Conjunctival Autograft Versus Amniotic Membrane Transplantation After Double Pterygium Excision: A Randomized Trial

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Purpose: To compare the outcome of amniotic membrane transplantation (AMT) and conjunctival autograft (CAG) after pterygium excision in patients with nasal and temporal pterygium (double pterygium) in the same eye.

Methods: Tertiary care medical center. A total of 33 eyes of 33 patients with previously unoperated double pterygium were enrolled in the randomized trial, of which 31 remained in follow-up at 1 year. Eyes with double pterygium were randomized to either nasal AMT and temporal CAG (nasal AMT group) or to temporal AMT and nasal CAG (temporal AMT group). The primary prespecified outcome was pterygium recurrence at the excised site 1 year after pterygium excision.

Results: At 1 year none of the 31 pterygia randomized to CAG showed recurrence in either the nasal or temporal location (0%, 95% confidence interval, 0%–11.2%). In contrast, 8 of 31 pterygia randomized to AMT exhibited recurrence at 1 year (25.8%, 95% confidence interval, 11.9%–44.6%), with 4 temporal recurrences and 4 nasal recurrences. The recurrence rate was significantly higher for AMT than CAG ($P = 0.005$: primary analysis), but not significantly different between the nasal and temporal sites ($P \geq 0.99$).

Conclusions: The use of CAG in pterygium surgery led to fewer recurrences than AMT, irrespective of the site of replacement.

Key Words: conjunctival autograft, amniotic membrane graft, double pterygium

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Pterygium is a common ocular disorder wherein a wing-shaped fibrovascular growth of conjunctiva extends up to or over the cornea. Smaller pterygia are symptomless, whereas larger pterygia can cause irritation and reduce visual acuity. Pterygia occur worldwide but the prevalence is high particularly within the periequatorial "pterygium belt," 30° N and 30° S of the equator.[1] Surgical intervention is typically considered for pterygia that cause irregular astigmatism, restriction of ocular movements, unacceptable cosmetic appearance, occurrence of secondary degenerative changes, or persistent irritation.[2]

Several modalities of surgical treatment have been described for this condition,[3] including the bare sclera technique,[4] translocation of pterygium head, use of adjuvants like mitomycin C,[5,6] and beta irradiation.[7] Recently, many surgeons have incorporated tissue transplantations after pterygium excision in an effort to reduce recurrence. The most common tissues that have been used as replacements are conjunctival autograft (CAG) and amniotic membrane transplantation (AMT). Randomized studies have shown the superiority of CAG over AMT in pterygium surgery.[8,9] It is not rare for nasal and temporal pterygium to coexist in the same eye. In such instances, a larger tissue is required to cover both raw surfaces. Although CAG may be taken from the superior and inferior bulbar regions, it may not be possible in all circumstances. The need to preserve enough conjunctiva, for example, in conditions which might warrant future filtering surgery has led to the consideration of alternate tissue supplementations. AMT is a commonly used tissue replacement in such circumstances.[9] Since nasal pterygia are usually larger than temporal pterygia, patients with double pterygium often have CAG transplanted in the nasal aspect. Anecdotally, it had been our impression that temporal pterygia recur more commonly after excision than do nasal pterygia, although we recognized that this observation could have been biased by our routine use of CAG for the nasal pterygium. This study was performed to compare the efficacy of CAG and AMT in preventing recurrence of pterygium, independent of the site of pterygium excision.

MATERIALS AND METHODS

Ethics Statement

Ethical approval for this randomized trial was obtained from the Aravind Eye Care System Institutional Review Board; the trial conformed to the Declaration of Helsinki. The trial was registered with Clinical Trials Registry of India, registration number CTRI/2015/07/005960.

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Study Population

Patients older than 18 years diagnosed with operable primary double pterygium at Aravind Eye Hospital Madurai between April 1, 2012, and March 31, 2013, were invited to be part of this study. Primary double pterygium was defined as the occurrence of significant nasal and temporal pterygium in the same eye without any obvious precipitating factors and without prior conjunctival surgery. Eyes were considered for surgery of both pterygia if they met at least 1 of the following criteria: (1) keratometric astigmatism of more than 1.5 diopters, (2) encroachment of both pterygia up to or over the cornea, (3) moderate to severe degenerative changes in both pterygia (eg, cystic structures), (4) repeated inflammation of both pterygia causing discomfort, or (5) restriction of extraocular motility. Exclusion criteria included unwillingness to commit to follow-up, a history of trauma thought to play a causative role in the formation of the pterygium, pregnancy, and prior enrollment of the contralateral eye in the trial.

Randomization

After obtaining written informed consent, participants were randomized in a 1:1 ratio to one of 2 groups: nasal AMT with temporal CAG (nasal AMT group) or temporal AMT with nasal CAG (temporal AMT group). Randomization was performed by the trial biostatistician with the *rand* and *sort* functions in Excel (Microsoft, Redmond, WA) and the randomization sequence was stored in a series of sealed envelopes labeled with sequential numbers. Envelopes were opened by the assisting nurse in numerical order in the operation theater just before the start of the surgery.

Preoperative Assessment

A complete ophthalmic examination was done before the surgery. Study participants underwent Snellen visual acuity measurement, slit lamp examination of the anterior segment, evaluation of extraocular movements, keratometry, and fundus examination.

Preparation of Amniotic Membrane Graft

Amniotic membrane graft was prepared and procured according to standard technique.

Surgical Procedure

All surgeries were performed by a single surgeon who was not involved in the process of postoperative evaluation. The nasal and temporal pterygia were operated in the same sitting. Surgeries were performed under peribulbar anesthesia.

Excision was performed similarly for nasal and temporal pterygia. Briefly, the head of the pterygium was dissected from the apex using a No. 15 surgical blade. The superficial conjunctival tissue was then excised. The underlying Tenon capsule and subconjunctival tissue were dissected beyond the area of the superficial conjunctival excision. The bleeding vessels were cauterized with wet field cautery. The CAG was prepared from the superior bulbar conjunctiva and care was taken to prepare it without disturbing the underlying Tenon capsule. For both CAG and AMT transplantations, the conjunctival side of the transplant was sutured using 8-0 vicryl suture, while the limbal side was anchored using 10-0 nylon suture. The postoperative medical regimen consisted of a topical antibiotic–steroid combination (gatifloxacin 0.3%–dexamethasone 0.1%) in tapering doses for a period of 3 weeks.

Postoperative Assessment

Postoperative slit lamp examinations were performed at 3 weeks (±2 weeks), 6 months (±2 months), and 1 year (±2 months). Recurrence was graded separately for the nasal and temporal sides (according to the grading system reported by Prabhasawat et al[10]). Grade 1 indicates that the appearance of the operated site was not different from the normal appearance; grade 2 indicates the presence of some fine episcleral vessels in the excised area extending up to, but not beyond, the limbus and without any fibrous tissue; grade 3 indicates the presence of additional fibrous tissue in the excised area that did not invade the cornea; and grade 4 represents true recurrence, with fibrovascular tissue invading the cornea. We defined recurrence in this study as grades 3 or 4. All postoperative evaluations were performed by 2 ophthalmologists who were not involved in the clinical care of the study participants and who were not informed of the treatment allocation.

Statistical Considerations

The primary comparison was pterygium recurrence at 1 year in pterygia treated with AMT versus CAG. The 2 pterygia from each eye were treated as a pair and the recurrences were compared between the 2 treatment groups in a McNemar test. As a secondary analysis, a subgroup analysis was performed using the same statistic based on whether the CAG had been randomized to the nasal or temporal side. Assuming a 22% recurrence rate for pterygia treated with AMT and 5% loss to follow-up, including 18 participants per group would provide 80% power to detect a significant difference with a McNemar test assuming a 2-sided alpha of 0.05 (*power paired proportions* command in Stata).

RESULTS

A total of 37 eyes of 37 patients were deemed eligible for enrollment during the period April 1, 2012, to March 31, 2013. Of these, 4 patients were not willing to be part of the study. Table 1 shows the baseline characteristics of study participants and eyes enrolled in the study; the median age of participants was 59 years (interquartile range 44–64 years), and 22 (60.6%) were female. A total of 16 eyes were randomized to the nasal AMT group and 17 to the temporal AMT group. Table 2 shows the baseline characteristics of pterygia randomized to AMT versus CAG; the size and grading of the pterygia between the 2 groups and also

TABLE 1. Baseline Characteristics of Study Participants Randomized to Nasal AMT and Temporal AMT Group

Characteristics	Number (%) or Median (IQR), N = 33
Participant characteristics	
Age, yrs	59 (44–64)
Female	22 (60.6)
Eye characteristics	
Right eye, N (%)	17 (51.5)
Visual acuity	6/18 (6/6 to HM+)
Keratometry	43.50 (42.87–45.12)
Extraocular motility restriction	0 (0)

HM, hand movements; IQR, interquartile range.

between nasal and temporal pterygia was not significantly different. A single surgeon performed all the surgeries and similar technique was performed for all. There were no intraoperative or postoperative complications or any serious adverse effects.

Two study participants did not complete the 1-year follow-up visit, leaving 31 pairs of pterygia for the primary analysis. Of these, 8 pterygia from 8 eyes had a recurrence at 1 year. All 8 recurrences were classified as grade 3 according to the prespecified grading scale. None of the 31 pterygia randomized to CAG had recurrence (0%, 95% confidence interval, 0%–11.2%), compared with 8 of the 31 pterygia randomized to AMT (25.8%, 95% confidence interval, 11.9%–44.6%); $P = 0.005$, McNemar test, primary analysis. Among the 8 recurrences from pterygia treated with AMT, 4 occurred in nasal pterygia and 4 in temporal pterygia. The same result was observed in subgroup analyses in which eyes were stratified by randomization group ($P = 0.045$ for the nasal AMT group and $P = 0.045$ for the temporal AMT group). The rate of recurrence was no different in nasal pterygia compared with temporal pterygia ($P > 0.99$: McNemar test).

TABLE 2. Baseline Characteristics of Pterygia

Pterygium Characteristic	Amniotic Membrane Transplant, N = 33	Conjunctival Autograft, N = 33
Nasal, N (%)	16 (48.5)	17 (51.5)
Length, median (IQR), mm		
Nasal pterygium	2.2 (1.6–3.4)	3.0 (1.8–4.0)
Temporal pterygium	2.0 (1.6–3.0)	2.0 (1.2–3.1)
Grade, N (%)		
Nasal pterygium		
T1	1 (3.0)	0 (0)
T2	12 (36.3)	15 (45.4)
T3	3 (9.0)	2 (6.0)
Temporal pterygium		
T1	3 (9.0)	0 (0)
T2	11 (33.3)	14 (42.4)
T3	3 (9.0)	2 (6.0)
History of inflamed pterygium, N (%)	0 (0)	0 (0)

IQR, interquartile range.

DISCUSSION

We found that at 1-year follow-up, 25.8% of double pterygia cases had experienced recurrence, with all recurrences occurring at the site where AMT was used. This confirms the results of previous studies that have found CAG to be superior to AMT and extend the results to the case of double pterygium.[8–10] This study also provided an unbiased assessment of recurrence after nasal versus temporal pterygium excision, and contrary to our hypothesis, failed to find a difference in recurrence between the 2 surgical sites. CAG is widely used as a tissue replacement after pterygium excision because of its ease of procurement and the excellent anatomical and functional results after this technique. CAG provides a source of healthy conjunctival epithelium and acts by contact inhibition effect on the residual abnormal tissue. In addition, CAG including the limbus may yield a better result by acting as a barrier against fibrovascular invasion of the cornea and supplying stem cells to the corneal epithelium. AMT may help by suppressing transforming growth factor-β signaling and thus acting as an antifibrotic agent.[12] Additionally, amniotic membrane acts as a basement membrane substrate that allows epithelium to grow over it, perhaps speeding the healing process. AMT is considerably more expensive than CAG and is often reserved for cases like double pterygium and recurrent pterygium (in the absence of adequate conjunctiva for securing a CAG) and for patients with glaucoma (to preserve conjunctiva for future filtration surgeries).[13]

We graded pterygium recurrences based on the criteria suggested by Prabhasawat et al.[10] It is worthwhile to note that all recurrences in this trial were of grade 3 (fibrovascular tissue at the site of the pterygium, but not extending over the cornea). We did not observe a single grade 4 recurrence (fibrovascular growth over the corneal surface), and none of the recurrences observed in the trial were scheduled for a second pterygium surgery. Thus, although CAG was superior to AMT in this study, the latter technique still performed reasonably well.

In our study, at 1-year follow-up, there were no recurrences when CAG was used either at the nasal or temporal site, although our confidence intervals indicated that we would expect to observe up to 11% recurrences with this technique. In contrast, about one-quarter of nasal pterygia did experience recurrence. Our results are consistent with several prior randomized trials that found higher rates of recurrence in eyes treated with AMT than in eyes treated with CAG (5%–12%),[8,9] although a different trial failed to find any difference between the 2 treatments.[11]

This trial is novel because it randomized AMT and CAG to either the nasal or temporal pterygium, which eliminated any potential bias that the surgeon might have had related to whether nasal pterygia would be more likely to recur. Based on anecdotal experiences, we thought that temporal pterygia would be more likely to recur. However, this trial provided no evidence to support that hypothesis. Thus, in cases of double pterygium, factors other than pterygium side may be more important for determining which pterygium to treat with CAG and which to treat with AMT, such as size and inflammatory activity.

The study also has several limitations. Although we attempted to mask the assessment of the primary outcome by having follow-up evaluations for the trial performed by separate ophthalmologists not involved in the care of the patient, it was impossible to mask the surgeon. In addition, since AMT often appears more transparent than CAG, complete masking at the postoperative examinations might not have been achieved. The trial was performed in South India, so the generalizability of the results to other races and settings is unclear.

To the best of our knowledge, this is the first randomized trial comparing the efficacy of CAG and AMT in pterygia from the same eye for preventing recurrence after pterygium surgery. We found no difference in recurrence between nasal and temporal pterygia, and hence no evidence to support the routine use of CAG for either the nasal or temporal side during pterygium surgery. CAG was superior to AMT as a tissue replacement after pterygium surgery irrespective of the site of transplantation and should be considered as the technique of choice for tissue replacement in pterygium surgery.

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