

Long Term Follow Up Results of Pterygium Excision with Conjunctival Autograft using Fibrin Glue: A Retrospective Study

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Purpose: To determine the long term follow up results and recurrence rates after pterygium excision with conjunctival autograft using fibrin glue.

Methods: A total of 1439 eyes operated for pterygium were retrospectively evaluated for recurrence rates and postoperative complications. Of 1434 patients, 1346 had primary pterygium, of which 1276 had nasal pterygium and 70 patients had both nasal and temporal pterygium, 93 patients had recurrent pterygium. All patients were operated using conjunctival autograft using fibrin glue and followed up for recurrences. Only cases with minimum of 6 months follow up were included in the study.

Abstract

Results: The mean recurrence rate in the primary pterygium group was 0.89% (n=12 of 1346) and in the recurrent pterygium group, it was 12.9% (n=12 of 93). An overwhelming majority of conjunctival grafts were secured adequately with fibrin glue, with postoperative complications like graft displacement noted in only 0.48%(n=7). Other complications like donor site granuloma were noted in 2.36% (n=34) patients.

Conclusion: Use of fibrin glue for securing conjunctival autografts reduces recurrence rates significantly and is safe due to fewer postoperative complications.

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Keywords: Pterygium, Fibrin glue, Conjunctival autograft

Introduction

Pterygium is a fibrovascular wing of tissue extending onto the cornea. This disease is more commonly seen in tropical countries where exposure to UV sunlight is high.^{1,2} The primary outcome measure of a successful pterygium surgery is low recurrence. Several surgical techniques have been developed to decrease recurrence rates, these include beta – radiation, excimer laser and antimetabolite drugs to prevent return of pterygium but these may sometimes be associated with serious complications. Conjunctival autografting after pterygium excision is associated with lower recurrence rates (2%–9%) and relatively few sight-threatening complications³⁻⁵ and has become the standard of surgery. The most common method of securing conjunctival autografts to the sclera is by suturing. Recently, fibrin glue was reported as being a successful alternative to conventional suturing in ocular surgery.⁶

Tissue adhesives are alternative means for attaching conjunctival grafts and shorten the operating time, improve postoperative comfort, and avoid suture-related complications.^{7,8} In the present study, we retrospectively studied the safety and efficacy of fibrin glue and rate of recurrence after conjunctival auto graft secured with fibrin glue for pterygium surgery.

Materials and Methods

We conducted a retrospective study of 1434 patients from our hospital between January 2009-December 2017 who underwent pterygium excision and conjunctival autografting with fibrin glue. The pterygium were grouped into primary pterygium and recurrent pterygium groups. The surgical procedures were performed by 5 surgeons. The primary

outcome measure was to define the recurrence rate using this surgical technique. Ethical clearance was obtained from the Institutional review board of our hospital.

Surgical Technique

The surgical procedures were performed by 5 surgeons. All patients received peribulbar anaesthesia with 2% lignocaine for the surgery. The pterygium was cut near the neck at the limbus and head severed off the cornea using Hoskins forceps. Fibrovascular tissue underlying the pterygium was exposed and dissected up to point of insertion of medial rectus and then excised with Westcott conjunctival scissors. The conjunctival defect was measured and free conjunctival autograft of the same size was harvested from the ipsilateral superior conjunctiva with Westcott scissors and Hoskins forceps. Minimum inclusion of Tenon's tissue was ensured to have a thin tension free graft which does not retract and shrink after surgery.

The graft was then rotated onto the area of bare sclera with care taken to match limbal tissue to limbus. The two components of glue were separated in two syringes and the fibrinogen and thrombin component were placed underneath the graft and the graft was ironed. Excess glue was trimmed away and the grafts were confirmed to have good adherence.

Post operatively, the patients were started on steroid & antibiotic drops six times daily which were gradually tapered over a duration of six weeks and lubricants four to six times a day. Topical cyclosporine 0.1% was used twice daily for three months in recurrent pterygium cases. Patients were followed up for a minimum duration of six months and then every year for any signs of recurrence. Recurrence

was defined as any fibrovascular growth two mm past the corneoscleral limbus onto the clear cornea. Time to recurrence was also studied.

Statistical Analysis

Recurrence was considered as the primary outcome variable. Study group type (Primary pterygium vs recurrent pterygium) were considered as Primary explanatory variable. Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency and proportion for categorical variables. All quantitative variables were checked for normal distribution within each category of explanatory variable by using visual inspection of histograms and normality Q-Q plots. Shapiro- Wilk test was also conducted to assess normal distribution and a p value of >0.05 was considered as normal distribution. For normally distributed quantitative parameters, the mean values were compared between the study groups using Independent sample t-test (2 groups). Categorical outcomes were compared between study groups using Chi square test. A p value < 0.05 was considered statistically significant. IBM SPSS version 22 was used for statistical analysis.⁹

Results

The cohort of 1439 patients consisted of 764 males and 675 females. There were 1346 (93.54%) primary pterygium patients, of which, 1276 had nasal pterygium and 70 patients had both nasal and temporal pterygium, 93 (6.46%) had a recurrent pterygium (for all, this was the first recurrence). The mean age of the population was 46.83 ± 13.32 years, the minimum age was 17 years and maximum age was 83 years (95% CI 46.14 to 47.52). The mean follow up was 3.2 years (maximum of six years and minimum of six months). Details are given in Table 1.

Table 1: Demographic data and descriptive analysis of age, gender, recurrence and time to recurrence in primary and recurrent pterygium

	Primary pterygium	Recurrent pterygium
Total (N=1439)	N=1346 (93.54%)	N=93 (6.46%)
Male	N=705 (52.37%)	N=59 (63.44%)
Female	N=641 (47.62%)	N=34 (36.55%)
Mean age	47.44 ± 13.26 years	38.04 ± 10.98 years
Recurrence rate	0.89% (N=12)	12.90% (N=12)
Time to recurrence	8-12 months	3-6 months

The primary pterygium group had 12 recurrences (0.89%, n=12 of 1346) of which, six were male and six were female patients and the mean age was 47.44 ± 13.26 years. The recurrence was noted to occur between 8-12 months. The recurrent pterygium group had 12 recurrences (12.9%, n=12 of 93) of which seven were male, five were female patients and the mean age of patients was 38.04 ± 10.98 years. Time to recurrence was noted as 3-6 months in this group. The difference in the proportion of recurrence and mean age between primary and recurrent pterygium groups was statistically significant (P value < 0.001). Details are given in Table 2.

Post-operative complications like displaced graft were seen in seven eyes (0.48%) operated with fibrin glue. Patients were reassured and taken for repair wherein the excess glue was trimmed off and the graft repositioned. Donor site complications like Tenon's granuloma was noted in 34 eyes (2.36%), of which eight were excised and no recurrence was seen and the others resolved with steroid use. No case of graft loss was noted in this study. No adverse events from the use of fibrin glue like anaphylactic reaction were observed.

Table 2: Comparison between primary and recurrent pterygium (N=1439)

	Type		P-value
	Primary pterygium (N=1346)	Recurrent pterygium (N=93)	
Recurrence			
Yes	12 (0.89%)	12 (12.90%)	<0.001
No	1334 (99.10%)	81 (87.09%)	
Age (Mean \pm SD)	47.44 ± 13.26	38.04 ± 10.98	<0.001

SD=Standard Deviation

Discussion

Tissue adhesives have a wide range of application in ophthalmology as an alternative to sutures. Fibrin glue has previously been used in ophthalmology for conjunctival wound closure, cataract surgery, oculoplasty and orbital surgery, repair of leaking glaucoma filtering blebs, lamellar keratoplasty, and attachment of an amniotic membrane patch.¹⁰⁻¹⁶

Various surgical techniques have been described for pterygium excision. Current surgical techniques to prevent pterygium recurrence include conjunctival autograft, limbal and limbal-conjunctival transplant, conjunctival flap and conjunctival rotation autograft surgery, amniotic membrane transplant, cultivated conjunctival transplant, lamellar keratoplasty, and the use of fibrin glue.¹⁷ Kenyon et al introduced the surgical technique of using conjunctival autograft in the management of primary advanced and recurrent pterygium.³ Although more time-consuming, this technique was found to be safe and effective in reducing the number of recurrences while avoiding the risk of potentially serious complications.^{4,5} Traditionally, during pterygium surgery the conjunctival autografts are secured in place with either absorbable or non-absorbable sutures. Tisseel (Tisseel, Baxter Corporation, Mississauga, Canada) is a two-component tissue adhesive which mimics the natural fibrin formation. The use of fibrin glue during pterygium surgery was first described by Cohen et al in 1993.⁷ Since then, there have been several reports on the safety and efficacy of fibrin glue during pterygium surgery.^{8,18,19}

To the best of our knowledge, this is the largest and longest retrospective study evaluating recurrence rates after conjunctival autografting with glue for pterygium excision. The study lends further evidence that use of conjunctival autograft in conjunction with fibrin glue reduces recurrences. Fibrin glue accelerates the normal process of fibrin formation by creating strong adherence of graft to underlying episclera

within minutes of application. Koranyi et al²⁰ proposed that the immediate adhesion of the entire graft provided by the glue may help to inhibit the proliferation of the fibroblasts of adjacent Tenon's tissue and therefore contribute to reducing the recurrence rate. The extensive contact of the grafted tissue with the entire underlying surface, provided by the use of fibrin glue, facilitates earlier vascularization of the graft, and hence its viability. This more rapid healing process may prevent further fibroblast migration from adjacent tissues. Koranyi et al reported their findings in a randomized control trial comparing fibrin glue with conventional sutures in 43 cases of pterygium autografting, in which surgery time and postoperative discomfort was significantly reduced in those patients receiving fibrin glue.

Evidence suggests that increased ocular surface inflammation during the postoperative period may increase the risk of pterygium recurrence.^{8,21,22} Suturing may cause additional trauma to the surgical site and up-regulate the post-operative reparative inflammation. Use of fibrin glue for conjunctival autograft fixation has reduced operating time, patient discomfort and lower reported recurrence and complications.^{23,24}

Of the 1439 patients who were included in the study, 764 were male and 675 were female. This is not surprising as men tend to be more involved in outdoor activity and hence are exposed to greater ultraviolet radiation. The mean age of the patients was 46.83 ± 13.32 years. Age has also been implicated with recurrence, more commonly seen in younger age-groups, the highest incidence occurs between ages of 20 and 49 years.²⁵ However, this may be because of the fact that younger age-groups tend to have thicker pterygium before surgery.

With regards to type of pterygium, the majority of our patients had primary nasal pterygium (n=1346, of which 1276 had primary nasal pterygium and 70 cases had combined nasal and temporal pterygium), 93 had recurrent pterygium. In this large retrospective study, we have found that the recurrence rate in primary pterygium group using fibrin glue was 0.89% and in the recurrent pterygium group with fibrin glue, it was 12.9%. This correlated with a study by Masters et al²⁶ in which recurrence rate was 0.57% in primary pterygium and 6.9% in recurrent pterygium. In a study by Ti et al,²⁷ the overall mean recurrence rates for conjunctival autografting was 20.8% and 31.2% for primary and recurrent groups respectively. In another large retrospective study by Koranyi et al²⁰ in 461 eyes and long follow up of 6-12 months, the recurrence rate was 5.34% in the glue group and 13.5% with sutures. Another randomised clinical trial by Ratnalingam et al²⁸ reported a recurrence rate of 4.41% with fibrin glue and 15.9% with sutures. The reduction in recurrence rate is believed to be due to less postoperative inflammation. Since this was a retrospective study, data on pre-operative pterygium morphology was inadequately recorded and it is possible that recurrence rates would be higher in cases with pterygium having more aggressive morphology.

The time to recurrence was also studied in this retrospective study. The recurrence in the primary pterygium group occurred within 8-12 months and in recurrent pterygium

group at 3-6 months. Ti et al²⁷ reported 29 recurrences in the primary pterygium group, 25 (86%) and 27 (93%) had recurred by 6 and 9 months after surgery respectively. In the recurrent pterygium group, 17 out of 20 (85%) had recurred by 6 months, with a total of 18 cases (90%) by 9 months. That is, most recurrences following conjunctival autografting tend to occur early, within 6 months of surgery. In another study, Hirst²⁸ reported that the recurrence occurs within 4 months in 50% cases and within 1 year in 97% of cases. The recurrences happen more quickly with each subsequent removal, regardless of type of surgery, and raises the probability that there may be a host specific resistance to regrowth that surgical removal may destroy.

In this large retrospective study, no sight threatening complications developed. We observed graft displacement in 7 eyes, these were taken to OT for repair and no recurrence was noted during follow up. There were no cases of graft loss in our study. Other complications like donor site granuloma was noted in 34 (2.36%) eyes in the follow up period, of which 8 were excised and no recurrence was seen and the others resolved with steroid use.

A recent study²⁷ reported that the success rate of sutured conjunctival autograft can vary widely among different surgeons (range, 5%–82%). This variability was attributed to significant learning curves and different surgical skill levels among different ophthalmologists. Because the use of fibrin glue removes the need for the tedious suturing process, the learning curve can be shortened, and better results may be more consistently achieved despite differences in surgical expertise. Five surgeons were involved in this study, the individual technique may vary but the overall very low recurrence rate demonstrates the universal applicability of this technique. de Wit et al³⁰ described another technique of sutureless and glueless technique of conjunctival autograft in a case series and concluded that it provides good cosmesis and no post-operative complications. This technique of sutureless and glueless technique was used by Jain et al³¹ which demonstrated the rate of recurrence of pterygium to be same in sutureless and glueless conjunctival autograft and conjunctival autograft with glue but graft displacement and retraction were more in the former group, thus making fibrin glue usage for securing conjunctival autograft a more safe technique.

However, the main disadvantage of fibrin glue is its cost. Fibrin glue comes in ready to use pack. The cost of fibrin glue is 10000 INR for two millilitres. Our practice is to pool and schedule pterygium patients on the same day. By use of sterile techniques, the same preparation can be divided into aliquots and used without cross contamination. By dividing it, we can reduce the cost to 1000 which is ten times less.

To the best of our knowledge, this is the largest retrospective study demonstrating the recurrence rate in pterygium surgery with fibrin glue. The low recurrence rate shows low inter-surgeon variability of this technique and its universal applicability. Another strength is the follow up period. All cases had minimal follow up of 6 months and an average follow up of 3.2 years. The limitation of this study is that it is a retrospective series without a control group.

Conclusion

It has been proven by many studies that pterygium excision with conjunctival autograft decreases recurrences, but usage of glue seems to decrease this further. This large retrospective study showed that primary pterygium excision with conjunctival autograft using fibrin glue reduces recurrences significantly in primary pterygium. Recurrent pterygium is more at risk for recurrences despite reduced inflammation with fibrin glue due to various host factors and aggressive morphology of pterygium. Due to the long term safety and incidence of very few complications with fibrin glue in pterygium surgery, we suggest use of fibrin glue as a sutureless preferred technique of pterygium surgery.

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