Original Article

Phototherapeutic keratectomy for recurrent granular dystrophy in postpenetrating keratoplasty eyes

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Purpose: The purpose is to assess the clinical and visual outcome after phototherapeutic keratectomy (PTK) procedure in eyes with prior penetrating keratoplasty (PKP) for granular corneal dystrophy (GCD) and the time of performance of repeat PTK for recurrence. **Methods:** PTK was performed for visually significant recurrence: A reduction in best-corrected visual acuity (BCVA) by >2 lines over BCVA before recurrence was considered as visually significant recurrence. Three eyes had amniotic membrane patch performed with PTK. The main outcome measures were a recurrence of GCD, clinical course, and visual outcome. Intervals between repeat PTK procedures were noted. **Results:** Six patients (n = 10 eyes; males: 4, mean age 39 ± 13.97 years) underwent PTK. The mean pachymetry before first PTK was 527.1 ± 34 microns. The mean duration between PKP and first PTK was 85.1 months (range: 37–108 months). Two and three PTK procedures were done for seven and five eyes, respectively. Mean duration between first and second and second and third PTK was 62.12 ± 34.41 and 42.8 ± 13.54 months respectively. The average cut depth was 43.66 ± 19.57, 75 ± 43.30 and 39 ± 19.79 microns after the first, second and third PTK procedures, respectively. All eyes had a corneal haze. Prefirst PTK mean BCVA was 20/200 and improved significantly after the first two PTK procedures to 20/40 and after the third PTK procedure to 20/32 ($P < 0.001$). Five eyes had hyperopia. One acute graft rejection was managed successfully at 5 months with medical therapy. **Conclusion:** Multiple PTK procedures can be performed safely with improved visual acuity in grafts without compromising graft survival.

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Phototherapeutic keratectomy (PTK) is a safe and effective procedure for the treatment of corneal opacities located in the anterior one-third of the cornea.[1,2] The corneal opacities include corneal scars, spheroidal degeneration, band-shaped keratopathy, and corneal dystrophies. Granular corneal dystrophy (GCD) is clinically characterized by the presence of bilaterally progressive breadcrumb-like white opacities with intervening clear areas without the involvement of the limbus.[3] The treatment options include lamellar keratoplasty (LKP) or penetrating keratoplasty (PKP), alcohol epitheliectomy, superficial keratectomy and PTK.[4-7] Recurrences are common, though slower in GCD as compared to other stromal dystrophies, and may affect visual acuity.[8,9] LKP or PKP were performed before the availability of the excimer laser.[10,11] Since the recurrences are superficial,[12,13] a retreatment with an excimer laser is possible avoiding the complications of PKP.[11,14,15] The aim of this study is to assess the clinical and visual outcomes after performing PTK in eyes that had prior grafts.

Methods

This is a retrospective, noncomparative case series. PTK procedures performed for the recurrences of GCD in patients having prior PKP between January 1987 and October 2009 were included [Fig. 1]. All these patients had histopathologically proven diagnosis of GCD. Preoperative evaluation included complete comprehensive eye examination including best corrected Snellen visual acuity (BCVA), manifest refraction, if possible, slit-lamp biomicroscopy, Goldmann applanation tonometry for intraocular pressure measurement and dilated fundus examination. B-scan ultrasound was done when the view of fundus was hazy. Central corneal ultrasonic pachymetry was done in all cases. Topography was done when possible.

Surgical technique of the PTK procedure is described earlier in the literature.[1] The PTK procedure was performed using NIDEK EC-5000, Technolas 217, 217z (Bausch and Lomb, Rochester, USA) and Mel 80 excimer laser machines depending on the availability and use of these machines in the institute. PTK was performed under topical anesthesia using topical lignocaine 4% eye drops or proparacaine 0.5% eye drops. Under strict aseptic precautions, after draping, the lids were separated with a wire speculum. The epithelium was debrided manually with a hockey-stick knife. A target ablation was planned after assessing the depth of deposits and

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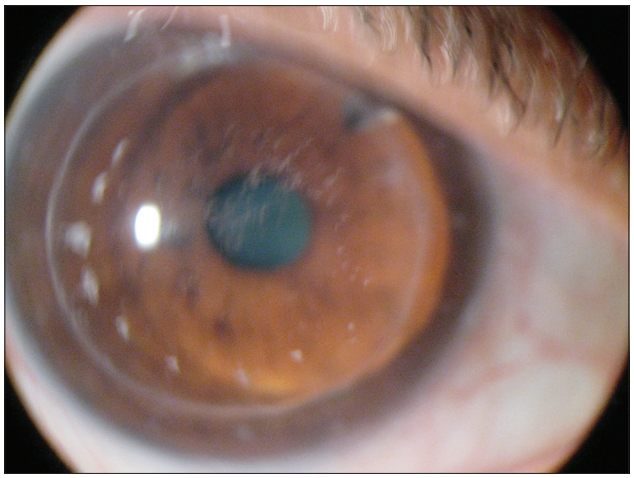

Figure 1: Diffuse slit-lamp photograph showing recurrence of granular dystrophy in a graft: multiple opacities, with clear areas in between are visible in the graft

opacities on slit-lamp biomicroscopy. The patient was asked to look at the fixation point when possible, or the ablation was centered on the entrance pupil. After performing 60–70% of the targeted ablation, the patient was reassessed for the clarity of the central visual axis and the ablation was continued if required. Hydroxypropyl methylcellulose (HPMC 0.7%) was used as a masking fluid to smoothen the corneal surface. A surgical sponge soaked in HPMC was applied on the surface, and excess HPMC was wiped out with a dry surgical sponge. This was reapplied as and when required during the procedure. The endpoint was achieved when a relatively clear visual axis with nil or a few opacities was noted, and the iris details were visible. Topical homatropine hydrobromide (2%), diclofenac sodium (0.3%) and antibiotic eye drops were instilled at the end of the procedure. The eye was either patched or a bandage contact lens (BCL) was placed until the defect healed. Amniotic membrane (AM) patch, sutured with 10-0 vicryl suture with the intention of reducing scar in three eyes was done.[16] Postoperatively, topical antibiotics were continued until the epithelial defect healed. Analgesics were prescribed as needed. Topical prednisolone acetate (1%) was added after the defect healed and BCL was removed. The steroids were given 4 times a day for a week and tapered gradually every week. The dose and the duration of topical steroids varied depending on the clinical examination. All patients received lubricating eye drops in the post-PTK period.

In the postoperative period, BCVA, healing of the epithelial defect, presence or absence of corneal haze, visually significant recurrence of GCD and graft rejection episodes, if any, were noted. Reduction in the BCVA by more than two lines over the highest value of BCVA recorded prior to the onset of recurrence was considered as visually significant recurrence. The retreatment protocol after a recurrence of dystrophy post-PTK was noted, including the number of repeat PTKs performed, the duration between the multiple PTK procedures and BCVA after each PTK procedure. Additional procedures if performed were noted.

Endothelial graft rejection was diagnosed by the classical appearance of rejection: the presence of Descemet's folds, keratic precipitates, stromal edema, and the loss of corneal transparency.

Data analysis

Snellen visual acuity was converted to logarithm of the minimum angle of resolution for statistical calculations. The preoperative BCVA before PTK was the last value recorded just before the PTK procedure. Postoperative BCVA was the highest BCVA recorded during the follow-up after the procedure.

After calculations, visual acuity is again reported in the Snellen fraction. A loss of BCVA of two lines or more after PTK was considered as compromised safety. The safety index was calculated by dividing the mean postoperative BCVA by the mean preoperative BCVA. The probability of the recurrence of GCD and the necessity of repeating surgery in the corneal grafts after PTK was calculated using the Kaplan–Meier method for survival analysis. $P < 0.05$ was considered statistically significant. R software version 2.14.1 (available from http://www.r-project.org/) was used for the statistical analysis.

Results

Six patients ($n = 10$ eyes) underwent PTK for the recurrent GCD in the grafted eyes. The indication for PTK was a reduction in BCVA by more than two lines over prerecurrence visual acuity. There were four males and two females. The mean age at the time of keratoplasty was 32.67 ± 10.17 years (range: 19–50 years). The mean age of the patients at the first PTK procedure was 39 ± 13.97 years (range: 21–61 years). The mean follow-up after PTK was 93.3 ± 60.25 months (range: 5–152 months). This follow-up was the time elapsed between the first PTK and the last follow-up. Two patients underwent cataract surgery during their follow-up; one patient had neodymium-doped yttrium aluminum garnet capsulotomy for posterior capsular opacification in the post-PTK period.

The mean pachymetry values before first PTK was 527.1 ± 34 microns (range: 485–587 microns). The mean pachymetry before the third PTK was 470.6 ± 31.52 microns (range: 439–512 microns). The sim *k* values were not available for all the eyes.

Ablation zone diameter was 6 mm zone in 8/10 eyes; 6.5 mm and 7 mm zone in one eye each at the time of first PTK. The mean zone diameter was 6 mm for subsequent PTK procedures. The average cut depth was 43.66 ± 19.57, 75 ± 43.30, and 39 ± 19.79 microns after the first, second and third PTK procedures, respectively.

Visual acuity

The mean BCVA before the first PTK was 20/200. The mean BCVA significantly improved after the first two PTK procedures to 20/40 and after the third PTK procedure to 20/32. The *P* value was statistically significant ($P < 0.001$) [Table 1]. BCVA improved by more than two lines in nine eyes except one eye when AM patch was used after the first PTK procedure. The safety indices were 0.37 after the first two PTK procedures and 0.33 after the third PTK procedure.

Refractive outcome

The mean spherical equivalent after last PTK was 1.3 ± 3.7 DS (range: −5.00 DS to + 8.00 DS) at the last follow-up. The mean hyperopia noted was 4.30 DS ± 2.7 D (range: +1.5 to + 8.00 DS) in five eyes and mean myopia noted was −2.43 DS ± 1.8 DS (range: −0.50 to − 5.00 DS) in four eyes. Mean astigmatism changed by

0.5 D ± 0.5 post-PTK. The range was −1.5 D to 4.5 D. Table 2 shows manifest refraction pre- and post-PTK.

Clinical outcome

Diffuse haze was noted in all patients. Complications such as persistent epithelial defects, recurrent corneal erosions or infections were not observed after PTK. None of the patients had clinical ectasia. One patient had a single episode of acute graft rejection at 5 months after the first PTK that resolved with intensive topical corticosteroids. This patient later had a recurrence of GCD after 115 months and underwent a second PTK procedure without having any complications.

Granular corneal dystrophy recurrence

Being a retrospective study, early clinical recurrences of the dystrophy after PTK was difficult to report with the assumption that patients may not report until they are symptomatic. Of the 10 eyes which underwent PTK, 7 eyes had two PTK procedures, and 5 eyes had three PTK procedures for recurrences to improve BCVA. Three eyes had PTK performed only once in the graft. The duration between PKP and first PTK was 95.9 ± 37.42 months. Table 3 shows the duration between repeat PTK procedures. Fig. 2 shows the Kaplan–Meier survival analysis.

Discussion

In this series, we performed multiple PTK procedures for the recurrences of GCD in grafts with the resultant improvement in the visual acuity without jeopardizing graft survival. Ninety percent of the patients had improvement in BCVA by two lines or more. BCVA did not improve in three eyes when AM was used as a patch. Post-PTK visual acuity was 20/40 even in the presence of corneal haze in this study. Ellies *et al*. had reported haze in all patients in their series.[11] However, 9.52% of patients in their series did not have a change in BCVA because of the presence of severe haze.[11] Reddy *et al*., had shown reduced visual acuity due to corneal haze after a repeat PTK in graft.[17] Bilgihan *et al*. had reported mild haze in all eyes (n = 19) and Grade 2 haze in six eyes when photorefractive keratectomy was performed for myopia and astigmatism in the grafted eyes.[18] Two patients underwent PTK (40 microns) in their series for haze: BCVA improved in one eye by one line, and no improvement was noted in the second patient because of residual astigmatism. The authors have reported 42% had reduced astigmatism, and 24% had reduced myopia when PRK was performed in graft.[18]

Limiting the depth of ablation zone to <100 microns may avoid hyperopia.[19,20] In our study, the ablation after every PTK procedure was <100 microns (average 53.33 ± 28 microns). Postoperative hyperopia was noted in 50% of eyes. Case 2 had +8.00 D of hyperopia after PTK; preoperative refraction was not possible, as against, Case 5 where hyperopia and astigmatism increased. Reddy *et al*., have reported comparable results of PTK in eyes with and without grafts for corneal dystrophy with

Table 1: Visual acuity before and after subsequent phototherapeutic keratectomy procedures

Eye	BCVA before PTK in PKP eyes	BCVA after first PTK	BCVA before second PTK	BCVA after second PTK	BCVA before third PTK	BCVA after third PTK
Case 1 OD	20/200	20/60	20/200	20/60		
Case 1 OS	20/80	20/80*				
Case 2 OS	20/200	20/40				
Case 3 OD	20/70	20/40	20/100	20/40	20/125	20/40
Case 3 OS	20/80	20/30	20/200	20/40	20/125	20/20
Case 4 OD	20/80	20/30	20/125	20/40	20/80	20/40
Case 4 OS	20/200	20/40	20/125	20/30	20/60	20/40
Case 5 OD	20/2000	20/40	20/60	20/20	20/400	20/50*
Case 5 OS	20/2000	20/30	20/160	20/80*		
Case 6 OS	20/100	20/60				

The BCVA before the first PTK and after subsequent PTK procedure/s. *Reduced visual acuity when amniotic membrane patch was used. PTK: Phototherapeutic keratectomy, BCVA: Best corrected visual acuity

Table 2: Manifest refraction before first phototherapeutic keratectomy and after phototherapeutic keratectomy procedures

Case number	Pre-PTK	After first PTK	After second PTK	After third PTK
Case 1 OD	−1.50 DS/−12 DCyl @180°	NA	−10 DCyl @25°	-
Case 1 OS	No glow	No glow	-	-
Case 2 OS	Dull glow	+8 DS	-	-
Case 3 OD	−6 DCyl @90°	−1.50 DS/−4 DCyl @115°	−3.50 DS/−5.50 DCyl @90°	−4 DCyl @90°
Case 3 OS	+2 DS/−6 Dcyl @50°	−5 Dcyl @70°	NA	+2 DS/−5 Dcyl @65°
Case 4 OD	+6 DS/−7.5 Dcyl @45°	−2.50 Dcyl @160°	No glow	+3 DS/−3 DCyl @45°
Case 4 OS	−2.50 Dcyl @160°	−0.50 DS/−2.50 Dcyl @40°	+1.25 DS/−2 Dcyl @30°	+4 DS/−4 DCyl @25°
Case 5 OD	+1 DS/−4 DCyl @30°	+3.50 DS/−4 DCyl @70°	Dull glow	+9 DS/−6 DCyl @180°
Case 5 OS	+8 DS/−5.50 DCyl @160°	+8 DS/−7.50 DCyl @160°	+8 DS/−8 DCyl @160°	-
Case 6 OS	Dull glow	−1.5 DS/−0.75 DCyl @90°	-	-

PTK: Phototherapeutic keratectomy

Table 3: Duration between repeat phototherapeutic keratectomy procedures in months

Case number	Duration between PKP and first PTK	Duration between first and second PTK	Duration between second and third PTK
Case 1 OD	72	120	-
Case 1 OS	72	-	-
Case 2 OS	180	-	-
Case 3 OD	108	84	48
Case 3 OS	108	48	36
Case 4 OD	108	72	46
Case 4 OS	108	84	60
Case 5 OD	82	24	24
Case 5 OS	84	17	-
Case 6 OS	37	-	-

PTK: Phototherapeutic keratectomy, PKP: Penetrating keratoplasty

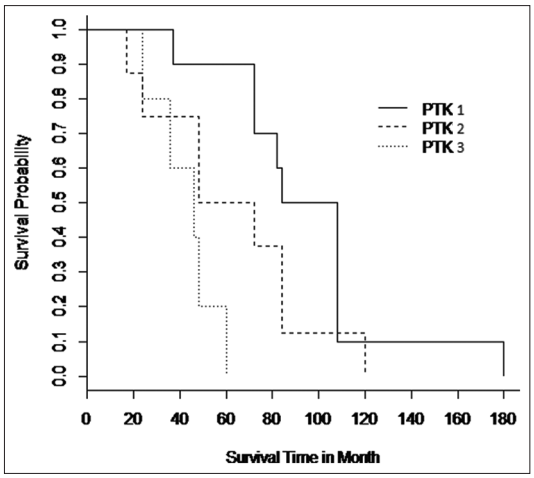

Figure 2: Graph showing probability of survival over repeat phototherapeutic keratectomy procedures

antihyperopia treatment performed only for patients without grafts.[17] Ablation in their series was 71 ± 24 microns in grafted eyes. Hyperopia was induced in the grafts in their series, as they wanted to reduce the preexisting myopia in the eyes grafted for various stromal dystrophies. The refractive error in their series before PTK was −5.1 DS and post-PTK was −1.8 DS indicating induced hyperopia.[17] Safety index in our series after multiple PTK procedures was comparable with Reddy *et al*., who have shown the safety indices after PTK procedures in dystrophy as 0.55 in the grafted eyes and 0.35 in eyes without grafts.[17] Safety index is used to know whether it is safe to perform the procedure.

Recurrence of GCD is known to occur.[4,8,21] Dinh *et al*., have described symptomatic, clinically significant, and visually significant recurrences of dystrophies after PTK.[8] However, no significant recurrences was reported after PTK in eyes having GCD with prior keratoplasty.[8] We considered only visually significant recurrence as our study design is retrospective. In our study, seven eyes had repeat PTK procedures and only three eyes had PTK performed only once. Roncon has shown effectiveness of mitomycin C (MMC) use along with PTK for prevention of recurrence in a case of GCD recurrence in a graft.[22] Similarly, Ayres *et al*., had shown effectiveness of MMC in prevention of recurrence and only minimal haze formation.[23]

The first PTK was performed in our series 95.9 ± 37.42 months after PKP (range: 37–108 months) and subsequently repeat PTKs were performed at a shorter interval (62.13 ± 34.42 months and 42.8 ± 13.53 months). Reddy *et al*., had shown significant recurrence in GCD in two out of five grafted eyes at an interval of 58 and 38 months.[17] Recurrences in GCD are superficial.[12,15] With multiple recurrences after PTK in eyes with prior keratoplasties, PTK can be safely repeated as was done in our series. The amount of ablation performed during third PTK procedure was 39 microns with clearing of visual axis. However, Chen and Xie had performed repeat keratoplasty for 6 out of total 15 eyes with GCD, where recurrences occurred after PTK.[9] The authors have reported recurrence at a mean depth of 118.5 microns with optical coherence tomography.[9]

Performing a repeat PTK procedure will be limited by the amount of ablation required to clear the opacities and the residual stromal bed thickness. It has been postulated that the residual stromal bed should not be <250 μm to avoid corneal ectasia. There are no reports of corneal ectasia after PTK for eyes with or without previous grafts for GCD. The corneal topography was not available in our series and we cannot comment on ectasia though clinical ectasia was not observed. The limitation of our study is lesser number of eyes and we have not used MMC to prevent recurrence or haze. Use of AM did not improve our outcomes. The strength of our study is shown by the improvement in visual acuity with multiple PTK procedures without compromising the graft survival.

Conclusion

PTK appears to be a safe and effective procedure for the treatment of recurrent GCD after PKP. PTK can be repeated a number of times as seen in our series with predictable improvement in the BCVA. This is especially important in developing countries like ours where tissue availability is less. Presence of haze does not preclude better vision. With the successive procedures, the time interval between repeat PTK procedures is shortened. Once PTK has reached its lower limit for the residual stromal bed thickness or the haze is severe, LKP or PKP can be performed to restore vision.

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Conflicts of interest

There are no conflicts of interest.

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