

Randomized interventional trial comparing conjunctival autograft secured with Sutures versus fibrin glue in primary pterygium excision

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Abstract

Background: An ideal pterygium surgery should achieve three principal goals: a low recurrence rate, absence of complications, and satisfactory cosmesis. Natural substances, such as fibrin, have significant advantage in achieving these goals. **Aim:** To compare the primary & secondary outcomes following primary pterygium excision with conjunctival auto graft using fibrin glue versus sutures. **Methodology:** A prospective interventional study was conducted at Department of Ophthalmology, Annapoorana medical college & Hospital, Salem, India, for a period of one year from June 2016 to May 2017. A total of 87 patients were included in the study. They were randomized into two groups. Group I received conjunctival auto graft secured with glue and Group II received conjunctival auto graft secured with suture. Postoperatively the patients were followed for a period of 6 months for measuring the primary and secondary outcomes. **Results:** The mean rank score for graft inflammation, and patients discomfort was less in fibrin glue group when compared to suture group during the follow-up period from 15th to 90th postoperative day and the difference was found to be statistically significant, whereas the mean rank for graft stability was lower in the suture group when compared to the fibrin glue group with a statistical significant difference between the two group. **Conclusion:** 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.

Keywords: Fibro vascular, Conjunctival, Aetiology

Introduction

Pterygium is an encroachment of fibro vascular tissue from the bulbar conjunctiva onto the cornea [1]. Various mechanisms have been suggested by previous studies, including degeneration, oxidative stress, antiapoptosis, extra cellular matrix remodeling, immunologic mechanisms, angiogenesis, viral infections, and genetic factors [2-5].

An increased incidence of pterygium is noted in the tropics in an equatorial zone between 30 degrees north and south latitudes. Though exact aetiology is not

known, risk factors include genetic predisposition, chronic environmental irritations like dust, dryness, heat and ultraviolet rays [6,7]. The prevalence of pterygium in India was reported between 8 and 15% from various studies and globally the prevalence was ranging between 2 and 30% [8,9].

Common indications for surgical excision of the pterygium include impending or manifest loss of visual acuity or persistent discomfort despite medical therapy. Visual acuity may be diminished secondary to growth within the visual axis or due to astigmatism induced by the flattening effect of the pterygium on the cornea. Other indications for surgical intervention include

Manuscript received: 4th April 2018
Reviewed 14th April 2018
Author Corrected: 20th April 2018
Accepted for Publication: 24th April 2018

ocular motility restriction, dysplastic looking lesions or for cosmetic purposes. Pterygium surgery today can be divided into four main groups: Bare sclera excision, excision with conjunctival closure / transposition, excision with antimetabolic adjunctive therapy, ocular surface transplantation techniques [10].

An ideal pterygium surgery should achieve three principal goals: a low recurrence rate, absence of complications, and satisfactory cosmesis [11]. The results of pterygium surgery are compromised by recurrence of the pterygium in a significant number of cases [12].

Traditionally, during pterygium surgery the conjunctival autografts are secured in place with either absorbable or non-absorbable sutures. The sutures had led to various levels of discomfort to the patients and it was also associated with increased risk of inflammation.

Later tissue adhesives have been used for closing and apposing wound edges. Synthetic tissue adhesives, such as cyanoacrylate, induce sufficient fibrin cross-linking kinetics but its use was limited because of its direct tissue toxicity and the barrier effect [13]. Natural substances, such as fibrin, have significant advantage in terms of minimal tissue reaction. The use of fibrin glue for pterygium surgery was first described by Cohen et al in 1993 [14]. Since then various reports have been published regarding the safety and efficacy of fibrin glue in ophthalmic surgery.

As of today, very few studies were conducted in this part of India to compare the efficacy between fibrin glue and sutures for primary pterygium excision surgery with conjunctival limbal auto graft.

Aim

To compare the primary & secondary outcomes following primary pterygium excision with conjunctival auto graft using fibrin glue versus sutures.

Methodology

Study area: Department of Ophthalmology, Annapoorna medical college & Hospital, Salem, **Study design:** Prospective interventional study

Study period: one year from June 2016 to May 2017.

Sampling technique: simple random technique was followed for randomizing the subjects into two groups and purposive sampling was applied for determining the total study subjects.

Inclusion criteria: Men and women between 20 – 60 years of age requiring nasal pterygium excision for the first time were included for the study.

Exclusion criteria: Patients presenting with pseudo-terygium, recurrent pterygium, double headed pterygium (nasal and temporal), age group less than 20 years and more than 60 years, one eyed patient, patients with ocular surface pathology and collagen vascular disease, patients with visually significant cataract were excluded from the study.

Study procedure: The study was started after getting the clearance from the institutional ethical committee and the informed consent from the patients who had participated in the study. A total of 87 patients were included in the study. Through a computer generated random number table all the 87 patients were randomized into two groups. Group I (44 patients) received conjunctival auto graft secured with glue and Group II (43 patients) received conjunctival auto graft secured with suture.

The socio-demographic details was obtained from the patients and a complete ophthalmological examination including visual acuity assessment and refraction with Snellen's chart. Thorough examination of anterior segment was done with slit lamp biomicroscopy at each visit. Intraocular pressure was measured with non-contact tonometer before surgery & at 2 & 4 weeks after surgery. Keratometry reading was obtained using Bausch & Lomb manual keratometer preoperatively & at 1st / 3rd / 6th month. Fundus examination was done using slit lamp biomicroscope and 90D lens.

Patients with ocular pathology other than error of refraction, with a history of previous ocular surgery or trauma, narrow occludable angles, ocular hypertension, physiologic or glaucomatous optic disc cupping, a family history of glaucoma were excluded. Anterior segment photography was also taken preoperatively and on postoperative follow up visits. If any complications were encountered during follow up, photographic documentation was done. Pterygium grading was done according to morphology grading of Donald Tan, as T1, T2 and T3. Grade T1(atrophic)- pterygium in which episcleral vessels underlying the body of the pterygium were unobscured and clearly distinguished, Grade T3 (fleshy)- thick pterygium in which episcleral vessels underlying the body of the pterygium are totally obscured by fibrovascular tissue • Grade T2 (intermediate) - All other pterygia that do not fall into these two categories [15].

All cases were taken up under regional anesthesia. The pterygium was excised with Westcott scissors over the sclera and removed from the cornea with toothed forceps and crescent blade. The conjunctival donor graft site was marked on all sides with gentian violet to outline an oversized graft with an additional 1.0 mm of length and width relative to the dimensions of the graft bed.

The epithelial side was marked to prevent graft inversion. The free graft then was placed on top of the cornea and kept moist using sterile normal saline solution. The conjunctival graft was positioned on the cornea so that limbal edge matched the donor site.

Sutured auto grafts: The conjunctival graft was slid into position and sutured with multiple interrupted 8.0 Vicryl polyglactin sutures. The knots were not buried but cut short. A minimum of eight and maximum of 10 sutures were required.

Results

The age and gender wise distribution of the study subjects was shown in table 1. It is seen from the table that majority of the study subjects in both the groups are in the age group between 30 and 50 years and the mean age among both the suture group and the fibrin glue group were almost similar. Similarly the male and female distribution in both the groups also did not show a statistical significant difference (table 1). The pterygium grading was done based on Donald Tan system of grading and in our study subjects majority of the patients was in either grade II or grade III and no statistically significant difference was observed between the two groups with respect to grading of pterygium (table 2). The mean duration of surgery in suture group was found to be much longer (20.6 mins) than the fibrin glue group (12.2 mins) and the difference was found to be statistical significant (table 3). The various outcome measures which were measured during the follow up period was assessed by Man-whitney U test, in which the outcome measures were ranked and the mean rank was compared between the two groups and it is interpreted as lower the rank better the outcome. The mean rank score for graft inflammation, and patients discomfort was less in fibrin glue group when compared to suture group during the follow-up period from 15th to 90th postoperative day and the difference was found to be statistically significant, whereas the mean rank for graft stability was lower in the suture group when compared to the fibrin glue group with a statistical significant difference between the two group. During the 180th day examination no inflammation and patients discomfort was reported in both the groups whereas the graft stability score was almost similar in both the groups. Among the various complications reported donor site granuloma and suture granuloma was found to be higher in the suture group compared to the fibrin glue group and the difference was found to be statistically significant, where as the incidence of pyogenic granuloma was found to be higher in the fibrin glue group and other complications like reverse

Fibrin glued auto grafts: The scleral bed was dried and diathermy was used to cauterize any bleeding vessels. The fibrin glue was applied to the bed and the graft was slid across into position. The graft was manipulated during the first 30 seconds and then left untouched for the cure time of 3 minutes. Any excess glue was removed with a dry spear after the 3-minutes cure time and the graft was trimmed if necessary.

Post-operatively topical antibiotic-steroid drops were prescribed. Subjective sensations of pain, foreign body sensation, tearing, and discomfort were evaluated on the first postoperative day and on weeks 2, and on 1/ 3/ 6 months using a 5-point scale adapted from Lim-Bon-Siong et al [16]. The primary outcome measure was graft success and stability which was defined as presence of intact graft at six months after surgery. The secondary outcome measures are in terms of recurrence, complications and cosmetic appearance at the end of follow up.

Table-1: Age and gender wise distribution of the study subjects.

Age group	Group I (suture) (n=44)		Group II (fibrin glue) (n=43)		P value
	Male	Female	Male	Female	
21 – 30	5 (21.7%)	4 (19%)	4 (20%)	6 (26%)	0.318
31 – 40	8 (34.7%)	6 (28.5%)	6 (30%)	7 (30.4%)	0.621
41 – 50	9 (39.1%)	10 (47.6%)	9 (45%)	8 (34.7%)	0.581
51 – 60	1 (4.3%)	1 (4.7%)	1 (5%)	2 (8.6%)	0.319
Total	23 (100%)	21 (100%)	20 (100%)	23 (100%)	
Mean ± SD	44.5±6.4	42.6±6.8	41.4±5.2	43.5±5.8	0.486*

P value derived by chi-square test

* P value derived by student T test.

graft had occurred only in two patients in the fibrin glue group and all these complications had occurred between 15th and 30th day of the post-operative period. Among the patients in the suture group 3 patients reported with recurrence during the 180th day of follow-up and none of the patients in the fibrin glue group had recurrence and the difference was found to be statistically significant.

Table-2: Distribution of the study subjects based on the grading of pterygium.

Grading	Group I (suture) (n=44)	Group II (fibrin glue) (n=43)	P value
I	4 (9%)	6 (13.9%)	0.618
II	24 (54.5%)	20 (46.5%)	
III	16 (36.3%)	17 (39.5%)	
Total	44 (100%)	43 (100%)	

P value derived by chi-square test

Table-3: Comparison of mean surgery time between the two groups.

Duration of surgery in minutes	Group I (suture) (n=44) Mean ± SD	Group II (fibrin glue) (n=43) Mean ± SD	P value
Mean	20.67 ± 4.89	12.22 ± 3.12	<.0001
Min	10	8	
Max	30	19	

P value derived by student T test

Table-4: Outcome measures during the follow-up period among the two groups

Outcome measure	Group I (suture) (n=44)				Group II (fibrin glue) (n=43)				P value
	15 th day (mean rank)	30 th day (mean rank)	90 th day (mean rank)	180 th day (mean rank)	15 th day (mean rank)	30 th day (mean rank)	90 th day (mean rank)	180 th day (mean rank)	
Graft inflammation	31.54	28.2	24.89	No inflammation reported	18.41	21	24	No inflammation reported	<.0001
Graft stability	24.13	22.5	23.5	24	26.67	27.04	25.28	24.89	<.001
Patients discomfort	30.80	27.26	25.28	No discomfort	19.28	22.23	23.5	No discomfort	<.001

P value derived by applying Man-Whitney U test

Table-5: Incidence of the various complications occurred during the follow up period between the two groups

Complication	Group I (suture) (n=44)	Group II (fibrin glue) (n=43)	P value
Donor site granuloma	5 (11.3%)	0	<.001
Pyogenic granuloma	0	3 (6.9%)	<.01
Suture granuloma	8 (18.1%)	0	<.001
Reverse graft	0	2 (4.6%)	0.071
Sub-conjunctival hemorrhage	1 (2.2%)	2 (4.6%)	0.362
Recurrence	3 (6.8%)	0	<.001

P value derived by chi-square test

Discussions

The present study which was conducted on 87 patients had proved that using fibrin glue shortens the duration of surgery time and also the discomfort in patients during the post-operative period. The recurrence rate was also found to be lesser in the fibrin glue group than that of patients who had sutures for the treatment of pterygium. Koranyi et al published the first randomized trial that compared pterygium surgery with sutures to surgery with tissue glue (Tisseel Duo Quick).

Their study was only slightly smaller than this one (43 patients) and, as in this study they showed a significant reduction in surgical time in their glue group of 9.7 min versus 18.5 min with 7-0 Vicryl [17]. They also showed a significant reduction in average pain for all days in the first week.

There were no significant differences in outcomes at the end of the 6-month follow-up period. Uy et al published a small randomized trial of fibrin glue (Beriplast P) with 11 eyes per group in 2005 [18].

They described similar results to our study; reduced operating time and fewer postoperative symptoms. Bahar et al published a report in 2006 with 65 patients and confirmed decreased surgical time and reduced symptoms and signs out to day 10 [19]. Fibrin glue (Quixil) was used and compared with 8.0 Vicryl.

In the present study we found the graft stability is better in the suture group patients than that of the patients in the fibrin glue group and the similar results was also proven by Vichare et al in their study showed a (16%) retraction rate with tissue glue compared to (10%) with sutures and in another study by Milind Surayanshi reported an equal retraction in both the suture and fibrin glue group [20,21].

A slightly higher rate of graft retraction in the non-suture group in the present study can be due to movement of the graft, due to lid movement causing displacement of the graft and tissue glue is vulnerable to mechanical forces hence the importance of post-operative care must be explained to the patients in detail.

The present study had shown that the recurrence rate was higher among the suture group than the fibrin glue group and it was substantiated by a study done by B M Oswald et al where they had reported the recurrence rate of 5.3% for fibrin glue versus 13.5% for sutures and

he also quoted that the lesser incidence of recurrence in the fibrin glue group might be due to the immediate adherence of the graft and lack of post operative inflammation in glue technique which would inhibit fibroblast in-growth and reduce the recurrence [22]. Another study done by Alok Sati et al in their study of 90 eyes comparing the efficacy of three surgical methods of conjunctival autograft fixation in the treatment of pterygium using sutures, tissue glue and autologous blood had found a similar recurrence rate amongst the three groups ($p=0.585$) [23].

The added cost of the Tisseel glue compared with the cost of Vicryl sutures does not make it economically justifiable. These costs have been approximated to one glue cost equals four to five sutures cost in other countries. Koranyi suggests using the same Tisseel syringe on six to seven patients on the same operating list and using sterile techniques without the risk of cross-contamination would possibly reduce the cost or in par with the cost of the sutures [17].

Conclusion

To conclude both glued and sutured conjunctival auto grafting procedures are safe and effective methods for pterygium surgery. Given the savings in operating time and using one glue kit for six to seven patients, we believe that fibrin glue technique may be cost-effective overall. In addition, the decreased postoperative patient discomfort with fibrin glue is a significant advantage for up to 15 days.

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. A disadvantage is the possibility of complications like subconjunctival hemorrhage / granuloma / reduced graft stability in early postoperative period, but with good surgical technique and patient selection these could be minimized.

Current study adding to the existing knowledge:

Usage of fibrin glue for pterygium surgeries will add on to the more stability of the autograft rather than suturing.

Contributions by the authors

- Keerthivarman Rukmangathan (corresponding author) – designing the entire study

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- Dhivya Ramakrishnan, Vasudharini Sundararajan, Ranjan Chandrasekaran– Operating surgeons
- Ramusiddharthan Ravichandran– Preparing the manuscript
- Shankar Radhakrishnan– statistical analysis.

Funding: Nil, **Conflict of interest:** Nil

Permission from IRB: Yes

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How to cite this article?

Keerthivarman Rukmangathan, Dhivya Ramakrishnan, Vasudarini Sundararajan, Ranjan Chandrasekaran, Ramusiddharthan Ravichandran, Shankar Radhakrishnan. Randomized interventional trial comparing conjunctival autograft secured with Sutures versus fibrin glue in primary pterygium excision. *Trop J Ophthalmol Otolaryngol*.2018;3 (2):1-7. doi: 10.17511/jooo.2018.i02.01

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