Amniotic membrane transplant with superficial keratectomy in superficial corneal degenerations: Efficacy in a rural population of north India

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Aim: To evaluate the applicability and efficacy of superficial keratectomy with transplantation of preserved amniotic membrane in superficial corneal degenerations in a rural population of Northern India in terms of visual improvement and surface regularization.

Settings: Peripheral referral center in rural north India.

Materials and Methods: This was a prospective non-comparative interventional case series where 24 eyes of 20 farmers from peripheral rural areas (M:F = 19:1) with visually significant superficial degenerative disorders (15 eyes with climatic droplet keratopathy one of which was associated with Salzmann nodular degeneration and nine eyes with band-shaped keratopathy) were subjected to amniotic membrane transplantation (single or multiple layer) combined with superficial keratectomy. Subjective and objective outcomes after surgery were evaluated and analyzed and statistical significance of the outcomes in various disorders was evaluated.

Results: Eighty-eight per cent (21 eyes) had symptomatic relief from distressing preoperative symptoms while postoperative visual improvement by two or more lines was achieved in 23 eyes (96%) over a mean follow-up period of 26.8 ± 10.2 months. The surface irregularity present preoperatively was relieved in 23 cases while postoperative decline of vision with visually significant scarring was seen in one case (4%), which was labeled as failure.

Conclusions: Amniotic membrane transplant with superficial keratectomy helped achieve subjective comfort, visual rehabilitation and clinical regularization of the corneal surface in superficial corneal degenerations during the mean followup of 26.8 ± 10.2 months in rural setups.

Key words: Amniotic membrane, phototherapeutic keratectomy, superficial corneal degeneration

Indian J Ophthalmol 2008;56:297-302

Superficial corneal degenerations like climatic droplet keratopathy (CDK), band-shaped keratopathy (BSK), and Salzmann nodular degeneration cause pain, irritation, irregularity of the corneal surface, deterioration of vision by involving the central visual axis and vascularization accounting for a resultant decrease in the quality of life. The older methods of treatment for these disorders (like lubricants, contact lens) provide only temporary symptomatic relief while more invasive procedures like penetrating or lamellar keratoplasty are fraught with many other problems like the need for long-term follow-up and medications, high rate of complications like rejection or infections. These are therefore not suitable options for patients from remote rural areas with poor follow-up and questionable compliance. Amniotic membrane transplant

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Manuscript received: 21.10.07; Revision accepted: 06.03.08

Presented at: Best Free paper award at Annual UP state Ophthalmological Society, Ghaziabad 2005 and Annual Delhi Ophthalmological Society, Delhi 2006.

has been proven effective for ocular surface reconstruction and regularization after pterygium surgery, ocular burns and other cicatrizing corneal conditions owing to its advantageous properties like anti-inflammatory, aid in epithelization and anti-scarring properties in particular.³ Newer modes of treatment for superficial corneal degeneration include phototherapeutic keratectomy (PTK) which calls for expensive instrumentation that may not be feasible in rural areas.⁴⁻¹¹ By this study, we therefore endeavored to study the surgical outcomes after keratectomy coupled with amniotic membrane transplant in patients with superficial corneal degenerations like CDK and BSK in a rural setup.

Materials and Methods

This was a prospective non-comparative interventional case series of 24 eyes of 20 patients with superficial corneal degenerations, namely CDK, BSK and Salzmann nodular degeneration, who were subjected to superficial keratectomy with preserved amniotic membrane graft at our peripheral referral center in rural north India between June 2004 and July 2006. This study was conducted in accordance with the ethical standards (institutional) and with the Helsinki Declaration.

Detailed history was obtained from all the patients, including their preoperative symptoms, history of previous medications or relevant surgical history. Preoperative assessment of all the patients included the best corrected visual acuity, applanation tonometry and fundus examination. Ultrasound (B scan) examination was done for assessing the posterior segment in cases of media opacities precluding fundus examination. The corneal pathology was assessed by slit-lamp examination in terms of the type of lesion, the area involved and depth of involvement and extent of preoperative thinning. Ultrasound pachymetry was attempted in all cases to assess the corneal thickness. Qualitative placido disc images were studied at baseline and at each follow-up in all the cases to assess the amount of surface irregularity in the involved eye.

Patients with corneal perforation or active ulcers, high intraocular pressure, coexisting fundus abnormalities, significant cataract, associated surface problems like trichiasis, entropion and most importantly, patients with corneal thinning >30%, involvement of the middle or posterior stroma were excluded from the study. All patients were counseled in detail about their condition and a well-informed consent, explaining the purpose and potential risk of surgery, was taken from them before surgery.

Surgical technique

Preserved amniotic membrane for this study was procured from LV Prasad Eye Institute, Hyderabad. Frozen pieces of the membrane preserved in Dulbecco's modified Eagle's medium (DMEM) as 4×4 cm pieces and spread on nitrocellulose paper were used for the study (prepared and preserved according to that prescribed by Kim and Tseng).¹²

All eyes were operated by the same surgeons (AR and US). The procedure was performed under peribulbar anesthesia. The level and extent of dissection was determined based on preoperative findings, i.e. extent of involvement of the cornea, depth of involvement and the amount of corneal thinning. After epithelial debridement with a micro sponge or crescent knife in the involved area [Fig. 1A], lamellar dissection was performed in the involved area. Overzealous dissection was avoided in eyes with preexisting corneal thinning. Ethylene diamine tetra acetic acid (EDTA) (if available) was used in cases with BSK after epithelectomy to aid in the lamellar dissection and removal of calcium deposits.

The membrane was sutured to the involved ocular surface with the epithelial side down and secured with interrupted 10-0 nylon sutures to the cornea [Fig. 1B]. Limbus to limbus total cover was done in cases with diffuse lesions while the membrane was cut to the desired size in selected cases with less extensive involvement. Multiple layers of the membrane were used in cases with preoperative thinning >20% with one layer used as filler (placed epithelial side down, left unsutured) and another outer layer sutured to the cornea, epithelial side up. A large therapeutic contact lens (No 16) was placed over the membrane for comfort of the patient.

Postoperatively, the patients were routinely treated with topical antibiotic drops (Tobramycin, 0.14%) and cycloplegics (tropicamide 0.5%). Cornea was assessed with regard to epithelization (demonstrated by regularity of the surface in all areas and restoration of normal luster of the cornea under the contact lens), surface regularity of the cornea, residual disease and scarring. The amniotic membrane was inspected for evidence of any retraction or loss of the membrane in the postoperative period. Bandage contact lens was left *in situ*

till the interrupted sutures securing the graft were removed (recycling of the lens done every week). Suture removal was done by three weeks and any complication noted in the postoperative period was identified and treated accordingly. The patients were followed up on an outpatient basis (three-monthly). In the postoperative period, complaints pertaining to relief from the preoperative symptoms like watering, irritation, foreign body sensation were assessed through enquiry from the patients (no grading of the symptoms was done due to inconsistent responses from the patients with regards to the severity). Placido images were acquired in the postoperative period after suture removal and during each follow-up.

The results were analyzed and divided into subjective and objective success or failure (depending on set criteria) and the causes of failure, if any, were evaluated. Subjective success was defined as relief of all preoperative symptoms and subjective visual recovery. Partial success was defined as relief of only one symptom (watering, irritation with or without visual recovery) or only subjective improvement in vision and no relief of other symptoms. Failure was defined as deterioration of preoperative vision with or without relief of symptoms. Objective success was defined as visual recovery postoperatively by at least two or more lines, mild (not visually significant) scarring, regular corneal surface and qualitative improvement in surface regularity by placido disc images. Partial success was defined as having moderate scarring with reduced vision, residual disease, recurrence, or surface irregularity (visually significant). Failure was defined by decrease in postoperative vision, need for repeat surgery or need for penetrating keratoplasty.

Statistical analysis was done using SPSS version 10 and statistical significance was defined as *P* value <0.05 with student "t" test. Correlation was done using Pearson's correlation coefficient.

Results

Twenty-four eyes of 20 patients (15 CDK, of which one was associated with Salzmann degeneration, nine BSK) from peripheral rural areas in north India were included in the study. No ocular pathology was found in any case of BSK (ruled out on slit-lamp and fundus examination); though a screening for systemic causes could not be done in these rural patients, systemic examination did not reveal any signs of hypercalcemia or any other systemic disorder in any of our cases. There were 23 males (96%) and one female (4%) with the mean age of the patients being 69.2% \pm 7.4 years (ranging from 56-80 years). The patients were followed up for a mean period of 26.8 \pm 10.2 months. Table 1 shows the demographic and clinical characteristics of the cases included in the study. All patients were found to have preoperative symptoms interfering with their daily activities. Fig. 2A-D depicts the preoperative and postoperative photographs of a case of CDK.

Fourteen eyes (58%) had lesions involving the whole of the cornea while in 10 eyes (42%) the central 4-6 mm of the cornea was involved. Central corneal thickness could not be assessed in any case by pachymetry due to involvement of the central visual axis in all the eyes [Fig. 2A]. Preoperative thinning (therefore demonstrated on slit-lamp examination) up to 10-20 % was present in five eyes (21%). Seventeen eyes had a preoperative visual acuity less than 20/200 while seven

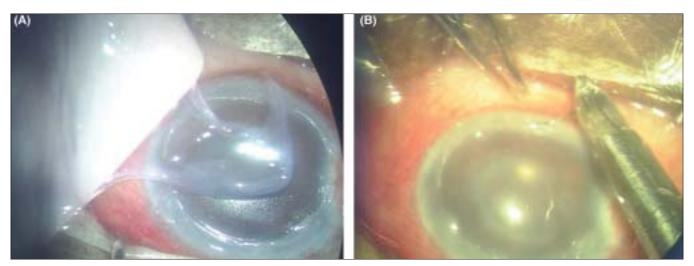


Figure 1: Surgical procedure of superficial keratectomy with amniotic membrane grafting (see text-surgical technique). (A) Intraoperative photograph showing the amniotic membrane placement over dissected bed after lamellar dissection with crescent knife (B) Intraoperative photograph showing amniotic membrane (figure showing total limbus to limbus cover) being secured to the cornea

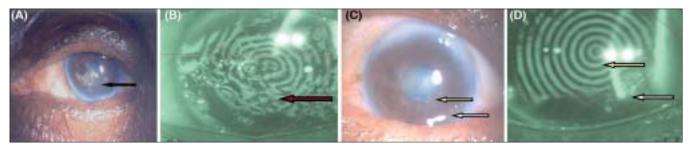


Figure 2: Pre- and postoperative clinical photographs of operated eyes with climatic droplet keratopathy. (A) Preoperative photo showing elevated lesions of spheroidal degeneration (red arrow) involving central cornea. (B) Preoperative placido images of same patient showing severe distortion of central rings (red arrow). (C) Postoperative slit-lamp photograph showing clearing of central cornea with minimal scarring (yellow arrow) and residual lesions (white arrow). (D) Postoperative placido images showing regularization of the central rings in the visual axis (yellow arrow) with residual irregularity in the periphery (White arrow)

had visual acuity between 20/200-20/60 [Table 1].

Three cases with corneal thinning by 20% were grafted with multiple layers of amniotic membrane. Only two cases with BSK underwent EDTA application with superficial keratectomy. No intraoperative complications were noted in any case.

Postoperatively, subjective relief of preoperative watering due to the corneal disease was achieved in 88% cases (21 patients) while irritation was relieved in 83% cases (20 patients). Overall, relief of one or more symptoms was seen in 23 eyes. More eyes with BSK experienced subjective relief than CDK.

Subjective visual recovery was felt in 88% patients (21 cases; though objectively visual improvement by more than two lines occurred in 23 eyes, two patients denied any subjective improvement in their vision postoperatively). The overall postoperative vision improved after the procedure with 23 eyes gaining two-line improvement (P<0.001). While 67% (16/24 eyes) of eyes had a vision <20/200 preoperatively, only 17% of eyes (4/24 eyes) had similar acuity postoperatively (P<0.001, Fig. 3). Objective visual improvement was seen in 12 of 15 eyes of CDK [Table 2] as opposed to six of nine eyes with BSK though this was not statistically significant.

The surface regularity improved after the procedure in 23 cases (96%) as observed in placido disc images evidenced by decreased distortion of the rings in the involved area with decrease in the area of distorted mires.

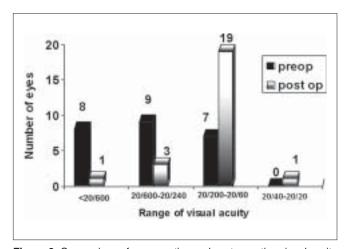


Figure 3: Comparison of preoperative and postoperative visual acuity of all patients subjected to the study

Table 1: Demographic characteristics of patients subjected to superficial keratectomy and amniotic membrane grafting for superficial corneal degenerations

Age (yrs)	Sex	Diagnosis	Thinning	Symptoms		Visual acuity		Outcome		Complications
				Preoperative	Post operative	Preoperative	Post operative	Subjective	Objective	
60	М	CDK	20%	W,I,VC	-	FC	20/400	S	PS	Recurrence
60	M	CDK	-	W,I,VC	-	20/600	20/300	S	S	-
70	M	CDK	-	W,I,VC	-	20/600	20/60	S	S	Retraction
60	M	BSK	-	W,I,VC	-	20/400	20/60	S	S	-
80	М	BSK	10%	W,I,VC	I,VC	FC	20/600	PS	PS	Moderate scarring
60	F	CDK	-	W,I,VC	-	20/300	20/60	S	S	-
74	M	CDK	-	W,I,VC	-	FC	20/200	S	S	-
74	M	CDK	-	W,I,VC	-	FC	20/300	S	S	-
70	M	CDK	10%	W,I,VC	-	20/1200	20/200	S	PS	Retraction
56	M	CDK	-	W,I,VC	-	20/400	20/200	S	S	-
70	M	CDK	-	W,I,VC	I	FC	20/200	S	S	-
65	M	BSK	20%	W,I,VC	W,VC	20/120	20/200	Fa	Fa	Graft loss, ED
60	M	CDK	-	W,I,VC	-	20/200	20/80	S	PS	Residual
60	M	CDK	-	W,I,VC	-	20/200	20/80	S	S	-
67	M	CDK	-	W,I,VC	-	20/80	20/40	S	S	Retraction, ED
80	M	BSK	-	W,I,VC	-	20/200	20/80	S	S	-
80	M	CDK	-	W,I,VC	I,VC	20/120	20/40	PS	S	-
70	M	CDK	-	W,I,VC	W	20/1200	20/200	PS	S	-
80	M	BSK	-	W,I,VC	-	20/200	20/80	S	S	Retraction
70	М	BSK	20%	W,I,VC	I	20/1200	20/200	PS	PS	ED, Moderate scarring
70	M	BSK	-	W,I,VC	-	20/400	20/200	S	S	-
70	M	BSK	-	W,I,VC	-	20/400	20/200	S	S	-
75	M	BSK	-	W,I,VC	-	20/600	20/200	S	S	-
80	M	CDK	-	W,I,VC	W	20/400	20/200	PS	S	-

W - watering, I - irritation, VC - visual compromise, BSK - band-shaped keratopathy, CDK - climatic droplet keratopathy, FC - finger counting close to face, S - success, PS - partial success, Fa - failure, ED - epithelial defect, M - male, F - female

Subjective success was obtained in 17 cases (71%) and objective success was seen in 18 cases (75%) [Table 2]. Patients with BSK had a better subjective success while CDK had a better postoperative objective success.

One case of BSK was labeled as a failure with postoperative decline in vision and severe scarring. Loss of the graft was seen in this patient on the 12th postoperative day associated with loose sutures.

Postoperative complications were few. Central epithelial defect <3 mm (detected after suture removal at three weeks) was noted in three patients, which healed within five days on conservative treatment (liberal topical lubricants) after suture removal and did not require any repeat procedures. A total limbus to limbus cover was used in these three patients with evidence of retraction in one case on the 10th postoperative day and loss of the membrane in another while the third case had the graft *in situ*. Amniotic membrane graft (AMG) retraction was seen in four cases involving the inferior peripheral cornea only. Recurrence of the lesion around the periphery of previously dissected bed was seen in one eye with CDK at nine months (not involving the visual axis) and loss of the graft was

encountered in one case which was labeled as postoperative failure

Comparison of similar age groups with both disorders gave similar results. There was no correlation between the age and the final visual acuity, subjective or objective outcomes. Preoperative corneal thinning was associated with postoperative scarring (r = 0.4, P = 0.002) while no correlation was found between the extent of corneal involvement and the postoperative visual acuity. None of our patients required penetrating keratoplasty or repeat procedure in the follow-up period.

Discussion

Despite good results in previous studies,⁴⁻¹¹ the need for a safe and effective alternative to PTK and keratoplasty for visually incapacitating degenerative diseases of the cornea, has been felt at centers where such facilities are not available, or in rural places where the compliance and long-term follow-up of the patient is doubtful. Since most of our patients were from a rural setting, we did not prefer a controlled study and therefore recruited no controls (superficial keratectomy alone) in the study, keeping in mind the poor ocular hygiene and high risk

Table 2: Comparison of objective and subjective outcomes after superficial keratectomy coupled with amniotic membrane grafting in superficial corneal degenerations

Result		Subjective*	Objective#			
	Success	Partial success	Failure	Success	Partial success	Failure*
CDK (n = 15)	10	5	0	12	3	0
BSK $(n = 9)$	7	1	1	6	2	1
Total $(n = 24)$	17 (71%)	6 (25%)	1 (4%)	18 (75%)	5 (21%)	1 (4%)

Subjective* - refer to the text, Objective# - refer to the text, CDK - Climatic droplet keratopathy, BSK - Band shaped keratopathy

of postoperative infections over a de-epithelized corneal bed. In this study, we obtained only a 71% subjective and 75% objective success with the procedure. While objective improvement of vision was obtained in 23 of 24 eyes, two patients denied a subjective improvement. The overall subjective success as regards the relief of preoperative symptoms was observed to be less than the objective success. This difference may in part reflect the severity of symptoms caused by the surface irregularity in such patients.

Earlier reports have stated good results of the use of the membrane in cases of BSK, where visual acuity improved in five of nine (44%) sighted eyes and remained unchanged in four. 12 Kwon and associates have reported the safety and efficacy of superficial lamellar keratectomy with amniotic membrane in BSK in two cases. 13 Phototherapeutic keratectomy in BSK has also been reported to have successful outcomes. 14-16 Our study showed more success objectively (six of nine eyes) than subjectively success (seven of nine eyes), with eight of nine eyes achieving two-line improvement in vision postoperatively, in BSK. One case had loss of the graft on the 12th postoperative day with resultant scarring and decrease in vision which was therefore labeled as failure.

Al-Towerki¹⁷ has studied the surgical outcome of superficial keratectomy using microkeratome (free flap) for treatment of irregular CDK. Successful outcomes of laser procedures have also been reported in CDK. ⁹⁻¹¹ We obtained a better objective than subjective success in CDK, with improvement of >two lines in 15 eyes.

Studies of PTK in CDK have quoted success in reducing corneal opacification in 98% of cases of CDK.¹⁸ In a study by Peter Hersh and associates, of PTK in spheroidal degeneration, the uncorrected visual acuity improved in 20 eyes of 28 cases with loss of vision noted in two cases.¹⁹ Two patients subsequently underwent penetrating keratoplasty. In our study with amniotic membrane, objective success was obtained in 12 out of 15 cases with CDK while only 10 of 15 eyes were relieved of their symptoms. None of the cases required penetrating keratoplasty or a repeat procedure.

Recurrence of CDK has been reported in two eyes after keratoplasty, 3.5 years after lamellar and six years after penetrating keratoplasty.²⁰ A similar study reported favorable outcomes of lamellar keratoplasty for indications including CDK and BSK, though graft infection was seen in seven eyes.²¹ We did not encounter any case of postoperative infection in our study, though recurrence of CDK around the dissected bed was seen at nine months postoperatively, which, however, did not affect the final visual outcome or necessitate a repeat procedure. Amniotic membrane grafting not only was easily

available but also obviated devastating complications and did not require any long-term treatment.

Eyes with CDK in this study experienced more objective improvement while those with BSK had better subjective relief in our study. The more diffuse involvement of the cornea in BSK could account for less objective improvement in this subset as compared to CDK, which is more localized, facilitating easy removal of the lesion. This also could in part explain the better subjective relief after surgery in eyes with BSK. We did not find any difference in the time for disintegration of the amniotic membrane in either of them (45-60 days after suture removal).

Quantitative analysis of corneal topography, though preferable for this study, was not possible owing to lack of necessary equipment for the same in a remote rural setup. Nevertheless, comparisons between the preoperative and postoperative placido images in our study showed decreased distortion of the rings in the involved area with decrease in the area of distorted mires in all the cases though no definite conclusion of the effect of this procedure on the corneal topography could be drawn from the study due to lack of quantitative data.

The learning curve for the surgical procedure was steep with no major intraoperative or postoperative complications encountered. The procurement of the membrane was easy and one membrane could be used collectively for two to three eyes when cut to the desired size of the lesion.

Amniotic membrane grafting with superficial keratectomy proved to be an effective alternative in rural patients with superficial corneal degenerations, both in terms of subjective relief to the patient with improved vision and objective regularization of the corneal surface in a rural set up.

Acknowledgements

We would like to thank LVPEI for providing us with preserved amniotic membrane and whose cooperation was valuable in the completion of this study.

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Source of Support: Nil, Conflict of Interest: None declared.