Conjunctivolimbal autograft with and without Fibrin Adhesive in Pterygium Surgery

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Abstract: Aim: To compare between the use of biological fibrin adhesive and the current method of attaching conjunctivolimbal autograft with simple suturing during primary pterygium surgery. **Patients & methods:** Twenty-nine patients with thirty primary pterygia had pterygium excision using conjunctivolimbal autograft transplantation. They were classified into two groups regarding the method by which the transplanted conjunctivolimbal autograft was fixed as follows: Group I: Simple suturing was done for 15 eyes. Group II: Fibrin glue was done for 15 eyes. **Results:** Marked drop in tear production (around 10 mm) was reported in both groups and there was non significant statistical difference between both groups as regards the value of Schirmer's test (p-value > 0.05). Re-epithelialization of the corneal defect was complete in all cases of both groups by the end of the second postoperative week. There was marked reduction in the mean duration of surgery in group II (19.7±5.2 minutes) in comparison to 39.7 ± 3.9 minutes in group I. **Conclusion:** Fibrin glue is easy, safe and effective in fixing conjunctivolimbal autograft during primary pterygium excision. It reduces surgical time and is associated was less complications than simple suturing of the graft.

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1. Introduction

The recurrence of pterygium is closely associated with corneo-limbal stem cell deficiency, more severe conjunctival inflammation, corneal involvement, and adhesion with surrounding tissue than the primary pterygium[(1)].

Anti-metabolites such as mitomycin C (MMC) were introduced to prevent the recurrence of pterygium. The use of anti-metabolites is restricted by several complications including various ocular surface diseases, secondary glaucoma, and cataract[(2)].

The transplantation of conjunctivolimbal autograft (containing the limbal stem cells) was reported to be the most effective method of lowering recurrence rate (2-9%) and occurrence of complications. However, the suturing presents several disadvantages, including complicated surgical techniques, prolonged operating time, prolonged postoperative patient discomfort, and suture-related potential complications[(3)].

The use of tissue bio-adhesives as an alternative means of attaching the grafts may shorten operating time, improve postoperative discomfort, and possibly avoid suture-related complications [(4)].

The **aim** of this study was to compare between the use of biological fibrin adhesive and the current method of attaching conjunctivolimbal autograft with simple suturing during primary pterygium surgery considering mainly operating time, postoperative discomfort, and postoperative complications.

2. Patients and Methods

Twenty-nine patients with thirty pterygia were enrolled in this prospective study. All patients were attending the outpatient clinic of Al-Zahraa University Hospital over a period of 12 months, between October 2010 and October 2011.

All pterygia were primary, and all had pterygium excision using conjunctivolimbal autograft transplantation. They were classified into two groups regarding the method by which the transplanted conjunctivolimbal autograft was fixed as follows:

Group I: Pterygium excision using conjunctivolimbal autograft transplantation by simple suturing was done for 15 eyes.

Group II: Fifteen eyes had pterygium excision using conjunctivolimbal autograft transplantation by fibrin glue.

Patients with recurrent pterygium, pseudo pterygium and patients with any other ocular surface pathology were excluded.

All patients were subjected to complete preoperative ophthalmological examination including; visual acuity, refraction, slit lamp biomicroscopy to detect nature of pterygium, and tear film evaluation using Schirmer's test (Schirmer II).

Operative technique: All cases were operated upon using the surgical microscope under aseptic conditions, and all of them were managed on an outpatient bases.

Topical anesthesia was achieved by instillation of 0.4% benoxinate hydrochloride three

times at 5 minutes interval, together with subconjunctival infiltration anesthesia by injection of 2% lidocaine hydrochloride beneath the body of the pterygium and upper bulbar conjunctiva using 25-gauge needle.

Horizontal incisions were made with Westcott scissors in the bulbar conjunctiva above and below the body of the pterygium. The pterygium body was dissected from both the surface of the sclera and the overlaying conjunctiva by blunt dissection and then excised together with the involved conjunctiva and the underlying subconjunctival fibrovascular tissue and tenon's capsule. After dissecting the body off the sclera to the limbus with blunt Wescott scissors, the head is grasped with non-toothed Graefe forceps and avulsed off the cornea against counter pressure exerted at the opposite limbus. Any pterygial tissue left on the cornea was removed with a surgical blade. Hemostasis was insured by minimal cautery using bipolar diathermy when needed.

A graft about 0.5 mm larger in width than the excised area was taken from the superior temporal region, measured with Castroviejo calipers and the dissection was started from the conjunctival side to the limbus using Vannas scissors. Subconjunctival injection of local anesthetic was accomplished in the upper bulbar conjunctiva leading to ballooning of the conjunctiva and facilitated dissection. Care was taken to avoid dissecting the Tenon's in the graft as much as possible and to prevent buttonholes and graft rollover. The dissection was extended 0.5 mm to the adjacent cornea between two shallow radial incisions of both sides using disposable surgical knife. The graft was transferred to the excised pterygium site. Care should be taken to the proper orientation of the graft. Haemostasis using a bipolar cautery had been applied to the donor site when needed.

Fixation of the graft

Group I (suture group): In this group, the limbal portion of the graft was secured to the limbus with two 10-0 nylon sutures, followed by anchoring the conjunctival portion to the underlying episclera and surrounding conjunctiva by interrupted 8-0 virgin silk sutures.

Group II (fibrin group): In this group, the graft just after excision was placed on the cornea with the stromal side facing upwards. One drop of the thrombin component was placed on the scleral bed and one drop of the fibrinogen solution was put onto the graft. Thereafter, the graft coated with thrombin solution was then immediately flipped over and spread out onto the bare sclera coated with fibrinogen solution by using two McPherson forceps, and soon thrombin and fibrinogen reacted forming the fibrin glue to seal the donor graft to bare sclera. After the graft was positioned, there was about 30 seconds to smooth out the graft and press it gently to the scleral bed, attaching the graft firmly but not stiffly. Excess glue was removed and the graft was trimmed if necessary**.**

Postoperative treatment was 0.3% Ofloxacin antibiotic eye drops 4 times daily for two weeks, 0.1% dexamethasone eye drops 4 times daily for two weeks, and then tapered during the next two weeks, and 0.2% sodium hyaluronate eye drops 4 times daily for one month. Eye patching was continued until corneal epithelialization was complete.

Patients were followed-up for at least 3 months after pterygium excision. Postoperative follow-up data were collected on the follow up visits after one day, one week, two weeks, one month, two months and three months and one year after surgery.

At day 7, all sutures were removed in the suture group I. On each follow up visit a complete ocular evaluation (similar to that done preoperatively) was carried out with particular attention to symptomatic complaints of patients including: pain, foreign body sensation, tearing, and discomfort), visual acuity and slit-lamp examination for healing of the corneal and scleral beds of excised pterygia, graft transplantation and re-epithelization of the donor sites.

Graft survival was defined as an intact graft by the fourth week after surgery, and graft failure was defined as the absence of the graft by the fourth week while, recurrence was defined as any growth of fibrovascular tissue into the cornea by slit lamp examination[(1)].

3. Results

The study included 30 eyes with primary pterygia in 29 patients. Seventeen patients were males (58.6%) and twelve patients were females (41.4%). Twenty-eight patients (96.6%) were operated upon unilaterally and one patient (3.4%) had a bilateral surgery.

The thirty pterygia included in this study were randomized according to surgical technique involved, into two groups:

Group I: Surgical excision with conjunctivolimbal autograft transplantation by simple suturing (15 pterygia).

Group II: Surgical excision with conjunctivo-limbal autograft transplantation by fibrin glue (15 pterygia).

The mean age of the patients $\pm$ SD in group (I) was (44.3 ± 11.2years), which was (47.7 ± 10.8years) in group (II). There was no significant statistical difference between both groups concerning age (p> 0.05). Regarding sex difference between both groups, there was no significant statistical difference between them. (Each group contains 9 males and 6 females).

Pterygium is more commonly seen in outdoor workers than in those working indoors. 63.3% of the patients were working outdoors as manual workers, whereas 36.7% were indoor workers (Table 1).

Regarding pterygium grading, we used both the extent of corneal involvement margin [(5)], and pterygium translucency; the visibility of the underling episcleral blood vessels [(6)].

We found that there was a marked drop in tear production after surgery in both groups (Table 2), Schirmer's test was 10.7± 1.6 mm in group I, while it was 10.9 ± 1.2 mm in group II. There was no significant difference between both groups as regards the value of Schirmer's test (p-value > 0.05).

There was marked reduction in the mean duration of surgery in group II (19.7± 5.2minutes) in comparison to 39.7 ± 3.9 minutes in group I (suture group). There was also a marked reduction in the mean duration of graft fixation in both groups (Table 3 & Figure 1).

Symptoms as ocular pain, photophobia, lacrimation and foreign body sensation or any of them were experienced, to varying degree of severity during the postoperative follow-up period mainly during the first postoperative month. There was marked shortening of the mean duration of postoperative symptoms relieve in group II (2.5 ± 1.2 weeks), compared to 4.1± 1.4 weeks in group I, that was a statistically significant difference (p-value<0.05) (Table 4).

There was a relation between duration of postoperative discomfort relieves and the grading of pterygia according to translucency. This relation was found to be statistically significant (p-value < 0.05) (Table 5).

In the first week postoperatively, there was contraction of the conjunctivolimbal graft and gaping between the graft and adjacent conjunctiva. Mild to moderate degrees of edema of the graft were observed in all cases. In the second week postoperatively, the gap was obliterated and edema was absorbed. By the end of the first month postoperatively, blood vessels of the nasal conjunctiva appeared less engorged and the graft was less hyperemic. At the second month postoperatively, most cases showed disappearance of conjunctival hyperemia and there was faint scar marking the border of the graft.

Postoperative conjunctival injection was mainly localized around the graft. By the end of the first week, there was a slight increase in graft injection with minimal edema due to vascularization of the graft. The graft was mostly vacularized 3-5 days postoperatively from the surrounding conjunctiva and adjacent episclera. There was no failure in the vascularization of the grafts, except in one case in group (II) (fibrin glue group) in which graft rejection occurred (6.67%).

Graft injection gradually decreased by the end of the first month postoperatively. Prolonged conjunctival injection more than 2 months was noted in one eye in group (I) in which granuloma occurred (6.67%).

Re-epithelialization of the corneal defect was complete in all cases by the end of the second postoperative week. The donor sites from which the grafts were taken were completely re-epithelialized in all cases after two weeks without significant scarring. There were no Tenon's granulomas or other problems in the donor areas. In addition, grafts were completely fixed in 27 eyes (90%) out of the total 30 eyes, 13 eyes (86.7%) in group I and 14 eyes (93.3%) in group II, while there were two eyes (13.3%) with partial graft dehiscent in group I with spontaneous healing by the end of the second month and no reoperation was needed. One eye (6.7%) in group (II) showed graft rejection at the first postoperative day.

The best corrected visual acuity (by decimal system) at three months postoperatively showed no significant changes in the majority of cases in the two groups. In group (I), the mean value of reduced astigmatism was 2.4 ± 1.8 diopters, while it was 1.9 ± 0.9 diopters in group (II). It is a definite reduction in the astigmatic diopteric power, but the difference between both values in the two groups was found to be of no statistical significance (p > 0.05)

There were two cases (6.7%) of recurrence, one in each group. In group I, recurrence (6.7%) was noted at the third postoperative month. In group II, recurrence (6.7%) was noted 6 month postoperatively. There was no difference in recurrence rate regarding sex in both groups (one was male and the other was female).

Complications were noted in 3 eyes in group (I) (20%) and in 2 eyes in group (II) (13.3%). In group (I) one eye showed both granuloma formation and recurrence. No statistically significant difference could be detected regarding the number of eyes with complications in both groups (p > 0.05) (Table 6).

The complications met with during the follow-up period were as follows: in group (I), wound dehiscence was noted in two cases (13.3%). The graft was small in size and under tension. Some sutures cut through the graft tissue leading to wound dehiscence. Epithelialization occurs in these 2 cases with no need for further surgical intervention. Wound dehiscence in group (II) was not reported.

One case (6.7%) with graft rejection was noted in group (II), while graft rejection was not reported in group (I).

Suture granuloma was observed after 2 weeks in one eye (6.7%) in group (I). Excision of the

granuloma was done under local anesthesia, but recurrence of pterygium was observed 3 months post-operatively.

Follow up was carried out for 12 months after surgery in both groups. Seven eyes in seven patients who did not complete the follow up period, and they were excluded from the study.

Table (1): Distribution of patients in both groups regarding to their occupation

Group	Group of simple suturing technique No.=15		Group of fibrin glue adhesive technique No.=15		Sign. test	*P*-value
Items	No	%	No	%		
Occupation						
-Manual worker	8	(53.3)	6	(40.0)	Chi – square(X^2) = 1.5	*P* = 0.6
- Farmer	3	(20.0)	2	(13.3)		
-Employee	1	(6.7)	1	(6.7)		
- House wife	3	(20.0)	6	(40.0)		

Table (2): Comparison between the results of Schirmer's test in each group

Group	Group of simple suturing technique No.=15	Group of fibrin glue adhesive technique No.=15	Sign. test	*P*-value
Items				
Schirmer's test (mm)				
-Range	8 -14	9 - 13	t-test = 0 .384	*P*= 0.7
-Mean ± SD	10.7± 1.6	10.9 ± 1.2		

Table (3): Comparison between the two groups regarding duration of surgery

Group	Group of simple suturing technique No.=15	Group of fibrin glue adhesive technique No.=15	Sign. test	*P*-value
Items				
Duration of surgery (minutes)				
P-value = 0.000 t-test = 11.8	15 - 30	35 - 45	-Range	
	19.7 ±5.2	39.7 ±3.9	-Mean ± SD	
Duration of graft fixation (minutes)				

Table (4): Comparison between the duration of postoperative subjective symptoms relieve in the two groups

P-value	Sign. test	Group of fibrin glue adhesive technique No.=15	Group of simple suturing technique No.=15	Group Items
Duration of postoperative discomfort relieve (wks)				
P= 0.003	t-test = 3.3	1 - 6	2 - 6	-Range
		2.5 ± 1.2	4.1± 1.4	-Mean ± SD

Table (5): The relation between duration of postoperative discomfort relieves (wks) and the grading of pterygia according translucency

P-value	Sign. test	Group of fibrin glue adhesive technique No.=15	Group of simple suturing technique No.=15	Group Items
Duration of postoperative discomfort relieve (wks)				
P-value = 0.003	t-test = 10.8	1 - 6	2 - 6	T1 -Range
		2.6 ±1.9	3.3±2.3	- Mean ± SD
		2 -3	2 - 4	T2 -Range
		2.1 ± 0.37	3.6 ±0.8	- Mean ± SD
		2 - 4	4 - 6	T3 -Range
		3.3 ±1.2	5.0 ±1.0	- Mean ± SD

Table (6): Complications in both groups

P-value	Sign. Test	Type of Surgery		Group
		Group of fibrin glue adhesive technique No.=15	Group of simple suturing technique No.=15	
		No %	No %	Items
Postoperative complication				
P = 0.385	(X^2) = 3.0	13 (86.7)	12 (80.0)	Absent
		0 (0.0)	2 (13.3)	Graft dehiscence
		1 (6.7)	0 (0.0)	Graft rejection
		1 (6.7)	1 (6.7)	Recurrence
		0 (0.0)	1 (6.7)	Granuloma
P-value = 0.000	t-test = 11.8	3 - 5 4.5 ± 3.2	22 - 25 24.7 ± 2.5	-Range -Mean ± SD

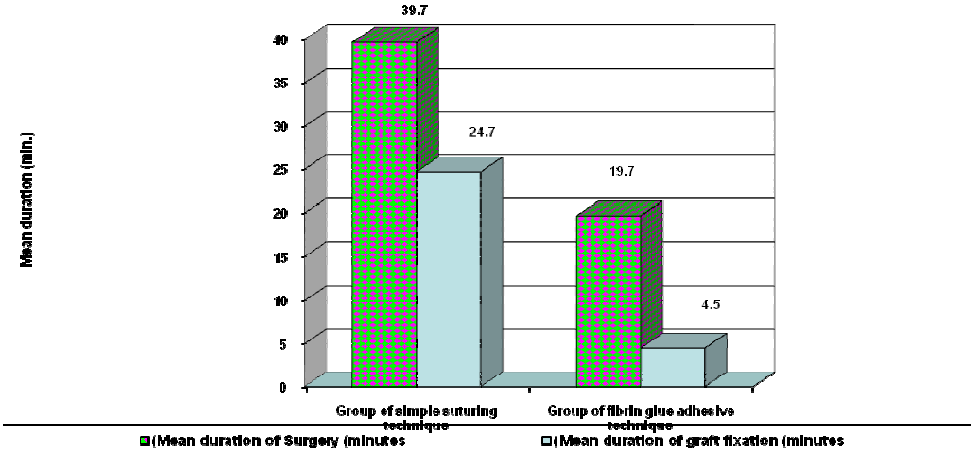

Figure (1): The mean duration of surgery among both groups

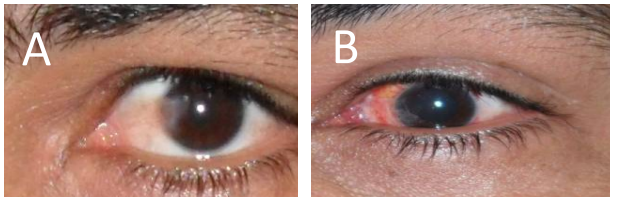

Figure (2): A case in group (I), **(A)** preoperatively**, and (B)** one day postoperatively**.**

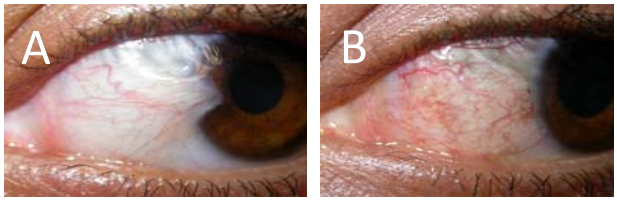

Figure (3):A case in group (I), **(A)** preoperatively **and (B)** 2 weeks postoperatively

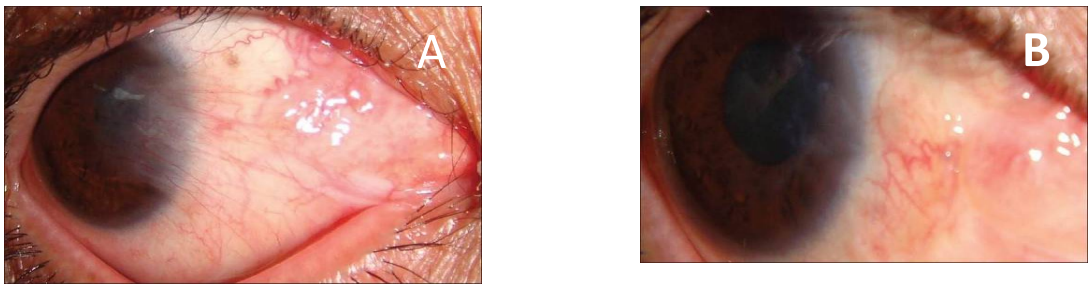

Figure (4): A case in group (II), (A) preoperatively and (B) one month postoperatively

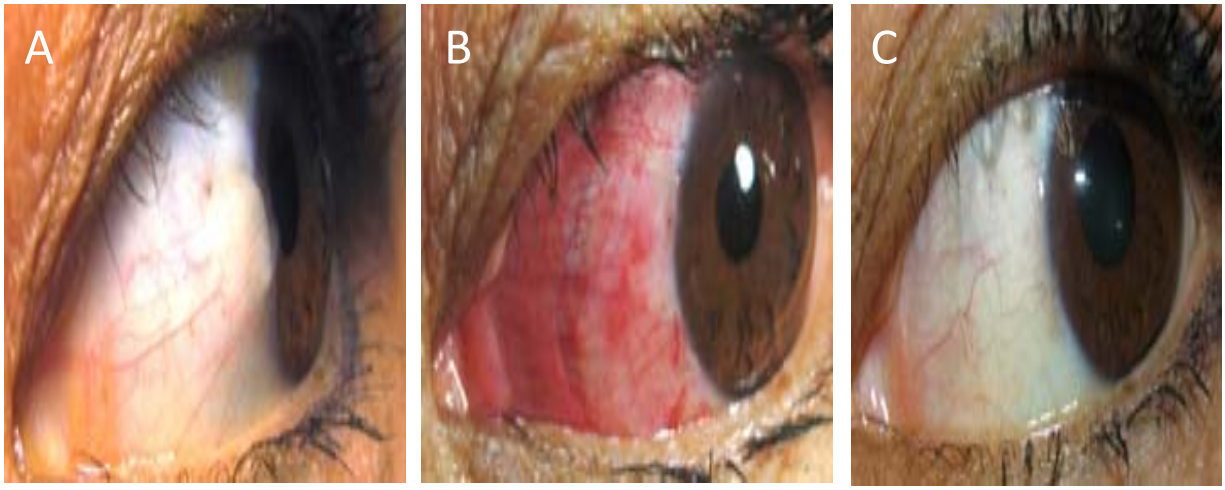

Figure (5):A case in group (II), (A) preoperatively, (B)one day postoperatively, and (C) 3 months postoperatively.

4. Discussion

All patients with pterygia in this study were ranging between 30 to 70 years old. These finding is in agreement with Viso *et al.*[7],Liang *et al.* [8]and Kheirkhah *et al.* [9] who found that the prevalence of pterygium increased significantly with aging.

The prevalence of pterygium in this study was higher in outdoor workers mostly manual workers and farmers (63%).These finding are in agreement with Sekelj *et al.* [10] who found that persons working in outside environments were more likely to have pterygia than those working indoors.

In the present study, 60% of the patients were males and 40% were females (3: 2). This result is similar to that of Tong *et al.* [11] who found that 56% of their patients were males and 44% were females. While, Mahar[12] in Saudi Arabia reported that 86% of his patients with pterygia were males and 16% were females and he attributed this to the fact that females stay indoors most of the time in Saudi Arabia.

We noted a definite decrease in the amount of tears production in all age groups and in both male and females (around 10 mm.). This was explained clinically as most of patients were suffering from burning sensation.

There were a negative significant Pearson Correlation (r) in our study between severity of preoperative subjective symptoms of patients with pterygia, and values of Schirmer's test (mm). The more severe the preoperative subjective symptoms, the more reduction of the Schirmer's test values after surgery. This supports the theory that implicates the ocular surface changes in the pathogenesis of pterygium.

Preventing pterygium recurrence is the main concern of pterygium surgery. Some authors revealed that the recurrence rate for primary closure varies from 5% to 69%, for sliding conjunctival autograft from 3.2% to 10.7% and for free conjunctival autograft it varies from 0% to 39% among different reports[13].

The technical difficulty of attaching the autograft and prolonged operation time with suturing can be a challenge for many surgeons. Furthermore, suture use is associated with patient discomfort and minor complications[14].

Biologic adhesives, such as fibrin glue, can be an alternative method of conjunctival or conjunctivolimbal graft attachment. The advantages of using fibrin glue for attaching graft include ease of use, shorter operating times, less postoperative discomforts and fewer complications [4].

In the present study, there was marked reduction of the mean operation time when using fibrin glue (19.7 ± 5.2 minutes) compared to (39.7 ± 3.9 minutes) for conjunctivolimbal autografting attached with suturing (Virgin 8-0) (*P*-value = 0.000). This is in agreement with the result of Harvey *et al.*[4] and Kim *et al.* [1] who reported 27.8 ± 1.0 minutes and 18.0 ± 5.7 minutes as a mean operation time for fibrin glue technique in attaching conjunctivolimbal autograft compared to (67.0 ± 3.6 minutes) for conjunctivolimbal autografting attached with suturing (Nylon 10-0) ($P<0.001$).

Postoperative complaints were relieved in group 2 (fibrin glue technique) by 2.5 ± 1.2 weeks, while in group1(simple suturing technique) they were relieved by 4.1± 1.4 weeks (*P*-value= 0.003). This was in agreement with the result of Koranyi *et al.* [15],Harvey *et al.* [4], and Srinivasan *et al.* [16].

In this study, a change of refraction was noted in most of the cases in the two groups. No significant differences were detected between the two groups as regards to their effect on the best corrected visual acuity. The change of refraction was related to

the surgical excision of the pterygium and its effect on the corneal curvature, not to the effect of conjunctivolimbal graft or methods used for its attachment. These results are in agreement with Allan *et al.* [17] who found that the visual acuity at 3 months postoperatively was not affected by conjunctival autograft transplantation in the majority of cases (72%) when compared with the preoperative level.

The mean astigmatic error in the present study was reduced by (2.4± 1.8 D) in the first group and by (1.9 ± 0.9 D) in the second group, with no significant difference between both groups (range: 0.5 – 6 D).

In the present study, there was no difference in recurrence between the two groups; the total recurrence rate was 6.7% (two recurrences), one case of recurrence was noted in each group. These results differ from Karalezli *et al.* [18] results, where they reported 4% recurrence in the fibrin glue group and 12% in the suture group.

Pan et al. [19] **in their meta analysis** supports that the use of fibrin glue can significantly reduce the recurrence rate without increasing the risk of complications (Peto odds ratio OR 0.33, 95% CI, 0.15–0.71, $P = 0.004$) compared with suture. There were no significant differences in the complication rate (Peto OR 1.82, 95% CI, 0.63–5.27, $P = 0.27$).
Kim *et al.* [1] recommended that long-term postoperative studies are needed to confirm whether the rate of pterygium recurrence and other complications are affected by the use of fibrin glue. The same thing in the present study, the results of recurrence could not be relied on, because long term follow up period and large scale study are needed.

We reported one patient with graft rejection (6.7%) in group2 (fibrin glue group), while there were two patients with partial graft dehiscence (13.3%) in group1 (suture group) for which no reoperations were required. They showed spontaneous healing by one month postoperatively. There were no complications at the donor graft site or button holes in the graft in both groups. These results were more or less similar to Harvey *et al.* [4]who reported 9% from the suture group experienced partial graft dehiscence and to Kim *et al.* [1] who reported 5.6% wound gapping.

Granuloma formation was recorded in one patient in the suture group compared to no granuloma formation in the fibrin glue group. No other complications were observed.

There are some concerns regarding the safety of fibrin glue use, including potential for anaphylactic reaction and disease transmission. None of the patients in the present study had anaphylactic reactions. Adherence to strict manufacturing processes can prevent transmission of pathogens.

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