visual acuity (BCVA), slit lamp bio-microscopy for tear film meniscus, other associated corneal abnormalities, and presence of any anterior segment inflammatory disorders. Eyes with any major ophthalmic ailments, pupillary area involvement, and ocular surface disorders were not included in the study. All the eyes received ciprofloxacin 0.3% eye drops thrice a day prior to the surgery, and the surgeries were performed on an out patient basis under topical and subconjunctival anesthesia.

Surgical techniques. *Pterygium excision.* The eye was draped, and a universal eye speculum was applied. Lidocaine 2% with adrenaline 1:2,00,000 was injected subconjunctivally and underneath the pterygial mass. The pterygial tissue was held at the body. With the help of an iris repository, total pterygium was avulsed from the corneal surface and then trimmed at the distal end. Removal of subconjunctival fibrous tissue was performed adjacent to and deeper to the removed mass. The complete removal of the fibrous tissue was judged meticulously. Any abnormal scar tissue on the cornea was also polished with a crescent knife. The conjunctival bare area, thus created, was measured both vertically and horizontally with a caliper.

Conjunctival autograft (CAG). To obtain the graft, the supero-temporal aspect of the bulbar conjunctiva of the same eye was exposed and a one mm larger area than the recipient bed was marked. Lidocaine 2% mixed with adrenaline 1:2,00,000 was injected subconjunctivally to make the conjunctiva free from the episcleral tissue and to reduce bleeding. The auto-conjunctival tissue was dissected along with the limbal area of the conjunctiva. The dissected conjunctival tissue was placed over the scleral bed, with limbal side of the donor tissue coinciding the limbus. For group I, fibrin glue was applied over the scleral bed and the obtained graft was completely spread. While waiting for the graft to adhere to the scleral bed, the exposed area created by the donor tissue removal was also closed by ballooning of the conjunctiva with subconjunctival injection for 24 hours with 2 mg Dexamethasone and 20 mg Gentamicin, followed by patching of the eye. For group II patients, the graft was sutured to the conjunctival edge by 3 interrupted 8-0 Vicryl sutures, and the limbus with 3 interrupted 10-0 monofilament nylon sutures with buried knots. The sutures were removed after 14 days. The donor site was not sutured and allowed to epithelize by itself in both the groups.

Postoperative therapy and follow up. All the eyes received 1% prednisolone acetate eye drops every 4 hours in the first week, 4 times a day in the second week, twice a day during the third and fourth weeks, and then stopped. Similarly, 0.3% Ciprofloxacin eye drops were instilled 4 times a day during the first week, twice a day during the second, third, and fourth week, and then discontinued. The patients were followed up one the first day, fourth day, first, second, and fourth

week, and then every month for 3 months and every 3 months thereafter. Any untoward effects noted were recorded in the preset ProForma.

Statistical analysis. Student t-test for proportions was used to test the significant difference in complications (superficial punctate keratitis and recurrence) and postoperative symptoms (irritation, watering, and redness) between the 2 groups at a 1% level of significance.

Results. Of the 50 patients, 36 were male and 14 were female. The mean age of the patients in group I was 60.08+3.92 years (range: 54-66 years) and in group II was 60.36+4.55 years (range: 49-68 years) (**Table 1**). The difference in mean age at surgery in the 2 groups was not statistically significant (p>0.01). Two eyes had temporal lesions and the rest had nasal lesions. Twenty-one eyes in group 1 and 20 eyes in group II had grade 3/fleshy pterygium. The rest had grade 2/intermediate pterygium. The extent of corneal involvement from the limbus in group I was 3.23+0.92 mm and in group II was 3.26+0.70 mm (p>0.01). Mean number of pterygium surgeries, prior to admission were 3.13± 3.357 in group I and 4.40±3.806 in group II (p>0.01). The primary outcome measure was the recurrence between the 2 groups. The recurrence rate was one eye (4%) in group I and 3 eyes (12%) in group II. Recurrence in group I was at 5 months and in group II was at 7 and 8 months. Recurrence was defined as postoperative growth of fibrovascular tissue over the corneoscleral limbus and into the clear cornea. In this particular patient in group I, the graft retracted postoperatively. This difference in recurrence rates between the 2 groups was not statistically significant (p>0.01). The secondary outcome measures were surgical time, postoperative discomfort, and complications in both groups. Average time taken for surgery in group I was 18.24±2.20 min (range 14-20 min) and in group II was 26.60±1.93 min (range 24-30 min). The surgical time was significantly reduced in group I (p<0.01). Group I had a mean pain score (based on Wong Bakers FACES Pain Rating Scale) of 0.44±0.583 as compared to group 2 with a mean score of 3.32±0.802. The postoperative discomfort was significantly greater in group II patients (p<0.01). The postoperative complications, in the form of superficial punctate keratitis (SPK) were greater in group II patients. However, there was no statistically significant difference in SPK's between the 2 groups (p>0.01). Five eyes were also operated for cataract (Phaco) along with pterygium surgery. All these 5 eyes underwent temporal phacoemulsification with a 2.8 mm incision. It obviated the need for repeat peribulbar/retrobulbar anesthesia. The pterygium was situated nasally and was operated with CAG using 10-0 nylon sutures (group 2). We did not encounter any major confounding effect due to simultaneous cataract and pterygium surgery. The mean postoperative follow up period in group I was 9.86+2.15 months and in group II was 13.00+1.25 months (p>0.01).

Table 2 - Comparison of complications (SPK and recurrance) between the 2 groups.

Complications	Group I (n=25)	Group II (n=25)	$t_{(cal.)}$	$t_{(48, .01)}$	*P*-value
SPK	2 (8)	7 (28)	1.90	1.96	>0.01*
Recurrence	1 (4)	3 (12)	0.84	1.96	>0.01*
Total	**3**	**10**	-	-	-

*not significant. SPK - superficial punctate keratitis

Table 1 - Demographic data.

Description	Conjunctival graft (with fibrin glue) Group I	Conjunctival graft (with sutures) Group II	*P*-value
Number of eyes operated	25	25	-
Gender (male to female ratio)	1:0.38	1:0.38	>0.01†
Mean age at surgery ± SD (years)	60.08±3.92 (range: 54-66)	60.36±4.55 (range: 49-68)	>0.01†
Mean corneal involvement ± SD in mm	3.23±0.92	3.26±0.70	>0.01†
Mean follow up in months ± SD	9.86±2.15	13.00±1.25	>0.01†
Recurrence (%)	1 (4)	3 (12)	>0.01†
Surgical time (minutes)	18.24 ± 2.20 range 14-20	26.60 ± 1.93 range 24-30	<0.01*
Post operative discomfort graded on Wong Bakers Visual Analogue Pain Scale	0.44±0.583	3.32±0.802	<0.01*

*p<0.01 shows a very significant difference at 1% level of significance. †non-signifiant

Discussion. The recurrence of pterygium is believed to be caused by induced trauma to the pterygial head during surgery, which releases the pterygial factor, namely, histamine and epidermal growth factors. Fibroblasts derived from human pterygia express functionally active histamine and epidermal growth factor receptors. Controlled modification of either the receptors or the appropriate ligands could have beneficial effects in pterygia treatment.[29] The strong immunoreactivity and the release of basic fibroblast growth factor (b-FGF), a fibroangiogenic growth factor, in cultured fibroblasts of recurrent pterygia suggests that fibroblasts may play an important role in the recurrence of pterygium.[30] To reduce the recurrence, a number of adjunctive therapies, such as beta radiation, argon laser therapy, and topical thiotepa have been tried in the past with very little effect. Efforts have also been made to reduce the recurrence by using intraoperative mitomycin C (MMC) application with or without conjunctival graft.[1,2,4] Comparative studies have been conducted by various authors on the role of amniotic membrane graft and conjunctival graft with encouraging results,[3-13] thus making the procedure more popular and more acceptable because of a low recurrence rate, maintenance of normal anatomical integrity, less post-operative complications, and surgical ease. Recurrence rates following these procedures are reported to be 5.3-13.3%.[10,11,24] Our study is also in concurrence with that of literature with a recurrence of 12%.

Recently, fibrin glue application to fix the graft has come into vogue for the management of primary and recurrent pterygium.[14,16-26] Authors have claimed that the technique is not only feasible but provides surgical ease and less postoperative pain, and takes less surgical time.[18,20,29] Less postoperative inflammation may be the cause of a lower recurrence rate than in the suturing group. Our results are comparable to the literature both in terms of postoperative ease and lower recurrence. However, further studies with a larger sample size are required to make a concrete conclusion.

The limitation of a short follow up of 8-16 months, and a small sample size in our study could have contributed to a lower recurrence rate. The importance of limbal conjunctival inclusion for reducing the rate of recurrence has been emphasized in the literature.[11] Available studies show that with limbal conjunctival inclusion, the rate of recurrence varied from 5.3-9% when limbal conjunctiva was included versus 14.3-21% when the limbal conjunctiva was not included.[11] In the present study, we included limbal conjunctiva in all, which might have acted as a barrier for prevention of recurrence.

In summary, CAG is a simple and safe modality for the management of recurrent pterygium and should be performed routinely by all the ophthalmologists. Further, fixing the graft with fibrin glue will be a viable option in terms of less surgical time and more postoperative patient comfort, and last but not the least, lens recurrence.

References

1. Díaz L, Villegas VM, Emanuelli A, Izquierdo NJ. Efficacy and safety of intraoperative mitomycin C as adjunct therapy for pterygium surgery. ***Cornea*** 2008; 27: 1119-1121.
2. Rahman A, Yahya K, Ul Hasan KS. Recurrence rate of pterygium following surgical excision with intraoperative versus postoperative mitomycin-C. ***J Coll Physicians Surg Pak*** 2008; 18: 489-492.
3. Luanratanakorn P, Ratanapakorn T, Suwan-Apichon O, Chuck RS. Randomised controlled study of conjunctival autograft versus amniotic membrane graft in pterygium excision. ***Br J Ophthalmol*** 2006; 90: 1476-1480.
4. Katircioğlu YA, Altiparmak UE, Duman S. Comparison of three methods for the treatment of pterygium: amniotic membrane graft, conjunctival autograft and conjunctival autograft plus mitomycin C. ***Orbit*** 2007; 26: 5-13.
5. Ozer A, Yildirim N, Erol N, Yurdakul S. Long-term results of bare sclera, limbal-conjunctival autograft and amniotic membrane graft techniques in primary pterygium excisions. ***Ophthalmologica*** 2009; 223: 269-273.
6. Memarzadeh F, Fahd AK, Shamie N, Chuck RS. Comparison of de-epithelialized amniotic membrane transplantation and conjunctival autograft after primary pterygium excision. ***Eye (Lond)*** 2008; 22: 107-112.
7. Oguz H. Amniotic membrane grafting versus conjunctival autografting in pterygium surgery. ***Clin Experiment Ophthalmol*** 2004; 32: 501-504.
8. Oguz H, Kilitcioglu A, Yasar M. Limbal conjunctival mini-autografting for preventing recurrence after pterygium surgery. ***Eur J Ophthalmol*** 2006; 16: 209-213.
9. Kuzmanović Elabjer B, Busić M, Elabjer E. Retrospective clinical analysis of free conjunctival autograft in treatment of pterygia. ***Coll Antropol*** 2008; 32: 303-306.
10. Syam PP, Eleftheriadis H, Liu CS. Inferior conjunctival autograft for primary pterygia. ***Ophthalmology*** 2003; 110; 806-810.
11. Dekaris I, Gabrie N, Karaman Z,Mravicic I, Kastelan S. Limbal conjunctival autograft transplantation for recurrent pterygium. ***Eur J Ophthalmol*** 2002; 12; 177-182.
12. Mejia LF, Sanchez JG, Escobar H. Management of primary pterygia using free conjunctival and limbal conjunctival autografts without antimetabolites. ***Cornea*** 2005; 24: 972-975.
13. Varssano D, Michaeli-Cohen A, Loewenstein A. Excision of pterygium and conjunctival autograft. ***Isr Med Assoc J*** 2002; 4: 1097-100.
14. Ayala M. Results of pterygium surgery using a biologic adhesive. ***Cornea*** 2008; 27: 663-667.
15. Kheirkhah A, Casas V, Sheha H, Raju VK, Tseng SC. Role of conjunctival inflammation in surgical outcome after amniotic membrane transplantation with or without fibrin glue for pterygium. ***Cornea*** 2008; 27: 56-63.
16. Jiang J, Yang Y, Zhang M, Fu X, Bao X, Yao K. Comparison of fibrin sealant and sutures for conjunctival autograft fixation in pterygium surgery: one-year follow-up. ***Ophthalmologica*** 2008; 222: 105-111.

17. Koranyi G, Seregard S, Kopp ED. Cut and paste: a no suture, small incision approach to pterygium surgery. ***Br J Ophthalmol*** 2005; 89: 392.
18. Karalezli A, Kucukerdonmez C, Akova YA, Altan-Yaycioglu R, Borazan M. Fibrin glue versus sutures for conjunctival autografting in pterygium surgery: a prospective comparative study. ***Br J Ophthalmol*** 2008; 92: 1206-1210.
19. Kim HH, Mun HJ, Park YJ, Lee KW, Shin JP. Conjunctivolimbal autograft using a fibrin adhesive in pterygium surgery. ***Korean J Ophthalmol*** 2008; 22: 147-154.
20. Srinivasan S, Dollin M, McAllum P, Berger Y, Rootman DS, Slomovic AR. Fibrin glue versus sutures for attaching the conjunctival autograft in pterygium surgery: a prospective observer masked clinical trial. ***Br J Ophthalmol*** 2009; 93: 215-218.
21. Marticornea J, Rodriguez-Ares MT, Tourino R, Mera P, Valladares MJ, Martinez-de-la-casa JM, et al. Pterygium surgery;conjunctival autograft using a fibrin adhesive. ***Cornea*** 2006; 25: 34-36.
22. Uy HS, Reyes JM,Flores JD, Lim-Bon-Siong R. Comparison of fibrin glue and sutures for attaching conjunctival autografts after pterygium excision. ***Ophthalmology*** 2005; 112: 667-671.
23. Ozdamar Y, Mutevelli S, Han U, Ileri D, Onal B, Ilhan O, et al. A comparative study of tissue glue and vicryl suture for closing limbal-conjunctival autografts and histologic evaluation after pterygium excision. ***Cornea*** 2008; 27: 552-558.
24. Sarnicola V, Vannozzi L, Motolese PA. Recurrence Rate Using Fibrin Glue-Assisted Ipsilateral Conjunctival Autograft in Pterygium Surgery: 2-Year Follow-up. ***Cornea*** 2010; 5. [Epub ahead of print]
25. Ratnalingam V, Eu AL, Ng GL, Taharin R, John E. Fibrin adhesive is better than sutures in pterygium. ***Cornea*** 2010; 29: 485-489.
26. Por YM, Tan DT. Assessment of fibrin glue in pterygium surgery. ***Cornea*** 2010; 29: 1-4.
27. Hall RC, Logan AJ, Wells AP. Comparison of fibrin glue with sutures for pterygium excision surgery with conjunctival autografts. ***Clin Experiment Ophthalmol*** 2009; 37: 584-589.
28. Wong DL, Hockenberry-Eaton M, Wilson D, Winkelstein ML, Schwartz P, editors. Wong's Essentials of Pediatric Nursing. 6th ed. St. Louis: Mosby; 2001. p.1301.
29. Maini R, Collison DJ, Maidment JM, Davies PD, Wormstone IM. Pterygial derived fibroblasts express functionally active histamine and epidermal growth factor receptors. ***Exp Eye Res*** 2002; 74: 237-244.
30. Kria L, Ohira A, Amemiya T. Growth factors in cultured pterygium fibroblasts: immunohistochemical and ELISA analysis. ***Graefes Arch Clin Exp Ophthalmol*** 1998; 236: 702-708.

Related topics

Haider TA, Al-Amin LM, Bamashmus MA, Ali SF. Ninety degree conjunctival rotation autograft versus zero and 180 degree rotation autograft for pterygium surgery. ***Saudi Med J*** 2009; 30: 519-523.

Al-Abdulkareem A. Treatment of chronic fistula-in-ano using commercial fibrin glue. ***Saudi Med J*** 2004; 25: 1127-1128.

Tinay OE, El-Bakry AA. Treatment of chronic fistula-in-ano using commercial fibrin glue. ***Saudi Med J*** 2003; 24: 1116-1117.

Meo SA, Al-Khlaiwi T. Health hazards of welding fumes. ***Saudi Med J*** 2003; 24: 1176-1182.