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To compare conjunctival autografting with autologous serum against fibrin glue in pterygium excision

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Abstract
The study included 60 eyes having all nasal primary pterygium. Simple excision was performed followed by closure of the bare sclera by conjunctival autograft by the known method of fibrin glue in 30 eyes (Group A) versus autologous serum (Group B). During follow-up of 3 months, the eyes were assessed in comprehensive manner on postop day one, one month and third month. Outcome measures were assessed by cosmesis, operative time, postoperative recovery, graft inflammation, sub-conjunctival haemorrhage [SCH], Graft stability and recurrence. Average operative time in group A and group B were 18 minutes and 27 minutes respectively. Postoperative findings like graft oedema in conjunctival inflammation were more or less similar in both groups. In terms of graft stability, there were 1 (3.3%) graft loss in group A versus 2 (6.7%) graft loss. 2 (6.7%) partial displacements seen in group A whereas 4 (13.3%) partial displacements in group B. Most common finding in group B was SCH which made poor cosmesis but it lasted 2-3 weeks. There was one granuloma in group A. Both groups had same recurrence rate of 6.7%. Also graft retraction seen in 2 eyes each in either group. Autologous serum glue method is safe, efficacious and cost effective yet not commonly performed. As per our study, this method is associated with less postoperative discomfort with success rates that are comparable to fibrin glue.

Keywords: Conjunctival autografting, autologous serum, pterygium excision

Introduction
Pterygium is a wing-shaped triangular encroachment of vascularized granulation tissue covered by conjunctiva in the palpebral area. It is a fairly common degenerative disease with 9.5% to 13% prevalence in India and is commonly seen in dry and sunny climates with increased exposure to UV radiation, particularly in rural areas. Pterygium can develop into a dense fibrous tissue covering the pupillary area.
It is due to the localized limbal stem cell deficiency and is thought as a causative factor in majority cases.
Excision of pterygium with conjunctival autograft (CAG) seems so far to be one of the safest and most promising methods [1, 2, 3, 4, 5, 6, 7, 8].

Rationale for the Study
The main indications for surgery are visual impairment, due to irregular astigmatism, chronic irritation, recurrent redness and poor cosmesis. However, this study focuses on the most effective surgically after the adherence of the conjunctival autograft to the bare sclera by using either fibrin glue or autologous serum. The autologous serum has been proposed to be equal or comparable to that of suture and fibrin glue techniques. The efficacy of autologous serum has been assessed before. This study is to measure its results under various aspects in postoperative recovery in a comprehensive manner.

AIM
To study and compare the efficacy of conjunctival autograft using autologous serum with fibrin glue in pterygium excision for the management of primary nasal pterygium.

Design
Prospective non randomized interventional study.

Inclusions
Patients of either sex and age group from 35 – 80 years presenting with primary nasal pterygium of grade 2 and grade 3.

Exclusions
Recurrent pterygium, glaucoma, any infections or inflammation, retinal pathology requiring surgical intervention, history of previous ocular trauma, systemically uncontrolled hypertension and patients on anticoagulants.

Methods
The method for pterygium surgery is that the autologous conjunctiva is harvested from the superior bulbar conjunctiva after pterygium excision.
Pterygium was graded by slit-lamp and the recurrence rate (defined as any kind of fibrous-vascular tissue detected over the limbus, invading the cornea). Pterygium was originally graded in four stages, based on similar findings of fibrous-vascular tissue, from nasal limbus to the visual axis, as follows; grade 1 (less than 2.0 mm), grade 2 (higher that 2.0 mm and less than 4.0 mm), grade 3 (higher than 4.00 mm, without covering the visual axis) and grade 4 (tissue covering the visual axis) [9].
All cases were operated under local anesthesia (peribulbar injection) with Xylocaine 2%. A suture is used to abduct by clipping next to the lateral canthus. Pterygium head was avulsed using a toothed forceps and was separated from the cornea. Abnormal scar tissue was scraped by Crescent Knife. The body of the pterygium with the involved tennis capsule was dissected and excised. An oversize thin Conjunctival autograft (CAG) by 1 mm in group A and 0.5 mm in group B, in length and breadth relative to bare sclera was harvested from the superior temporal region. Care was taken not to include Tenon's capsule in the graft. With epithelial side facing upward and limbal edge of the graft aligned to the nasal limbus. Cautery was not used.
In group A (GLUE), Graft was fixed using fibrin glue available belonging to one brand. The adhesive is a commercial substance (fibrin glue) composed by human fibrin, human clotting factor XIII, thrombin and aprotinin The extracted tissue was everted and placed over the cornea and one of the two components from the fibrin adhesive was added all over the conjunctival graft surface. The bare sclera was dried with sponge or bud. The second component of the fibrin adhesive was added over the bare sclera. the conjunctival graft tissue was moved and placed the graft over the scleral bed. One minute is required to wait until both tissues stick together completely.
In group B (Autologous serum) we took slightly oversized CAG of about 0.5 mm [10]. After harvesting free CAG, a small conjunctival blood vessel was nicked with 26-G needle, blood was allowed to ooze over the bare sclera, and the graft was placed over it. The graft edges were slightly tugged under the pocket of the conjunctiva at the site of the excised pterygium on all the sides except at the nasal limbus. The graft was fixed by applying gentle pressure with iris repositor for fixation of CAG. As blood clotting time is usually 4–10 min, the graft was not disturbed for further 3-5 min [10]. The adhesion of the graft to the bare sclera was confirmed by gently stroking Cotton, ensuring appropriate edge to edge apposition of the thin graft then patched for 48 hours instead common method of 24 hours. Patients given strict instructions of not touching eyes or rubbing eyes.
The following treatment was indicated: Mixture of gatifloxacin 0.3% / Prednisolone acetate 1.0% four times a day for first week and then tapered weekly till 4 weeks. Lubricating drops CMC 0.5% four times a day for 4-6 weeks as per requirement.

Follow-Up
Day 1, Day 7, Day 15, 1st Month, 3RD Month.
At each visit detailed eye checkup done with slit lamp examination.

Results
We operated 60 eyes with primary nasal pterygium of which 35 were grade 2 and 25 were grade 3 pterygium [Table 1]
The age distribution showed 32 patients belonging to the 35–50year age group (53.3%), and 28 patients in the 50–85year age group (46.6%). 28 (46.6%) patients were female and 32(53.3%) were Male [Table 1].
The graft size is determined by the length of the pterygium along the limbus. Group A had average graft size of 6.2 mm × 6.8 mm and group B had relatively smaller graft size of average 5.5 mm ×6.2 mm.
Since our study is comprehensive, we have considered surgical time, expertise and average time for postoperative treatment. All surgeries were done by a single surgeon who had previously operated around 20 pterygium excisions prior to this study. Surgically, it was not difficult to transition from glue to serum method. We observed group A took lesser time of 18 minutes versus 27 minutes in group B. Symptoms in postoperative period were of mild category like irritation, watering, redness and photophobia. On the scale of + to +++, group B had moderate complaints in first 7-15 days. Although later after a month, in both group patients were comfortable.
Our study focusses on time wise analysis. So, we divided postoperative time in two groups, early (<1month) and late (1 month to 3 months)

Table 1: General Information

	Group A (Glue)	Group B (Serum)
Males	14	18
Females	12	16
Age group 35- 55 years	14	18
Age group 56 years & above	14	14
Grade 2 pterygium	16	19
Grade 3 pterygium	11	14

Table 2: Clinical Profile

	Group A (Glue)	Group B(Serum)
Surgical time	18.3 min	27.4min
Symptoms	+	++
Expertise	+	++
Average graft size	6.2mm × 5.8mm	5.6mm × 6.2mm
Average postop Treatment time	3-4weeks	4-5 weeks

+ = mild/little ++ = moderate +++ = severe/major

Early postop
Group A
Out of 30 patients, 3 eyes had graft oedema, 2 eyes had SCH and 3 eyes had conjunctival inflammation. One eye had graft loss and 2 eyes had partial displacement of graft after 2 -3 weeks post operation. One graft loss patient needed regrafting and 2 displacements were fixed with anchoring sutures. There were no graft recurrence and granuloma seen, but one case of graft retraction [Table 3].

Group B
Out of 30 patients, 2 eyes had graft oedema and two eyes had conjunctival inflammation. Most common adverse event was SCH which was seen in 7 eyes. With regards to graft integrity, one graft loss seen where regrafting was done

using conjunctival autograft from another site. Also observed, 2 eyes had partial displacement in immediate postoperative period which were fixed with few anchoring sutures. We saw one graft retraction towards the end of early postoperative period and no case of recurrence in group B. [Table 3]

Late postop

Group A

No SCH identified, one eye had granuloma and same patient had graft oedema. There has been one partial displacement fixed by anchoring sutures. No Graft loss identified and Graft retraction seen in two eyes.

Group B

It had one persistent SCH and same eye had persistent graft oedema. There was no conjunctival inflammation and no granuloma. There have been 2 partial displacements which was fixed by anchoring sutures on immediate day one postoperative. Two patients had graft loss, of which One had refused re-surgery and another got regrafting done from another site [Table 3]. Graft retraction was seen in two eyes. In both the groups, recurrence rate was same (6.7%) and observed in late postoperative period.

Table 3: Outcome

	Group A (Glue) Early Postop	Group A (Glue) Late Postop	Group B (Serum) Early Postop	Group B (Serum) Late Postop
Cosmesis	++	+++	+	+++
Graft oedema	3	1	2	1
SCH	2	0	7	1
Conjunctival inflammation	3	1	2	0
Graft loss	1	0	1	1
Graft partial displacement	2	1	2	2
Graft retraction	1	1	1	2
Granuloma		1	0	0
Recurrence	0	2	0	2

+Bad ++ good +++ very good

Discussion

The use of CAG following the pterygium excision was first described by Kenyon *et al.* in 1985 [11]. Surgical techniques have evolved from the bare sclera technique, auto-rotation of conjunctival flap, usage of amniotic membrane graft, or conjunctival graft to the recently developed conjunctival autograft, which is considered the current surgical gold standard. Fibrin glue has the advantage of better cosmesis but because of the biological origin of fibrin glue, its use carries a risk of postoperative inflammation, anaphylaxis, and transmission of prions and parvovirus B19, yet no such incidences recorded. Autologous serum forms a fibrin clot which adheres the conjunctival autograft to the bare sclera. As this is the patient's own serum, no foreign body reaction or rejection is seen hence inflammation will be minimum. Additional benefit of easy availability.

The present study showed a comparable outcome after pterygium surgery using both methods of conjunctival autograft with fibrin glue and autologous serum. Usually, the complexity of pterygium surgery is underestimated.

Conjunctival autografts in pterygium surgery follow a consistent healing pattern dominated by re-perfusion injury in early postoperative days [12]. Like our other studies also followed bandaging for 48 hours [13, 14].

We have considered surgical time, expertise and average time for postoperative treatment. We found out; group A took lesser time of average 18 mins versus 27 mins for group B.

Symptoms in postoperative period were of mild category like irritation, watering, redness and photophobia. Group B had more redness and less symptoms which was otherwise in group A. Similar findings in few other studies quoting better patient satisfaction and postoperative symptoms in the blood coagulum group than the other techniques [15, 16].

For more correlations, we recorded graft size in each case, graft size was measured in terms of breadth and length (longest measurement of graft from limbus)

Our study focusses on time wise analysis of outcomes of both the surgeries. We divided postoperative time in two groups, early (< 1 month) and late (> 1 month to 3 months)

Group A versus Group B

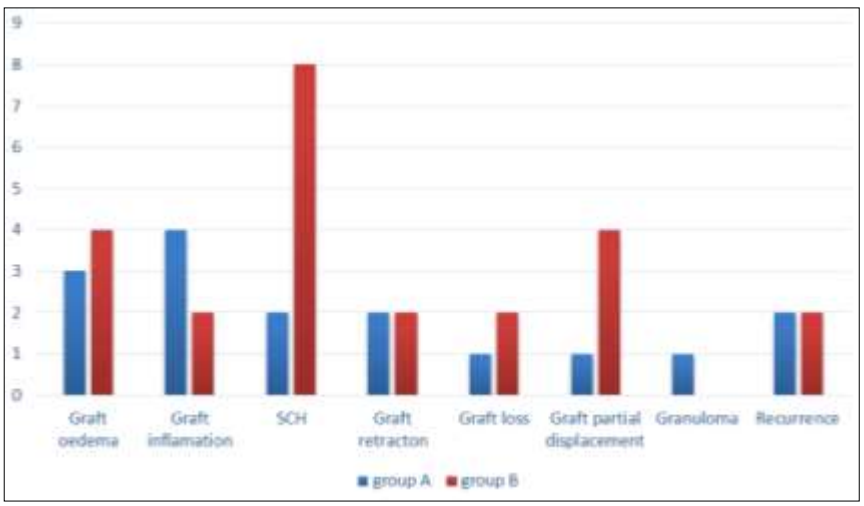

Fig 1: Comparison Group A and Group B

Table 4: Comparison between Group A and Group B

	Group A (Glue)		Group B (Serum)	
Graft oedema	4	10%	3	13.3%
SCH	2	6.7%	8	26.7%
Conjunctival inflammation	4	13.3%	2	6.6%
Graft loss	1	3.3%	2	6.6%
Graft partial displacement	2	6.7%	4	13.3%
Graft retraction	2	6.7%	2	6.7%
Granuloma	1	3.3%	0	0%
Recurrence	2	6.7%	2	6.6%

Group A had 4 graft oedema (13.3%) which is more than group B (10%). Also, conjunctival inflammation was more in group A (13.3%) as compared to 6.6% in group B.
A similar conclusion has been indicated by different authors [9, 17].
SCH (subconjunctival hemorrhage) was observed to be predominantly high in group B in almost 26.7% eyes versus 6.7% in group A. This affected the postoperative cosmesis. The reason for SCH was occurrence of sub graft hemorrhage due to excessive ooze from the scleral bed. One study showed that the spontaneous sub graft hemorrhage occurred with no effect on graft stability [20]. There are Similar findings in our study, all cases with subconjunctival haemorrhage had no graft loss or partial displacement. Although it might suggest problem in preparing scleral bed and more ooze allowed than required.

Graft Integrity
Graft loss has happened in one case in group A, whereas group B had two cases of graft loss in 3 months of follow up.
Although regarding partial displacement. Group A had less numbers of 2 eyes (6.7%) versus 4 eyes (13.3%) in group B. All 5 cases were fixed with sutures immediately with only few anchoring sutures taken and one case needed regrafting from another site. Kodavoor *et al.* [18] observed that prompt regrafting reduced the risk of further complications like recurrence, retraction with autologous serum. Maximum graft loss and displacement was noted in early period in both groups. Conjunctival autografts in pterygium surgery follow a consistent healing pattern dominated by re-perfusion injury in early postoperative days [12]. Our study establishes this fact hence we advocate 48 hours of patching in group B is beneficial. Same method of 48 hours patching was done in other studies [13, 23].
After analysis rate of graft loss and partial displacements, our study shows promising outcome in group B. Glue is a better adhesive than autologous in relative manner but with improvisation of standard protocol, even the latter can achieve comparable results.
There was one case of conjunctival granuloma in group A which was treated with prednisolone drops. Also, we noticed two grafts retraction in both groups. Although this phenomenon can be attributed to graft size disparity, but more studies are needed.
Few other studies gave promising results with autologous serum. [19, 20] and even long-term outcome and recurrence is better according to another study [21].
Most important finding was recurrence rate of 6.7% (2 out of 30) in each group. Similar promising results in terms of recurrence rate in another study [17]. Kurian *et al.* [21] stated that recurrence rate was 6.25% and 8.16% in glue and autologous serum group respectively. The main aim should be on meticulous dissection of pterygium that is excision of the pterygium body and underlying Tenon's layer to the length of the pterygium head [22] to avoid recurrence.
With regards to age, we found all 4 recurrent cases were from the age group 35-50 years.
Same correlation in one study stating recurrences is more frequent in younger patients [23].
As opposed to a study where graft retraction is more common with grafting with autologous blood than with the glue [23], our study found same rate of graft retraction in both groups (6.6%). Graft retraction can also be attributed to grade of pterygium or incorrect graft size used [24]. Group A has an average graft size of 6.2 mm × 6.8 mm and group B a smaller graft size average 5.5 mm × 6.2 mm. In comparison, Group A has larger graft size than group B.
Another study [25] found no untoward complication in small to average graft size. Although this is to be evaluated and studied in detail.
There are few steps in surgery to highlight which are important to have better graft stability and low rates of recurrence in autologous serum method such as

- Standard patient selection
- Appropriate graft size in abducted eye (graft size 0.5 mm larger than bare sclera)
- Patching for 48 hours

Conclusion
We know autologous serum is a natural good adhesive, cost effective and not market dependent. SCH is most common adverse event in serum group, but it does not harm the graft integrity. For first few days, SCH causes poor cosmesis. Hence, there is a learning curve in knowing how much ooze quantity is enough for proper graft adherence. More prospective studies should be conducted to understand the pattern for adherence. Our study observes Graft losses and partial displacements are early phenomenon, so patching for 48 hours is beneficial in group B. Autologous serum method is safe, efficacious and cost effective yet not commonly performed and accepted. As per our study, this method is associated with less postoperative discomfort with success rates that are comparable to fibrin glue.

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