

Comparison between Autologous Blood and Fibrin Glue for Adhering Conjunctival Autografts after Pterygium Excision- A Randomised Clinical Trial

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ABSTRACT

Introduction: Fibrin glue is a biological tissue adhesive and acts on the principle of final stages of the coagulation cascade. The cost of commercially available products is very high and not affordable for the patients of low socio-economic strata. As an alternative, pterygium surgery was done using patient's own blood to adhere the conjunctival autograft to scleral bed by the process of coagulation of fibrin from the oozing blood from the blood vessels under the flap.

Aim: To compare autologous blood and fibrin glue for adhering conjunctival autografts after pterygium excision.

Materials and Methods: It was a randomised clinical trial. Total 97 subjects with primary pterygium who visited the Ophthalmology Department were randomised into two groups. In group A (n=31), patients had undergone pterygium excision wherein conjunctival autograft was attached by fibrin glue. In group B (n=66) the graft

was attached by autologous blood present on the scleral bed. Mean operative time for the procedures were compared. Follow-up was done for 12 months and all subjects were examined for postoperative pain, foreign body sensation, inflammation, graft stability and recurrence.

Results: The mean age of patients in group A was 48.32±14.3 years (21-65 years), and in group B was 54.48±15.67 (23-74 years). Mean operating time in group A was 23.21±9.4 minutes and 13.7±4.3 minutes in group B, (p-value=0.001). Postoperative pain of mild degree was present in all the 31 (100%) subjects of group A. In group B, pain was absent in 32 (48.5%) and mild degree in 34 (51.5%) subjects. No recurrence was found in both the groups. Mean follow-up period was 11.4 months.

Conclusion: This study concludes that autologous blood is a useful alternative method for graft attachment in pterygium surgery without the untoward complications related to fibrin glue.

Keywords: Biological adhesives, Blood components, Grafts, Pterygium surgery

INTRODUCTION

There is always a dilemma amongst the surgical and medical options available for the management of pterygium. To date, various treatment modalities have been practiced for the treatment of pterygium. However, most of these modalities have been bogged because of high recurrence rate as high as 46%. However, a high recurrence rate was found associated with other treatment modalities and not with conjunctival grafting [1]. Various materials have been used to attach the autograft. In the conjunctival autografting, as it needs suturing of graft, drawback of this technique is the relatively longer surgical time as compared to the bare sclera technique.

There is also a risk of complications such as granuloma formation, giant papillary conjunctivitis and significant patient discomfort after the surgery due to sutures [1]. With this background, in view of the biodegradable and biological properties, fibrin-based adhesives have been used to adhere either conjunctiva or amniotic membrane, without inducing inflammation. Fibrin glue is derived from blood and is absorbable, relatively easy to use, and can be kept at room temperature or stored in a refrigerator. Fibrin glue is a biological tissue adhesive and acts on the principle of the final stages of the coagulation cascade where a solution of human fibrinogen is activated by thrombin (the two components of fibrin glue) [2-4].

It consists of thrombin and fibrinogen component, both of which are prepared by processing plasma. It is prepared at a transfusion center of blood [3,5,6] or from patients own blood [2,7] or is commercially available. When this processing of plasma is delayed, it may have a low concentration of fibrinogen [2,8,9]. The commercially available adhesives are produced from pools of plasma and contain high yields

of fibrinogen which produce firm coagulums. The major limitations of using these adhesives are the risk of transmission of diseases from the blood donors [2,10,11]. This can be minimised to zero by obtaining the blood of screened healthy donors [2,10,12]. The safest approach is to use the patient's own blood to prepare fibrin glue. The cost of commercially available products is very high and not affordable for the patients of low socioeconomic strata. So, use of patient's own blood to adhere the graft to scleral bed by coagulation of fibrin can be done. This is derived from the blood vessel that ooze under the flap [13,14]. This study aims to compare the outcome of oozing autologous blood as tissue adhesive and fibrin glue for conjunctival graft fixation.

MATERIALS AND METHODS

It was a randomised clinical trial conducted from September 2013 to January 2016 including follow-up period of one year. Total 97 subjects of primary pterygium who visited the Department of Ophthalmology at Acharya Vinoba Bhave Rural Hospital (AVBRH), Maharashtra, India, were randomised into two groups A and B, by simple random table method. Study approval was taken from institutional ethical committee (Ref.No. DMIMS (DU)/IE/Sept-2013/3621). Prior informed consent was taken in each case before the procedure.

In group A, pterygium excision was done wherein conjunctival autograft was attached by fibrin sealant ReliSeal glue 0.5 mL. In group B conjunctival autograft was attached by autologous blood present on the scleral bed after excision of pterygium.

Inclusion criteria: Patients with pterygium of grade 1, 2 or 3, double headed pterygia and temporal pterygia.

Exclusion criteria: Patients with recurrent pterygium, patients with immune system diseases, eyelid or ocular surface diseases (e.g.,

blepharitis, Sjögren's syndrome and dry eyes), with a history of ocular surgery or trauma or known hypersensitivity to any component of fibrin glue.

Best Corrected Visual Acuity (BCVA) was taken in every patient before procedure and one month postoperatively. Grading of pterygium was done by the 'Morphological grading system on slit lamp', and is as follows [5]:

Grade T1 (Atrophic): Pterygium in which episcleral vessels underlying the body of the pterygium were clearly distinguished.

Grade T2 (Intermediate): Pterygia in which episcleral vessel details were indistinctly seen or partially obscured.

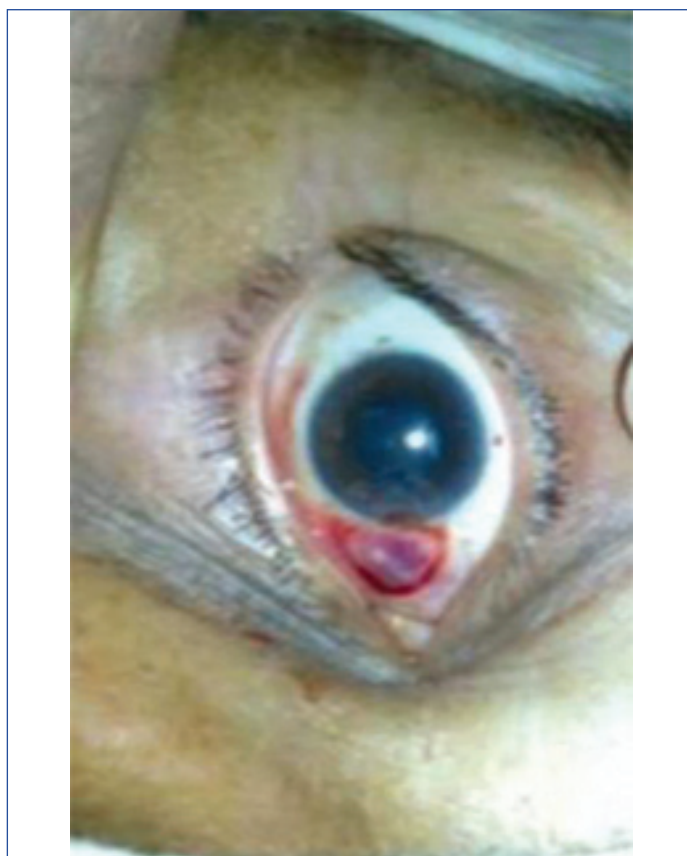
Grade T3 (Fleshy): In which episcleral vessels underlying the body of the pterygium were totally obscured by the fibrovascular tissue.

Study Procedure

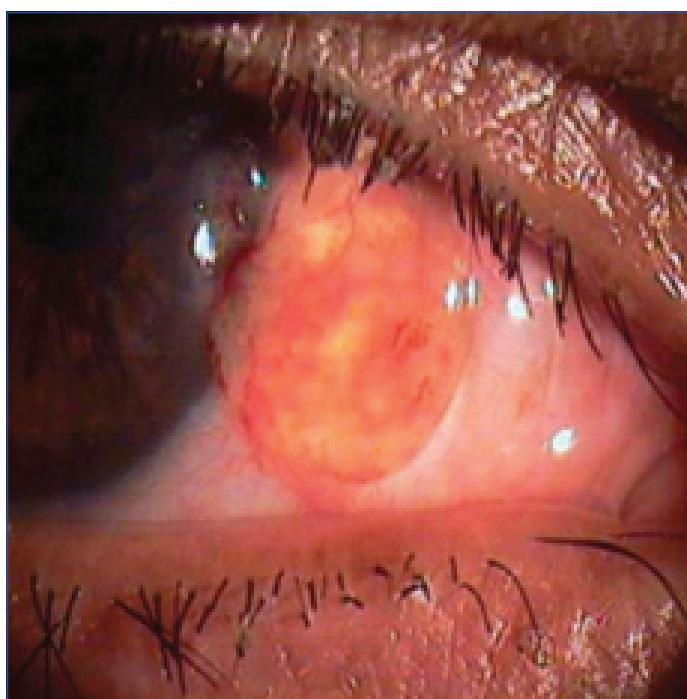
All procedures were performed by a single surgeon (MS) under local anaesthesia (peribulbar block). In patients of group A, under peribulbar block, maintaining all aseptic precautions, the globe was rotated inferiorly to expose the superior bulbar conjunctiva and then pterygium was excised. A thin free Tenon graft was obtained and kept over the cornea. The autograft was about 1.5 to 2 mm larger than the recipient bed. Care was taken not to displace the graft over the cornea. The graft was kept in place with blunt tipped forceps to prevent button holing of the graft. The graft extended beyond the recipient bed border by approximately 1 mm all around to avoid the chances of retraction.

The fibrin sealant ReliSeal glue 0.5 mL (Manufactured by Reliance Life Sciences Pvt. Ltd., Worli, Mumbai), was used in this prospective randomised trial to attach the graft. Fibrin glue was reconstituted before starting the procedure which was later included in the total time needed for the procedure. In group B, patient's own blood was used to adhere the graft instead of fibrin glue. After excision of pterygium was done, minimum bipolar wet field cautery was applied to stop the bleeding. Care was taken not to over-cauterise; as little oozing was useful in adherence of graft to the bed. Then the dissected tissue was avulsed from the cornea with a forceps or a needle holder, applying counter traction with a cotton bud. The autograft was about 1.5 to 2 mm bigger than the recipient bed. The graft was free of subconjunctival tissue. The graft was transferred to the recipient site carefully, realigning the donor limbus to recipient limbal bed. The graft was pressed against the sclera and extra fluid under the graft was expressed out using a flat spatula. The tissue was left for about three minutes in place. The cornea was covered with a wet weck sponge to protect macula from photo toxicity. After three minutes, tissue was checked for adherence to the bed and confirmed if it got attached to the bed due to coagulation of fibrin from the small amount of blood oozing under the flap [Table/Fig-1].

The donor site was left without any sutures. The speculum was removed taking care not to displace the graft. The lids were closed and pressure bandage was applied for 24 hours [13,14]. Each patient was followed-up for twelve months postoperatively on days 1, 7, 14, [Table/Fig-2] and then after 1, 3, 6, 9 and 12 months [Table/Fig-3]. The patients were asked about the presence of postoperative pain and foreign body sensation. These symptoms were segregated into mild (complication causing some discomfort), moderate (complication partially interfering with usual activity or sleep) and severe degree (complication completely interfering with usual activity or sleep). As defined by Hirst CW et al., recurrence was considered as the presence of fibrovascular tissue regrowth extending beyond the surgical limbus onto clear cornea [15]. Postoperative medication included topical dexamethasone (0.1%) and moxifloxacin eye drop, initially eight times for two weeks and then gradually tapered off over a period of eight weeks. Topical carboxymethyl cellulose 1% was also given for eight weeks in both groups.



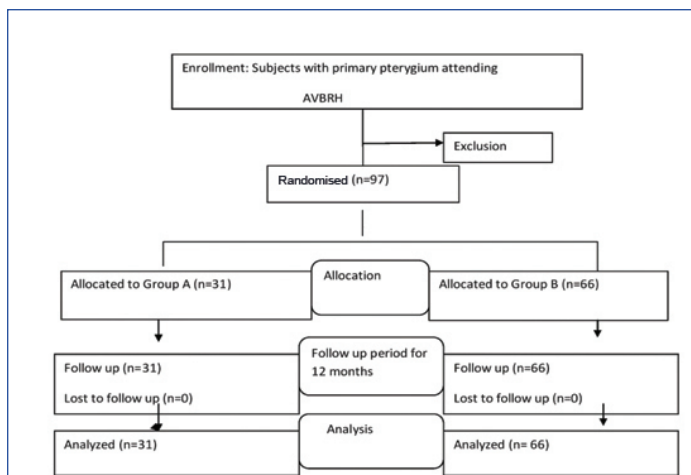
[Table/Fig-1]: Immediate postoperative picture of a patient from group B.



[Table/Fig-2]: Postoperative picture on 7th day.

STATISTICAL ANALYSIS

The statistical analysis was performed using Statistical Package for Social Sciences (SPSS) version 17 statistical software. The basic parameters like age and operation time were expressed in terms of mean and standard deviation. The difference for the parameters, age and operation time, between the two study groups was compared using independent t-test. Primary outcome variables such as surgery time, postoperative symptoms such as pain and foreign body sensations, rate of recurrence and secondary outcome variable such as postoperative complications between the two groups were compared using the nonparametric Mann-Whitney U Test. The significance were tested at $p < 0.001$ and $p < 0.05$ in all cases.



[Table/Fig-3]: CONSORT flow chart

RESULTS

In group A with 31 patients, pterygium excision was done wherein conjunctival autograft was attached by fibrin glue. In group B, in 66 subjects pterygium excision was done wherein conjunctival autograft was attached by patient's own blood. In group A, out of 31 subjects, 16 were male (51.6%) whereas in group B, 35 (53%) were male. Mean age in group A was 48.32 ± 14.3 years (21-65), and in group B was 54.48 ± 15.67 (23-74), p-value was 0.382 [Table/Fig-4]. The mean duration of surgery in group A subjects was longer than group B (p-value=0.001). It was observed that postoperative pain of mild degree was present in all of the 31 (100%) patients of group A. In group B, pain was absent in 32 (48.5%) subjects and mild degree of pain was present in 34 (51.5%) patients in first two postoperative days but it was absent afterwards. Postoperative foreign body sensation in both the groups was also compared [Table/Fig 5].

Study variables	Group A (n=31)	Group B (n=66)	p-value
Age in years (Mean \pm SD)	48.32 \pm 14.3	54.48 \pm 15.67	0.382
Sex (Male/Female (n))	16/15	35/31	0.388
Operation Time in minutes Mean (SD)	23.21 (\pm 3.1)	13.7 (\pm 4.3)	0.001

[Table/Fig-4]: Patients characteristics in both the groups.

*independent t-test

Nature of complications	Group A (n=31)	Group B (n=66)
Postoperative pain		
Absent	-	32 (48.5%)
Mild	31 (100%)	34 (51.5%)
Moderate	-	-
Severe	-	-
Foreign body sensation		
Absent	8 (25.8%)	43 (65%)
Mild	17 (54.8%)	23 (34.8%)
Moderate	6 (19.3%)	-
Severe	-	-

[Table/Fig-5]: Percentage wise distribution of complications.

It was seen that age, sex, and morphological grading of pterygium as variables amongst the subjects, does not have any effect on the outcome as whole in the present study. One patient in group A had graft loss; however, the graft was successfully reattached with fibrin glue. No recurrence of pterygium was observed in both the groups. Present study showed graft retraction (0.5-1.0 mm) in 3 eyes (10%) in group A and 11 (16.6%) eyes in group B in the first postoperative week, that went off gradually and spontaneously within first postoperative month. The present study showed total graft dehiscence in 2 eyes (3.03%) in group B. No patient developed corneal

ulcer, scleral melting, conjunctivitis, corneal dellen, hypersensitivity to fibrin adhesives, symblepharon formation in either of the groups postoperatively during the first month.

DISCUSSION

Commonly, autograft fixation is done by suturing. The associated disadvantages are prolonged operating time, postoperative discomfort due to sutures, suture abscesses, granuloma formation and buttonholes which needs suture removal [15]. Commercially available fibrin adhesive has been used widely in neurosurgery, plastic surgery, and ear, nose, and throat surgery. Report shows that fibrin adhesive is useful in ophthalmology for conjunctival wound repair, repairing leaking filtering blebs in trabeculectomies, lamellar keratoplasty, and closure of perforations in the lens capsule perforated corneal ulcer, ocular plastic and orbital surgery [16-21].

Aim of the present study was to compare the outcome of fibrin glue and autologous blood to attach the conjunctival graft in pterygium surgery. In both the groups there was no recurrence and no significant difference in postoperative complications.

Koranyi G et al., conducted a randomised clinical trial, and concluded that fibrin glue TISSEEL Duo Quick (Baxter, Vienna, Austria) could be used to attach the conjunctival autograft instead of sutures, with lesser operating time and postoperative discomfort [22]. The study showed a pterygium recurrence rate of 5.3% with glue versus 13.5% with sutures. Many studies that have been conducted comparing fibrin adhesive and sutures for attaching conjunctival grafts demonstrated better results with fibrin glue [23-25]. The risk of using commercial fibrin glue is the transmission of infectious agents despite viral inactivation techniques. With the use of commercially available fibrin glue products, human infection of Parvovirus B19 (HPV B19) has been reported [26]. Reports in the literature show three cases of anaphylactic reaction after use of TISSEEL fibrin sealant, one of which resulted in death [26]. Bovine proteonine aprotinin was thought to be the allergen, which was induced in the product as an antifibrinolytic to promote the dissolution of the fibrin clot.

In the present study, tranexamic capsules were used for antifibrinolytic effect, and steroid drops were used so that no hypersensitivity reactions occur. The lid closure provides a natural biological dressing and confers a natural bandage for adhering the graft. Lids provide compression, a smooth frictionless surface, and a vascular bed with good immune response in close proximity to the injury site. A study conducted by de Wit D et al., enrolled fifteen patients on whom autologous fibrin glue was used for pterygium surgery [27]. They showed well-positioned grafts in all four cases after six weeks of follow-up, whereas in the present study there was total graft dehiscence in two eyes (3.03%) group B. One of the two cases was an initial case, and it might have occurred due to inexperience and technical factors. This complication may also have resulted from a low concentration of thrombin and fibrinogen in the autologous blood compared to the commercially available fibrin glue. These patients did not undergo coagulation profile study preoperatively. Also, graft dehiscence is a recognised complication of using tissue glue and has been previously reported [28].

Mean operative time in present study in group A showed similarity with findings reported by Ratnalingam V et al., and Karalezli A et al., where the mean surgery time was 15.7 ± 2.4 and 16.93 ± 2.85 min. respectively [29,30]. Study conducted by Uy HS et al., showed mean surgical duration to be 67.0 ± 3.6 minutes for the suture group and 27.8 ± 1.0 minute for the fibrin glue group (p<0.001) [31].

In the study conducted by Alireza F et al., they prepared thrombin and fibrinogen in two separate syringes from patient's own blood and applied at the time of surgeries, but they had very small sample size (15 eyes) as compared to the present study (group B, n=66) [32].

In the present study, the graft retraction and recurrence was found in 14 eyes and two eyes, respectively. In the study conducted by

Singh PK, 10 eyes in each group were evaluated and they found similar recurrences in each group (10%). Mean operation time in autologous group was 14.74±2.35 minutes and in fibrin glue group it was 11.745±2.89 minutes [14]. In the present study, procedure time was found to be more in group A as it included the reconstitution of glue from three vials of fibrinogen, bovine proteonine and thrombin. Pain and foreign body sensation was not significant in both the groups though it was mild in group A in all patients as compared to group B in which only 50% patients had mild pain in first two postoperative days which might be due to fibrin glue present on the ocular surface though every care was taken to avoid excess of it. As it is biodegradable this discomfort was no longer present for more than a week.

Limitation(s)

Sample size in both the groups was unequal due to non affordability of the fibrin glue for the patients and the study was not granted any funds. Coagulation profile was not checked preoperatively in autologous group.

CONCLUSION(S)

This study concludes that autologous blood is a useful alternative method for fixing graft in pterygium surgery especially where there is financial constraint. We can save the time needed to reconstitute the fibrin glue and safeguard the patients from the diseases which can be transmitted through these market preparations. We found this procedure of autografting free of any untoward complications like disease transmission which can occur with fibrin glue.

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