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Research Article

A COMPARATIVE STUDY TO EVALUATE THE CLINICAL OUTCOME OF CONJUNCTIVAL LIMBAL AUTOGRAFT AND AMNIOTIC MEMBRANE TRANSPLANT FOR THE TREATMENT OF PRIMARY PTERYGIUM

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ABSTRACT

Objective: The aim of the study was to assess the safety and effectiveness of the conjunctival limbal autograft (CLAG) and amniotic membrane transplantation (AMT).

Methods: After a full pre-operative assessment 100 patients with primary pterygium attending the ophthalmology outpatient department of a teaching hospital in Eastern India, fulfilling the inclusion and exclusion criteria were selected for our study. The patients were explained the procedure of the study and possible outcomes. They were divided into two groups. Group A: Where 10-0 nylon was to be used for CLAG after pterygium excision. Group B: Where 10-0 nylon was to be used for AMT after pterygium excision.

Results: There was marked improvement in vision postoperatively more in the AMT group than CLAG. In the AMT group: 34% had a visual acuity of LogMAR 0.00, 30% had LogMAR 0.12, 12% had LogMAR 0.18, and 24% had LogMAR 0.30 after the surgery. In the CLAG group: 52% had a visual acuity of LogMAR, 20% had LogMAR 0.12, 22% had LogMAR 0.18, and 6% had LogMAR 0.30 after the surgery. Graft and suture-related complications were more in the CLAG group than in the amniotic membrane (AM) graft group.

Conclusion: In the present study, The CLAG group was found to be associated with more discomfort, and more post-operative complications than AMT. AM may provide a basement membrane rich in various growth factors and matrix proteins, which promotes epithelial cell migration, adhesion, and differentiation. It is also believed to have anti-inflammatory and antifibrotic effects and exerts anti-scarring effects through the transforming growth factor-β pathway. AMT may be a superior treatment in primary pterygium due to lower recurrence rate, shorter surgical times, and better visual and cosmetic outcomes.

Keywords: Pterygium, Conjunctival limbal autograft, Amniotic membrane transplant.

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INTRODUCTION

Etymologically speaking the word pterygium is derived from the Greek word "Pterygos" which means "wing." It is a triangular fibrovascular subepithelial ingrowth of the degenerative bulbar conjunctival tissue over the limbus extending onto the cornea. Pterygium is not just a degenerative disease but may be a proliferative disorder of the ocular surface. [1] Pterygium is especially prevalent in the so-called "pterygium belt" that extends across the tropics [2]. Histologically, pterygium shows elastotic degeneration in the vascularized subepithelial stromal collagen [3]. The factors implicated in the formation of pterygium include excessive light exposure, heat, dryness, dust, and wind. It has been shown that it is twice as common among people working outdoors. However, the incidence decreases by up to five among people who wear sunglasses in outdoor working environments [4,5]. Among the various factors thought to be responsible for pathogenesis of pterygium, ultraviolet radiation [6-8] remains the most common, but the main mechanism through which it results in pterygium formation is unclear [9]. Histopathologically, pterygium is characterized by the centripetal growth of a cluster of altered limbal stem cells (LSCs) followed by squamous metaplasia and an epithelium containing hyperplastic goblet cells along with Bowman's membrane dissolution accompanied by abundant active fibroblasts, a proliferative stroma with inflammation and neovascularization and extracellular matrix [10]. Recent studies reveal increased levels of the transcription factors cAMP response element-binding protein [11,12], cytochrome P450 1A1 protein [13], phospholipase D [14], and aquaporin-1 and -3 [15] as risk factors for pterygia development.

Conjunctival limbal autografting is a well-accepted procedure and has proven to be both safe and effective in reducing pterygium recurrence. The LSCs are important in maintaining the limbal barrier between the cornea and the conjunctiva. Chronic focal UV radiation-mediated alterations in nasal LSCs [16] may result in a failure of the limbal barrier, providing a sound explanation for the nasal predisposition of pterygium. The human amniotic membrane (AM) has anti-scarring, antiangiogenic, and anti-inflammatory properties. The basement membrane acts as a substrate to allow healing and epithelialization, and these properties lend themselves to pterygium surgery [17,18].

METHODS

This study was a hospital-based, longitudinal, prospective, and observational study. The study population comprised adult patients with primary pterygium. All the patients enrolled volunteered to take part in the study, and all of them gave informed written consent for this study. The study had the approval of the institutional scientific review committee. 100 patients in the age group of 20–80 years were enrolled. The patients were divided into two groups of 50 each. The patients with progressive pterygium that caused a significant decrease in vision, persistent irritation, and patients with pterygium which were cosmetically bothersome to them were included in the study. Patients with atrophic pterygium, pseudopterygium, recurrent pterygium, patients on anticoagulants, or those with a history of ocular surgery or trauma, and all those patients who had any form of ocular surface disorders were excluded from the study.

Sampling method

Convenience sampling.

Study technique

Following a complete pre-operative assessment, patients with primary pterygium attending the ophthalmology outpatient department of a teaching hospital in Eastern India were shortlisted for enrolment into the study. A comprehensive medical and ocular history was obtained. Patients underwent visual acuity measurement, thorough slit lamp examination, and a careful fundus examination. A total of 100 patients who matched the predetermined inclusion criteria were enrolled. Patients were randomly divided into two equal groups of 50 each, the first group, or Group A was the conjunctival limbal autograft (CLAG) group and the second group was Group B, or the AM transplantation (AMT) group. A single surgeon performed all surgeries. The patient was laid down in a supine position on the operating table. The initial antiseptic dressing was done with a 5% povidone-iodine solution. Peribulbar block was administered with 4–5 mL of 2% lignocaine and adrenaline mixed with hyaluronidase. Repeat antiseptic dressing was done with a povidone-iodine solution followed by sterile surgical draping.

For Group A, the CLAG graft was placed onto the bare sclera, and its four corners were anchored to the conjunctiva and episclera with 10-0 nylon sutures. Care was taken to maintain the spatial orientation of the graft about the limbus. Then, more stitches were given to adequately fix the graft. This required five stitches on average. The sutures were removed 1-month postoperatively. For Group B, the AM graft (AMG) was taken and cut into the desired measurement. The nitrocellulose paper was removed from the AMG. The four corners of the graft were anchored to the conjunctiva and episclera with 10-0 nylon sutures. Care was taken to maintain the spatial orientation of the graft about the limbus. Then, more stitches were given to adequately fix the graft. This required five stitches on average. The sutures were removed 1-month postoperatively.

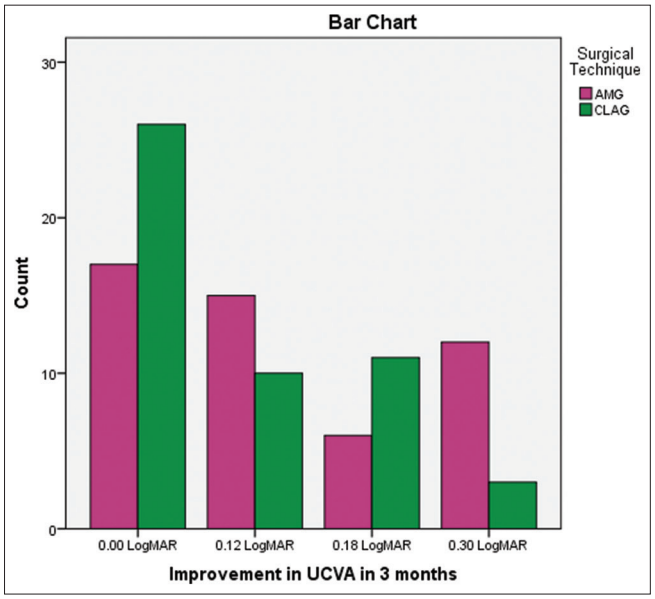

Fig. 1: Improvement in visual acuity (uncorrected) between the amniotic membrane transplantation group and conjunctival limbal autograft group at 3-month post-operative

Table 1: Improvement in uncorrected visual acuity after 3-month postoperatively compared between the two groups

Improvement in UCVA in 3 months	Surgical technique		Total
	AMG (%)	CLAG (%)	
0.00	17 (34)	26 (52)	43
0.12	15 (30)	10 (20)	25
0.18	6 (12)	11 (22)	17
0.30	12 (24)	3 (6)	15
Total	50	50	100

AMG: Amniotic membrane graft, CLAG: Conjunctival limbal autograft

Table 2: Distribution of graft-related complications on post-operative day 1, day 7, 1st month, and 3rd month

Graft related complications	Surgical technique	
	AMG (%)	CLAG (%)
Graft-related complications on Day 1		
Graft buttonhole	3 (6)	3 (6)
Graft dehiscence	2 (4)	2 (4)
Graft laceration	2 (4)	2 (4)
Graft edema	8 (16)	3 (6)
Graft retraction	0 (0)	1 (2)
Graft size disparity	3 (6)	5 (10)
Nil	32 (64)	34 (68)
Graft-related complications at Day 7		
Graft button hole	1 (2)	3 (6)
Graft laceration	1 (2)	1 (2)
Graft edema	6 (12)	2 (4)
Graft size disparity	0 (0)	7 (14)
Nil	42 (84)	37 (74)
Graft-related complications at 1 month		
Graft edema	0 (0)	1 (2)
Nil	50 (100)	49 (98)
Graft-related complications at 3 months		
Nil	50 (100)	50 (100)

AMG: Amniotic membrane graft, CLAG: Conjunctival limbal autograft

Table 3: Distribution of suture related complications on post-operative day 1, day 7, 1st month, and 3rd month

Suture related complications	Surgical technique	
	AMG (%)	CLAG (%)
Suture complications on day 1		
Conjunctival cyst	1 (2)	5 (10)
Loose suture	2 (4)	9 (18)
Nil	47 (96)	36 (72)
Suture complications at day7		
Conjunctival cyst	1 (2)	5 (10)
Graft loss	1 (2)	0 (0)
Loose suture	2 (4)	8 (16)
Nil	46 (92)	37 (74)
Suture complications at 1 month		
Nil	50 (100)	50 (100)
Suture complications at 3 months		
Nil	50 (100)	50 (100)

AMG: Amniotic membrane graft, CLAG: Conjunctival limbal autograft

Table 4: A comparison between the present study and a few similar studies on uncorrected visual acuity

Name of study	No. of patients	Improvement in UCVA		
Malik *et al*. [19]	40	0.18–0.5 LogMar units in 17.5% of patients at 6 weeks		
Elwan [20]	150	0.2–0.5 LogMar units in 6.66% at 3 months		
Sharma *et al*. [21]	80	In 3.75% of patients gain in BCVA* by 1 line in Snellen's chart In 1.25% of patients gain in BCVA by 3 lines		
		LogMAR	AMG (%)	CLAG (%)
Present study	100	0.00–0.12	64	72
		0.18–0.3	32	28

*Best corrected visual acuity. *P*=0.021 (significant), AMG: Amniotic membrane graft, CLAG: Conjunctival limbal autograft

Table 5: Various similar studies and the graft-related complication rates compared

		In CLAG group				
Name of study	**Total no. of patients**	**Graft retraction**	**Graft edema**	**Graft dehiscence**	**Graft displacement**	**Graft loss**
Singh *et al*. [22]	50-	11%	55.5%	-	-	-
Malik *et al*. [19]	40	7.5%	-	5%	-	-
Kodavoor *et al*. [23]	681	6.94%	70%	-	-	1.73%
Choudhury [24]	32	6.25%	-	13.33%	-	-
In AMT group						
Toker [25]	65	-	CLAG- 32.4%	AMG-5.4% CLAG-5.5%	-	-
Present study	100	AMG- nil CLAG- 2%	AMG- 16% CLAG- 6%	AMG-4% CLAG-4%	CLAG-14%	-

AMT: Amniotic membrane transplantation, CLAG: Conjunctival limbal autograft, AMG: Amniotic membrane graft

Table 6: Various similar studies and the suture-related complication rates compared

Name of study	**Total no of patients**	**Suture related complications**
Singh [22]	50	Conjunctival granuloma-2.2%
Kodavoor *et al*. [23]	681	Granuloma-1.16%; not significant
Present study	100	AMG- 2% conjunctival cyst, 4% loose suture, 2% graft loss CLAG-10% conjunctival cyst, 16% loose suture

CLAG: Conjunctival limbal autograft, AMG: Amniotic membrane graft

Follow-up

Follow-up visits were scheduled on 1st post-operative day, 1st post-operative week, and 1st, 3rd, and 6th -month post-operative. On the 1st post-operative day, patients were started on steroid antibiotic eye drops and carboxy methyl cellulose eye drops 6 times and 4 times a day, respectively. Any loose sutures were removed during the follow-up. The remaining sutures were removed after 1 month. Steroid antibiotic drops were tapered depending on the resolution of inflammation. On each follow-up visit, patients were evaluated for graft edema, graft dehiscence, graft retraction, graft displacement, graft loss, and suture-related complications like granuloma. Uncorrected visual acuity was measured at each visit. Tonometry was done at each follow-up visit. Any signs of graft necrosis such as avascularity, retraction of graft edge, or exposure of bare sclera were noted as also signs of scleral necrosis like guttering or thinning of sclera and avascularity of the region were noted. Outcome measures that were considered were improvement in vision after the surgery and graft as well as suture-related complications.

Analysis of data

Data were entered into a Microsoft Excel spreadsheet and analyzed using IBM SPSS STATISTICS 20. Visual Acuity tested by Snellen's chart was converted into LogMAR units for statistical analysis. Statistical tests (Chi-square test, t-test, and Fisher's exact test) were applied as necessary. $p \leq 0.05$ was defined as statistically significant.

RESULTS

The improvement in uncorrected visual acuity at 3-month postoperatively was statistically significant in both groups. Quantum of improvement in visual acuity was better in the AMT group. However, final uncorrected visual acuity was better in the CLAG group. In the AMT group: 17 patients (34%) had a visual acuity of LogMAR 0.00, 15 patients (30%) had LogMAR 0.12, 6 patients (12%) had LogMAR 0.18, and 12 patients (24%) had LogMAR 0.30 after the surgery. In the CLAG group: 26 patients (52%) had a visual acuity of LogMAR 0.00, 10 patients (20%) had LogMAR 0.12, 11 patients (22%) had LogMAR 0.18, and 3 patients (6%) had LogMAR 0.30 after the surgery see Figure 1.

Early (1–7-day postoperatively) graft-related complications were more common in the AMT group. However, differences in graft-related complications were almost extinguished in the later post-operative period with both groups reporting nil complications 3-month postoperatively. Suture-related complications were much lesser in the AMT group as compared to the CLAG group. Early (within 7-day postoperatively) suture-related complications were more frequent in the CLAG group. Differences in suture-related complications between the two groups narrowed down during a later follow-up period and were extinguished at 3 months. The results have been tabulated in the tables 1-3.

DISCUSSION

In this study, 100 patients with primary pterygium were enrolled. They were divided into two groups of fifty each, one group of patients received CLAG and the other group received AMG. It is believed that CLAG is the best treatment for pterygium as it prevents recurrences to a large extent. However, the CLAG technique is associated with morbidity, long operative time, and graft-related or suture-related complications. In the present study, a statistically significant difference was found in the grades of the post-operative subconjunctival hemorrhage, foreign body sensation, pain, and suture-related complications between the patients of the two groups at post-op day 1 ($p<0.05$). The CLAG group was found to be associated with more discomfort, and more post-operative complications than AMT. Prasad *et al*. [26] in their study found that the sutureless technique of graft placement resulted in lesser post-operative morbidity. Clearfield *et al*. [27] preferred CLAG over AMT as it was associated with fewer complications and better recurrence control. Yin *et al*. [28] in their studies demonstrated that AMT after pterygium excision was a better alternative to CLAG especially in post-operative ocular surface health and tear film stability. A few other studies and their main features have been tabulated in Tables 4-6.

CONCLUSION

While conjunctival autografting has gained worldwide acceptance for the treatment of pterygium, it is not without its demerits such as a long surgical time, graft inversion, and iatrogenic injury to the rest of the conjunctiva. Conjunctival autograft is also associated with significant discomfort in the immediate post-operative period. AMT may be a superior treatment in primary pterygium due to its lower recurrence rate, shorter surgical times, and its proven superiority where ocular surface defects exist. Better ocular surface reconstruction means better tear film stability and comfort for the patient. Further studies are needed to determine the respective role of the ocular surface epithelium and fibroblasts in interacting with the AM matrix. We suggest that AMT can be considered for conjunctival surface reconstruction, especially when a large lesion on the inter-palpebral zone is operated on.

AUTHOR CONTRIBUTION

Preparation of this manuscript: Dr. Arkendu Chatterjee, Data Collection and Statistical Analysis: Dr. Shafaque Sahar. Design and monitoring of the study: Prof Dr. Udayaditya Mukherjee and Dr. Rupam Roy.

CONFLICTS OF INTEREST

The authors state that conflicts of interest exist.

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