



FIBRIN GLUE VERSUS AUTOLOGOUS BLOOD FOR FIXATION OF CONJUNCTIVAL AUTOGRAFT IN PTERYGIUM SURGERY

Ophthalmology

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ABSTRACT

Purpose: To compare mean surgical time and graft outcomes following pterygium excision and conjunctival autograft fixation using patient's in situ autologous blood or standard fibrin glue-assisted conjunctival autograft adhesion. **Methods:** Outcomes of 44 eyes which underwent pterygium excision and conjunctival autograft with autologous blood (group I) were compared with 41 eyes that underwent fibrin glue-assisted conjunctival autograft (group II). Average time required for surgery and graft behaviour was noted in subsequent follow ups over 3 months. Results were compared between both groups. **Results:** The two groups were similar regarding age and gender. Mean surgical time required for group II was significantly higher than that of group I (23.00 ± 1.71 min, group I; 26.37 ± 3.73 min, group II; P -value < 0.001). Graft behaviour was analysed by noting incidence of graft edema, graft retraction, subconjunctival haemorrhage and recurrence at the end of 3 months. Incidence of graft edema at day 1, day 3 and day 7 did not differ significantly between two study groups (P -value > 0.05). Postoperatively, subconjunctival haemorrhage was seen in 54.5% and 53.7% cases in group I and group II respectively. At the end of day 21, none of the cases from either groups had any significant graft edema or subconjunctival haemorrhage. Incidence of graft retraction at day 1 and day 3 was significantly higher in Group I as compared to Group II (P -value < 0.05 for all). However, none of the cases required any intervention for the same. No cases of graft loss or graft granuloma formation were noted in either groups in all the follow-ups. Recurrence rates of 2 cases (4.5%) and 3 cases (7.3%) were seen in group I and group II respectively at the end of 3 months. **Conclusion:** The technique employing the use of autologous blood for conjunctival autograft fixation in pterygium surgery has provided safe and comparable results to fibrin glue. In terms of recurrence also, autologous blood is not inferior to fibrin glue in pterygium surgery. Autologous blood can be an excellent replacement for fibrin glue.

KEYWORDS

pterygium, conjunctival autograft, fibrin glue, autologous blood, recurrence, graft edema

INTRODUCTION

Pterygium, meaning wing in Greek, derived from the word "pterygion", is a wing-shaped, fibrovascular overgrowth arising from subconjunctival tissue extending across the limbus onto the cornea [1]. The mainstay for the management of pterygium is surgical. The initially employed bare sclera technique was faced with the major challenge of pterygium recurrence. In 1985, Kenyon et al proposed that in the treatment of pterygium, a conjunctival autograft could be used to cover the bare sclera [2].

Surgically, this autograft can be secured in place by sutures. To halt the suture-related complications, recently, fibrin glue and autologous blood, the newer suture-less alternatives have become available.

Fibrin glue has its limitations due to higher expenses, potential risk of transmission of infections, hypersensitivity reactions and lack of availability universally. Therefore, we undertook this study to compare the efficacy of fibrin glue and autologous blood as a means to secure the conjunctival autograft.

MATERIAL AND METHODS

Patients: A total of 100 patients of both genders, 18 and above years of age, with primary pterygia, who were advised surgery were considered for enrolment in the study.

Exclusion Criteria

- subjects not willing to participate in the study
- subjects with recurrent pterygium
- significant ocular surface disease
- subjects with known hypersensitivity to any component of fibrin glue

- subjects with limbal stem cell deficiency or loss due to mechanical or chemical trauma
- patients on anticoagulants or antiplatelet agents
- known bleeding or coagulation disorder

Design

A single-centre, prospective, randomised trial. Institutional Ethics Committee approval was attained and informed consent obtained from all participants.

The study took place at a tertiary care centre in Maharashtra, India, from October 2019 to October 2021.

Enrolled patients were alternately assigned into two groups as — Group I (45 eyes) underwent conjunctival autograft with autologous blood. Group II (45 eyes) underwent conjunctival autograft with fibrin glue.

Preoperative Assessment

Before surgery, all patients underwent Snellen visual acuity documentation, intraocular pressure assessment, slit-lamp biomicroscopy, and fundus examination. Refraction and keratometry assessment was done whenever required.

All surgeries were performed by the same surgeon under local anaesthesia (peribulbar block). Topical proparacaine 0.5% was instilled into the eye to be operated. The surgical field was cleaned with povidone–iodine 5%, the area draped, and a lid speculum inserted into the eye.

Intraoperative Steps

A superior rectus bridle suture was taken to aid adequate exposure of superior bulbar conjunctiva when needed. The head of pterygium was dissected from the cornea toward the limbus using a crescent blade. Body of pterygium was excised and the surrounding Tenon tissue was removed as much as possible, with care taken not to damage the underlying recti. Haemostasis was secured by applying pressure with only a cotton bud. Cautery was not used. Residual fibrous tissue on the cornea was removed with a Crescent blade.

The area of bare sclera was measured with a Vernier calliper, and a corresponding sized graft was harvested from the superior bulbar conjunctiva. The bulbar conjunctiva was dissected carefully without swelling it up with subconjunctival anaesthesia, as it may lead to dissection in the wrong plane. Once a thin Tenon-free graft with a fair limbal rim was obtained, it was oriented correspondingly on the cornea adjacent to the wound. Blunt tipped forceps were used to avoid button holing of graft at any point.

Conjunctival Autograft With Fibrin Adhesive

The thrombin and fibrinogen components prepared at the start of surgery were drawn into 2 separate 1-mL syringes. The time required for reconstitution of fibrin glue at the beginning of surgery was included in the overall time required for the procedure. One drop of the thrombin component followed by a drop of the protein solution was placed on the scleral bed. The graft was slid over the bare sclera, ensuring epithelium side up and the limbal edge toward the cornea. The graft was then pressed gently, edges crimped together and left to dry for 2 minutes before removing the lid speculum. The cornea was covered with wet sponge to protect the macula from phototoxicity.

Conjunctival Autograft With Autologous Blood

A homogenous blood film was allowed to form on the scleral bed. In cases in which the blood film was exceptionally thin or clot formation was premature, a fresh blood film was created by purposefully pricking the scleral capillaries with a 20-G needle. The graft was then slid over the bare sclera, taking into consideration the orientation of the graft at all times, pressed gently and left for a minimum of 4 minutes, using the normal clotting time of 4 to 10 minutes as a guide. The graft edges were crimped together. Extra time was taken in cases where the graft was found loose.

While waiting for the adhesion, care was taken to ensure that excessive and prolonged bleeding did not displace the graft from the bed, and residual active haemorrhages beneath the graft, if any, were tamponaded by direct compression with a blunt instrument.

Donor site bare sclera was covered by gentle traction on the adjacent conjunctiva.

For all cases, the graft was checked and confirmed to be intact after removal of the lid speculum. Moxifloxacin eyedrop was applied into the eye, the lids were closed and the eye was pressure bandaged for 24 hours.

Follow-up

The first postoperative evaluation was done after 24 hrs and all patients were treated with topical antibiotics (eyedrop Moxifloxacin 0.5%), steroid (eyedrop Prednisolone acetate 1%) 4 times a day for 7 days which was tapered over 4 weeks and a lubricant (eyedrop HPMC 0.5%) 4 times a day for 4 weeks.

Patients were followed up for a period of 3 months (day 1, 3, 7, 21, 45, 90).

Graft success was defined as an intact graft by the end of 6 weeks after operation.

Graft loss was defined as complete absence of graft from the host site on any of the follow-ups.

Graft retraction was defined as gaping between graft and host conjunctiva of at least 1mm.

Recurrence was defined as 'the formation of a wing of fibrovascular tissue occurring at the position of a previously excised pterygium with the apex crossing the limbus and extending onto the cornea, 'as distinct from' simple vascularisation of the corneal stroma [3].

It was ensured that the follow-up schedule be strictly adhered to by

appropriate, adequate and multiple reminders whenever necessary from our doctors, to each enrolled participant.

Statistical Data Analysis

The inter-group statistical comparison of distribution of categorical variables is tested using Chi-Square test or Fisher's exact probability test if more than 20% cells have expected frequency less than 5. The inter-group statistical comparison of means of continuous variables is done using independent sample t test. The underlying normality assumption was tested before subjecting the study variables to t test. In the entire study, the p-values less than 0.05 are considered to be statistically significant. All hypotheses were formulated using two tailed alternatives against each null hypothesis (hypothesis of no difference). The entire data is statistically analysed using Statistical Package for Social Sciences (SPSS Ver 22.0, IBM Corporation, USA) for MS Windows [4-6].

RESULTS

Figure 1 shows the number of patients and dropouts at each stage. So, the final analysis had 85 eyes—Group I n=44 and group II n=41.

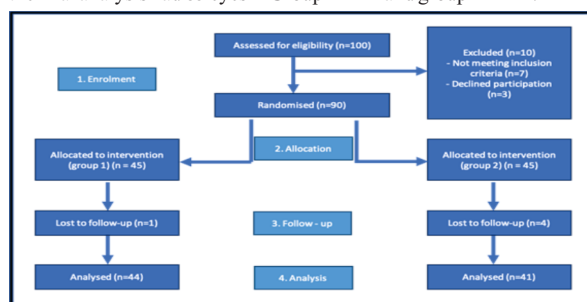


Figure 1 – Consort Diagram

Table 1 – Demographic data

	Group 1 (n=44)	Group 2 (n=41)
Age (years) (mean SD)	48.41 12.20	47.80 11.18
Male	25	22
Female	19	19
Right eye operated	28	22
Left eye operated	16	19

Table 1 summarises the patient demographics in the two groups which were comparable.

Table 2 – Inter-group comparison of mean time duration of surgery

Time (Min)	Group 1 (n=44)	Group 2 (n=41)	P-value
Time (Min) (mean SD)	23.00 1.71	26.37 3.73	0.001

P-value<0.05 is considered to be statistically significant.

Table 2 summarises the mean surgical time required in both groups.

The surgical time required for fibrin glue group was significantly higher than that of autologous blood group.

Table 3- Inter-group comparisons of incidence of Graft edema

Graft edema	Group 1 (n=44)		Group 2 (n=41)		P-value [Inter-group]
	n	%	n	%	
Day 1	4	9.1	5	12.2	0.733NS
Day 3	3	6.8	4	9.8	0.707NS
Day 7	2	4.5	2	4.9	0.999NS
Day 21	0	0.0	0	0.0	0.999NS

P-value<0.05 is considered to be statistically significant. NS – Statistically non-significant.

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Table 3 shows the incidence of graft edema in both the groups on days 1, 3, 7 and 21. It can be noted that there was absence of graft edema in both the groups on day 21.

Incidence of graft edema at day 1, day 3 and day 7 did not differ significantly between two study groups (P-value>0.05).

Table 4 – Inter-group comparisons of incidence of Subconjunctival haemorrhage

Subconjunctival haemorrhage	Group 1 (n=44)		Group 2 (n=41)		P-value [Inter- group]
	n	%	n	%	

Day 1	24	54.5	22	53.7	0.935NS
Day 3	24	54.5	24	58.5	0.711NS
Day 7	22	50.0	20	48.8	0.999NS
Day 21	0	0.0	0	0.0	0.999NS

P-value<0.05 is considered to be statistically significant. NS – Statistically non-significant.

Table 4 summarises the incidence of subconjunctival haemorrhage in both the groups.

Subconjunctival haemorrhage was seen in 54.5% and 53.7% cases in autologous blood and fibrin group respectively. At the end of day 21, none of the cases from either autologous group or fibrin group had any subconjunctival haemorrhage.

Table 5 – Inter-group comparisons of incidence of Graft retraction.

Retraction	Group 1 (n=44)		Group 2 (n=41)		P-value [Inter-group]
	n	%	n	%	
Day 1	28	63.6	16	39.0	0.023*
Day 3	14	31.8	4	9.8	0.017*
Day 7	4	9.1	4	9.8	0.999NS
Day 21	0	0.0	0	0.0	0.999NS

Values are n (% of cases), P-value [Inter-group] by Chi-Square test. P-value<0.05 is considered to be statistically significant. *P-value<0.05, NS – Statistically non-significant.

Table 5 summarises the incidence of graft retraction in both the groups.

Distribution of incidence of graft retraction at day 1 and day 3 was significantly higher in Group 1 as compared to Group 2 (P-value<0.05 for all).

On day 1, Graft retraction rates of 63.6% and 39.00% were seen in autologous blood and fibrin group respectively. This reduced to 31.8% in autologous blood group and 9.8% in fibrin group on day 3. Further reduction to 9.1% and 9.8% was seen on day 7 in autologous blood and fibrin glue group respectively. Complete resolution of retraction was seen in both the groups on day 21 visit.

Table 6 – Inter-group comparisons of incidence of Recurrence

Recurrence	Group 1 (n=44)	Group 2 (n=41)	P-value [Inter-group]
Day 90	2 (4.5 %)	3 (7.3 %)	0.669NS

P-value<0.05 is considered to be statistically significant. NS – Statistically non-significant.

Table 6 summarises the incidence of recurrence in both the groups.

Recurrence rates of 4.5% and 7.3% were seen in autologous blood and fibrin group respectively. All the recurrences were noted on the 3 month follow up visit.

DISCUSSION

The surgical time required for fibrin glue group was significantly higher than that of autologous blood group. In contrast, a comparative study of 60 patients conducted by S. Kumar et al [7] reported lesser time for conjunctival autografting using fibrin glue.

Different surgeons have reported different waiting times for the graft to get attached to bare sclera in autologous blood group. It ranged from 3 minutes to 10 minutes. Average reported time was 6 minutes considering the clotting time of 4-10 minutes. In our study we waited for 4 minutes after placing the graft in autologous blood method. The time required for the graft adherence in fibrin glue was 2 minutes and the time required for preparation of glue was 5 minutes. Even though the reconstitution was done before the procedure, the time required for the same was included in the overall time required for the procedure.

Graft edema was present in 9.1% and 12.2 % cases of autologous and fibrin group respectively on day 1 which reduced on day 3 and day 7 with no cases of inflammation on day 21 in both the groups. It was not statistically significant on any of the days (p value>0.05 on all occasions). G. Rathi et al [8] found chemosis in 4% eyes in autologous blood group. This graft edema can be attributed to intra-operative trauma while handling tissue.

Subconjunctival haemorrhage was seen in 54.5% and 53.7% cases in autologous blood and fibrin group respectively. The difference was not

statistically significant (p value>0.05). This was more as compared to the study by S. Thatte et al [9] which showed a rate of 36% in autologous group and S. Kumar et al [7] which showed zero cases in fibrin group. The incidence of zero subconjunctival hemorrhage in fibrin group in the study by S. Kumar et al [7] can be attributed to the use of cautery before placement of graft.

A larger subconjunctival haemorrhage has been seen if more blood is allowed to ooze at the bare sclera before placing the autograft. It has also been attributed to cause graft dislodgement due to contraction of the clot.

Subconjunctival hemorrhage has also been hypothesized to occur more in autologous blood group as a result of clot retraction and fibrinolysis resulting in entanglement of red blood cells within the clot. It is lesser in fibrin glue group probably due to presence of aprotinin which would have delayed the clot lysis.

Graft retraction rates of 63.6% and 39.00% were seen in autologous blood and fibrin group respectively. It was more in autologous blood group and was statistically significant (p value=0.023). All the cases healed spontaneously without any surgical intervention.

This was almost double the rate seen by J. Bhatia et al [10] who reported Nasal gaping in 36% cases in their study of 205 cases of pterygium which were operated using autologous blood and almost 5 times the rate seen by S. Thatte et al [9] who reported graft retraction rate of 13.5% in 151 eyes.

The donor graft size taken in our study was of the exact same size as that of bare sclera in both the groups, i.e., autologous blood group and fibrin group. An oversized graft by 0.25 mm was taken in autologous blood group by K. Mittal et al. [11] However, they took same sized grafts for the fibrin glue group.

G. Nadarajah et al [12] in their study of 120 eyes have taken 1 mm oversized graft and undermined the edges underneath the conjunctiva. Another study involving 97 subjects by M. Sune et al [13] have used oversized graft of 1.5 to 2 mm larger size. This was done to reduce the graft retraction postoperatively.

It is unlikely that autologous blood is not as adhesive as fibrin glue because fibrin glue only mimics the last few stages of the coagulation cascade that concludes with formation of a stable fibrin clot. The increased rate of graft retraction in our study is probably due to not using oversized grafts as has been done in various other studies.

No cases of graft loss or granuloma formation were seen in our study. A prospective, non-comparative, interventional case series by S. Mitra et al [14] who studied 19 cases found similar results.

Recurrence rates of 4.5% and 7.3% were seen in autologous blood and fibrin group respectively. This was not statistically significant (p value>0.05). This was in concordance to studies conducted by N. Vichare et al [15] who found recurrence rate of 3.33% in fibrin glue group at the end of 6 months in their study of 60 patients with primary pterygium and A. Kurian et al [16] who observed a recurrence rate of 6.25% in autologous blood group and 8.16% in fibrin glue group at the end of 1 year in a study of 200 cases of pterygium.

We did not observe any intra-operative complications. A retrospective analysis of 2356 eyes done by S. K. Kodavoor et al [17] has reported graft tear in 27 cases and buttonholing of the graft in 13 cases. Other intraoperative complications like globe perforation, thinning of sclera or cornea, excessive bleeding and muscle injury have also been reported by other studies.

CONCLUSION

It can be noted from our study that the technique employing the use of autologous blood for fixation of autologous blood in pterygium surgery may prevent potential adverse reactions encountered with the use of foreign materials and in this small series provided safe and comparable results to the use of fibrin glue.

However, it should also be noted that complete pterygium tissue excision, adequate sized conjunctival autograft, thin graft with minimal tenons, proper orientation of the graft, complete coverage of the bare sclera with proper fixation of the graft to the sclera, preventing

post-operative inflammation are all prerequisites to minimise the complications.

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