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# A Comparative Study and Histopathological Evaluation of Pterygium Excision with Amniotic Membrane Grafts Transplantation with Fibrin Glue and Vicryl Suture

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## ABSTRACT

**Aim:** To compare the clinical and the histopathological outcomes of fibrin glue versus vicryl sutures for fixing amniotic membrane grafts in patients undergoing pterygium excision.

**Methods:** The study was a randomized control study involving thirty patients with primary pterygium. All underwent pterygium surgery with amniotic membrane graft and every alternate patient had the graft secured with fibrin glue and 8 '0' vicryl sutures. Therefore 15 eyes had the grafts attached with fibrin glue and 15 eyes had it attached with 8 '0' vicryl suture in the recipient site. The patients were examined on 1<sup>st</sup>, 15<sup>th</sup> and 45<sup>th</sup> day to assess the patients comfort, duration of surgery, position of the graft and the histopathological examination of the edge of tissues on 1st and 15th day.

**Results:** Our results showed that amniotic membrane grafts are an effective alternative for conjunctival autografts in pterygium excision surgery in reducing inflammation and recurrence. The use of fibrin glue in attaching amniotic membrane grafts significantly reduces surgery time, improves post-operative patient comfort and results in decreased inflammation with faster healing

**Key Words:** Pterygium, Amniotic membrane graft, Fibrin glue, vicryl suture, Histology

## INTRODUCTION

Pterygium is a greek word derived from pterigion, meaning 'wing'. It is a wing shaped fibro-vascular sub-conjunctival tissue. Pterygium is a common external growth in the eye, growing over the conjunctiva and encroaching over the cornea.

It is more commonly seen in the tropical and sub tropical areas of the world. The pathogenesis of pterygia is still unclear. Some of the probable triggering mechanisms proposed for the growth of pterygium are the ultraviolet light, stimulation of fibroblasts, increased concentration of local growth factors and human papilloma infection. If the progressive pterygia are left untreated, the fleshy

growth encroaches the deeper layers of the cornea and may cover the pupillary axis.

The treatment options for progressive pterygium are essentially surgical excision but invariably are associated with recurrences. New approaches like adjunctive therapies, limbal conjunctival autografts and amniotic membrane grafts, are being tried to decrease the rate of recurrence after pterygium surgery<sup>1,2</sup>. Conjunctival autograft transplantation (CAT) is most commonly used to prevent recurrences after surgical excision of pterygium. CAT requires a skilled and a trained experienced surgeon to perform the surgery. Moreover, CAT cannot be used in conditions like double pterygium, severe dry eyes, cicatricial conditions of the eye, cystic pterygium or in patients with glaucoma in whom the superior conjunc-

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tiva needs to be preserved for future trabeculectomy. In these conditions, amniotic membrane grafts (AMG) can be an alternative<sup>3</sup>. The methods of attaching the AMG's can be by either sutures or fibrin glue.

In our study we compared the effectiveness of using fibrin glue (Reliseal, Baxter) and 8-0 vicryl sutures to attach amniotic membrane grafts in patients undergoing pterygium excision. This is a randomized clinical study to evaluate the operation time, postoperative patient's satisfaction, comfort and the histopathological co-relation.

## MATERIALS AND METHODS

Thirty patients (30 eyes) with primary nasal, temporal and double pterygium extending 3 mm or more on the cornea were enrolled in the study. Patients with recurrent pterygium, connective tissue disease, and trauma, hypersensitivity to any component of tissue glue or other pathologic features or infection of the ocular surface were excluded from the study. After approval from the ethics committee of the institute, all patients were informed about the study and written informed consent was obtained from all patients.

Patients were randomized to two groups: Fibrin glue group (FG) and Vicryl suture group (VG). Every alternative patient underwent AMG with glue and AMG with sutures after pterygium excision in the affected eye. The patients were also masked for the subjective evaluation of symptoms and comfort. Before surgery, detailed ophthalmologic examinations including biomicroscopic anterior segment examination, intraocular pressure measurements and funduscopy were performed. All surgical procedures were performed by the same surgeon (Dr. E.N). Tissue glue was used to close the amniotic membrane grafts in 15 patients, and 8-0 vicryl sutures was used to close the amniotic membrane grafts in another 15 patients. Histopathologic examination of the tissue on the edges of the graft-host junction was performed in both groups on postoperative days 1 and 15. The Main outcome measures were patient comfort, graft success, complications, histopathologic evaluation, and recurrence of pterygium.

### Preparation of Fibrin Tissue Glue

The fibrin glue (Reliseal, Baxter) was prepared according to the manufactures instructions. Freeze-dried protein concentrate and thrombin were reconstituted and were warmed for few minutes in a fibrino thermin device. Then each solution was withdrawn in two separate syringes and placed in a dual injection system in which both their contents were mixed in appropriate proportions.

### Preparation of amniotic membrane:

Processed and Cryopreserved amniotic membranes obtained from an eyebank authorized by 'Eyebank association of In-

dia' preserved in a cryofridge which maintains a temperature of about -70 degree is used. Serological tests on the grafts were done prior to the surgical procedures.

### Clinical Follow-up

All the patients underwent pterygium excision under local anaesthesia and they received AMG with fibrin glue and AMG with sutures alternatively. They were prescribed topical steroids in tapering doses weekly. Postoperative follow-up examinations were performed on 1, 3, 7, 15, 30, and 45 days after surgery. A small bit of tissue at the graft-host junction was taken on 1<sup>st</sup> and 15<sup>th</sup> day post op for histopathological examination. The anterior chamber, integrity of the graft, and the donor site were evaluated by slit-lamp biomicroscopic examination at each visit. All patients were evaluated with regard to subjective symptoms such as irritation, foreign-body sensation, and epiphora on the first postoperative day and 1, 2, 3, and 4 weeks after surgery. Subjective symptoms were graded according to patient satisfaction by using a scale of 0-3 as follows:

- 0: Complete satisfaction (no symptoms);
- 1: Moderate satisfaction (no interruption of daily activities);
- 2: Low satisfaction (partial interruption of daily activities);
- 3: Unsatisfied (complete interruption of daily activities).

### Histopathological examination

The histopathological examination and grading on day 1 and 15 were done. Four micrometer sections were prepared and stained with hematoxylin-eosin (H-E) for examination with light microscopy under low x 10 high x 40 magnification. The grading of inflammation was estimated as negative, mild (a few changes roughly estimated at 33% of the cross-section), moderate (changes roughly at 33%-66% of the cross section), and severe (changes estimated at 66% of the cross section). They were evaluated for the

- Presence or absence of fibrin glue
- Location of inflammation : Whether epithelial or stromal ( Acute, chronic or mixed )
- Degree of inflammation: Nil, Mild, Moderate and Severe
- Fibrosis: Nil, Mild, Moderate and Severe
- Congestion: Nil, Mild, Moderate and Severe
- Granulation tissue: Present or absent
- Others: Epithelial hyperplasia, Dysplasia, Pyogenic granuloma

Statistical analysis were done with SPSS soft ware version 23

## RESULTS

All patients had primary pterygia and were operated with AMG after pterygium excision and 15 patients had attachment

of the graft with 8-0 vicryl sutures and 15 patients had attachment with fibrin glue and completed the 45 days follow up. No patient was excluded from the study.

Of the 30 patients, 20 (66.67%) were men, and 10(33.33%) were females. Mean age of the patients was 42.9 years $\pm$  6.32 years (range, 32 -55 years). There were no significant differences in age between the FG and VG ( $p = 0.514$ ). No intra operative complication occurred in any group. No cases required sutures to close the AMG edges intra operatively. More bleeding was observed in the recipient bed after pterygium excision in the VG. The fibrin glue preventing the bleeding intra operatively was observed. Minimal congestion was observed in both the groups which gradually subsided over time. However, FG had subsided hyperemia by 1 week whereas, VG patients had extended hyperemia for over 15 days. No recurrence was observed in any group during the 45 day follow up period.

The overall mean duration of the surgery was 33.9 minutes  $\pm$  9.52 min (range 22 -55 min). The mean duration of the surgery was 25.5 minutes  $\pm$  3.41 min (range 22 -35 min) in the fibrin group and 42.23 min  $\pm$  4.8 min (range 39 -55 min) in the suture group. The operation time was significantly shorter in the fibrin glue group compared to that in the suture group ( $p < 0.05$ ).

Subjective symptoms were milder and were relieved more rapidly in the FG than the VG during the 1<sup>st</sup> post operative week. The patients in the FG improved completely within 2 weeks of surgery.

73.3% in the VG had moderate to severe postoperative complaints like pain, foreign body sensation, irritation and epiphora on the postoperative days 1 and 15 whereas all the patients in the FG experienced mild post operative complaints ( $p < 0.05$ ).

Patient satisfaction was significantly higher in the FG on the 1<sup>st</sup>, 15<sup>th</sup> and 45<sup>th</sup> post operative day than the VG ( $p = 0.033 < 0.05$ ).

On histopathological examination of the FG on the 1<sup>st</sup> post operative day, the fibrin glue was seen under the AMG as an eosinophilic substance. Mild congestion, acute inflammatory response and sub-epithelial and intra-epithelial leucocyte infiltration were observed in all eyes (fig.8). Stromal infiltration of leucocytes were seen in eyes with double pterygium. Fibrin glue was not seen on day 15 and minimal inflammation was present in only few patients who had double pterygium excision. Foreign body granulation tissue was not seen in any of the histopathological preparations of FG whereas in the VG, moderate inflammatory response with sub-epithelial and intra epithelial leucocyte infiltration were detected on 1 and 15<sup>th</sup> post operative day with foreign body granulation tissue and vascularisation (fig. 9).

The donor area healed in all patients by 15 days. No complication such as infection, intra ocular pressure elevation, allergic conjunctivitis, graft necrosis, pannus, granuloma formation, symblepharon or pseudopterygium were seen during the 45 day follow up period in either of the group. No adverse effects due to the fibrin glue were encountered.

All patients had a significant improvement in visual acuity due to the relieved astigmatism caused by the pterygium. However, in patients who had a pterygium extension of more than 3 mm in the cornea and with double pterygium had residual astigmatism and lower vision due to surgically induced corneal irregularity and scarring.

## DISCUSSION

Pterygium excision with bare sclera technique is associated with more recurrence rates and complications compared to conjunctival grafts and amniotic membrane grafts<sup>4</sup>. Although conjunctival autografts with sutures are safe and effective, more surgical expertise, technical ability and surgical time are required for the dissection of the graft and securing it with sutures<sup>5</sup>. Amniotic membrane grafts (AMG) is a new technology and can be used instead of conjunctival autografts after pterygium excision. Amniotic membrane is the innermost lining of the placenta. It contains natural growth factors and cytokines which are integral to the healthy development of the foetus. Amniotic membrane has a very unique property of not expressing human leucocyte antigens, therefore immunological responses are not initiated and inflammatory rejections do not occur following its transplantation after pterygium excision<sup>6</sup>. Sutures do not actively participate in wound healing and only causes additional trauma at the dissected site. There is also the danger of infectious agents entering along the suture tract or even the sutures might act as a nidus of inflammation itself which can predispose for recurrence. Loose or broken sutures can cause discomfort and foreign body sensation to patients and may require additional maneuvers to remove them and hence additional working time<sup>7</sup>.

Koranyi et al<sup>8</sup> were the first to report the use of fibrin glue for conjunctival grafts after pterygium surgery in a prospective randomized study. But the study was for conjunctival autografts and not for AMG's. Their study evaluated the post-operative pain and demonstrated that the use of fibrin glue significantly decreased the postoperative pain than that from sutures. They also postulated that the mean surgical time was significantly shorter in the fibrin glue group compared with the suture group. In our study we found that the symptoms of pain, watering, foreign body sensation were significantly lower on the 1<sup>st</sup> and the 7<sup>th</sup> postoperative day in the fibrin glue group than they were in the suture group. The duration of the surgical time also was significantly shorter which are

consistent with the earlier studies<sup>8</sup>. Also, the histopathological evaluation does not show any foreign body granulation tissue in eyes with fibrin glue, whereas it was observed in eyes with vicryl sutures from day 1 to day 15. The fibrin glue was seen under the conjunctiva on the first postoperative day but not seen on days 15 and 45. The location of inflammation was mostly epithelial and mild inflammation in the fibrin glue group on the 1<sup>st</sup> postoperative period which completely resolved by the 15<sup>th</sup> postoperative period whereas in the suture group, the inflammation was both epithelial and stromal with moderate inflammation on the 1<sup>st</sup> postoperative day which became mild by the 15<sup>th</sup> and subsided by the 45<sup>th</sup> postoperative day. Fibrosis and vascularisation was almost nil in the fibrin glue group whereas in the suture group it was comparatively higher. However, there was minimal fibrosis and vascularisation noted in both the groups who had double pterygium excision indicating that a larger surface area resection induces more inflammation. The inflammatory responses were lower than that seen in the conjunctival autografts due to the anti-inflammatory, anti-fibrosis and anti-vascularisation properties of the amniotic membrane<sup>6</sup>.

Transmission of infections like human immunodeficiency virus, Hepatitis or parvovirus from the amniotic membrane and the fibrin glue use during surgery continues to be a theoretic risk<sup>9</sup>. The manufacturer of the Baxter and Reliseal glue had used a double-barreled approach to safety by careful donor selection and two-step vapour heating treatment. No documented viral transmission have occurred due to use of Baxter or Reliseal fibrin glues, which agrees with our observations during follow up. The amniotic membranes that had been procured from authorized eyebanks had used stringent methods for processing the amniotic membranes. However serological tests had been done on the membranes before using the batch for surgery to rule out transmission of infections.

The combined properties of both the fibrin glue and amniotic membrane produce higher patient's postoperative comfort and satisfaction and reduced inflammation. Though the discomfort and inflammation was present in the AMG with suture group, the inflammation subsided after 15 days which were evident from the histopathological examination and the inflammation was not like that was seen in conjunctival autograft with sutures which were moderate to severe<sup>10</sup>.

## CONCLUSION

The use of many sutures in securing the edges of the AMG in the vicryl group, caused discomfort and foreign body sensa-

tion to the patients. Patients satisfaction was moderate and the inflammation persisted for 15 days. However, the anti-inflammatory, anti-fibrosis and anti-vascularisation properties of the AMG reduced the severity of inflammation and symptoms. The inflammatory responses that were seen due to the sutures could pre-dispose for recurrence of pterygium although there are reduced instances due to the amniotic membrane properties.

The use of fibrin glue to attach the amniotic membrane after pterygium excision is a safe and effective procedure to reduce the patients discomfort and complications in the postoperative period. The histopathological evidences also points out the inflammation in the AMG with fibrin glue group are milder and it is more epithelial and all the inflammatory changes subsided after 7 days. Furthermore, the shortened operating time saves the risk of infection, and the operating room time and the resources can be optimally used by this technique. Early postoperative recovery facilitates patients to return to their normal lifestyle and resume their work.

**Conflict of interest:** None

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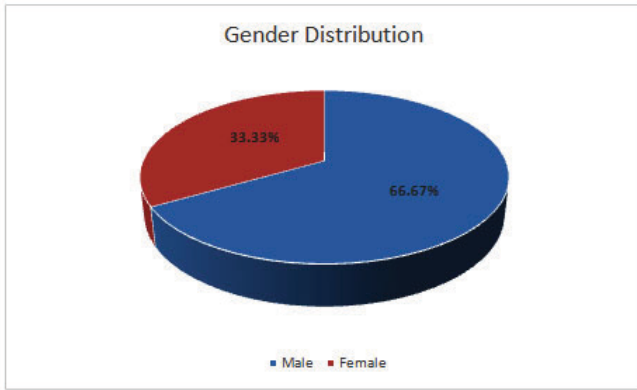


Figure 1: Gender distribution.

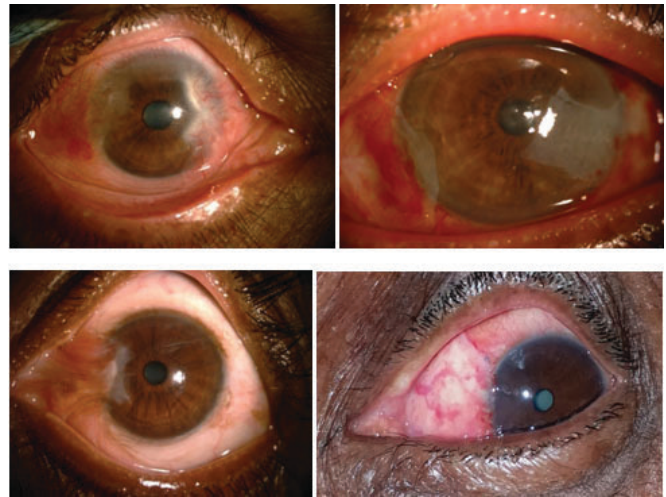


Figure 5: Pictures of the patients in both the groups, before and after surgery. (A) Pre-operative and postoperative day 1 and 15 of fibrin glue group. (B) Pre-operative and postoperative day 1 and 15 of the suture group.

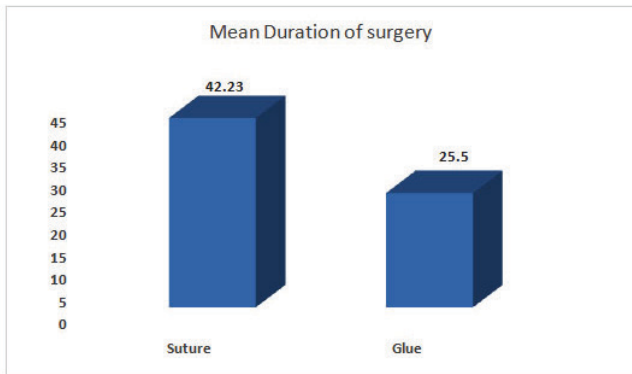


Figure 2: Duration of surgery.

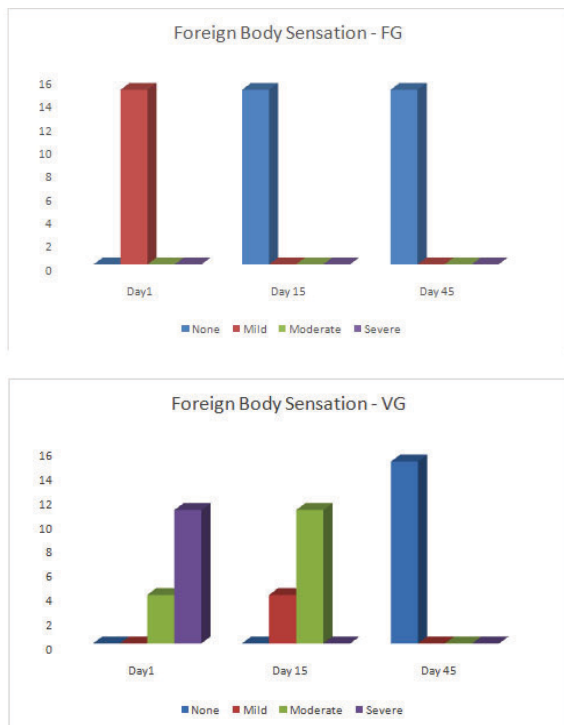


Figure 3 & 4: Subjective symptoms of patients in the FG and VG.

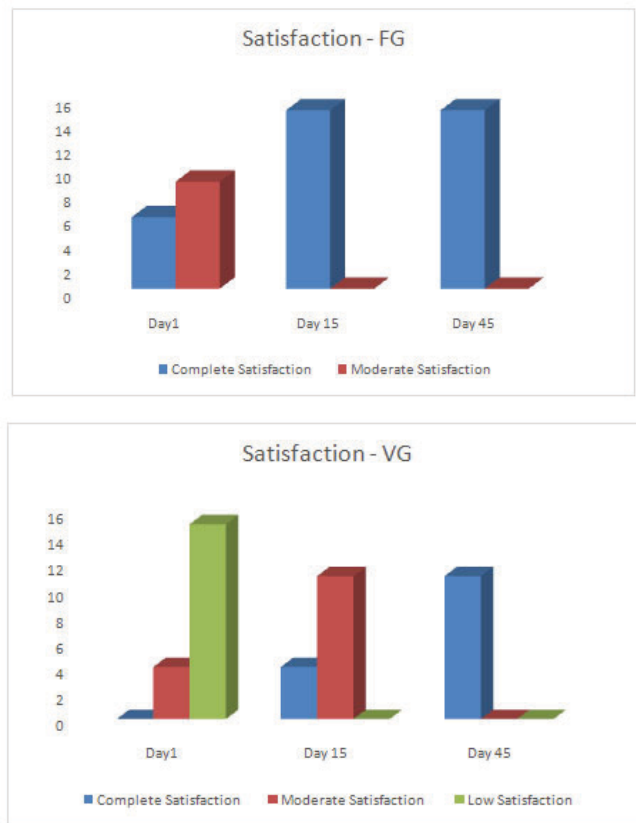
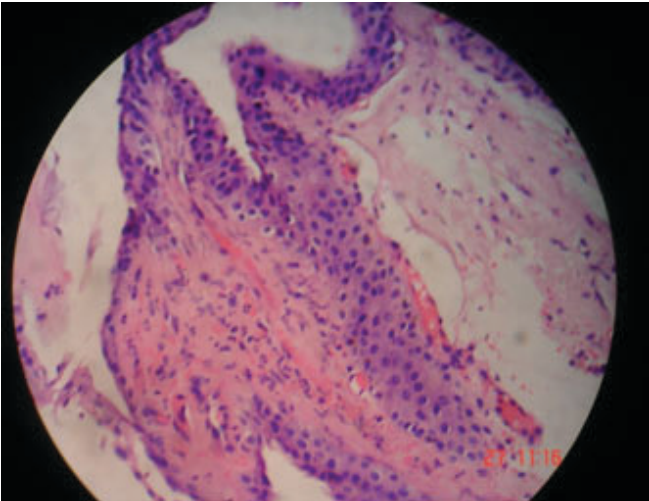
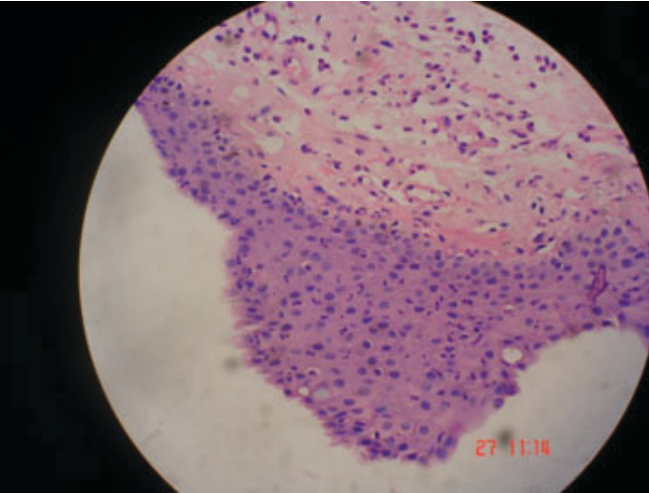


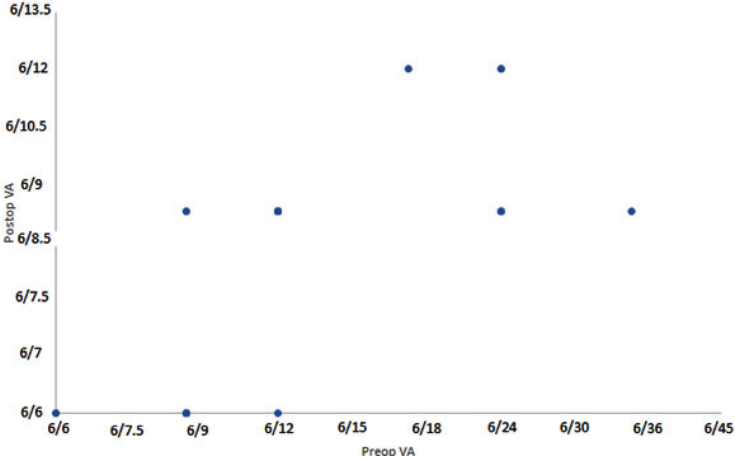
Figure 6 & 7: Shows patients' satisfaction in the FG and the VG.



**Figure 8:** Mild stromal and epithelial inflammation with stromal congestion in the fibrin glue group: H & E - Magnification: low x 10 high x 40.



**Figure 9:** Moderate epithelial and stromal mixed inflammation in the vicryl suture group: H & E - Magnification: Low x 10 high x 40.



**Figure 10:** Association between pre op and post op visual acuity.