Visual outcomes and recurrence rate of macular corneal dystrophy following phototherapeutic keratectomy in Saudi Arabia

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Abstract:

PURPOSE: The purpose of the study was to evaluate the visual outcomes and recurrence rate of patients with macular corneal dystrophy (MCD) who have undergone phototherapeutic keratectomy (PTK).

METHODS: This retrospective, single-centered study enrolled patients from King Khaled Eye Specialist Hospital who had undergone PTK for MCD between 2000 and 2020. Pre-, intra-, and post-operative data were collected, and the primary outcome measures included uncorrected visual acuity, best-corrected visual acuity (BCVA), spherical equivalent, central keratometry, keratometric astigmatism, recurrence rate, and necessity of subsequent surgery.

RESULTS: This study evaluated 42 eyes of 29 patients. BCVA improved from 0.41 (±0.17) preoperatively to 0.30 (±0.16) postoperatively. Sixteen out of 42 eyes (38%) had the recurrence of macular dystrophy deposits within the stroma; the average time from PTK to recurrence was 37 months (range: 5.5–115.4 months). The overall success rate of PTK at 2 years was 44.8%. Eleven eyes (26%) required subsequent surgery following PTK at an average of 43 months postoperatively. Deeper ablation and longer application of mitomycin C (MMC) were both found to be statistically significant factors associated with visual improvement and lower recurrence rate following PTK.

CONCLUSION: PTK can be considered a treatment modality for younger patients to defer keratoplasty to a later stage. Deeper ablation is associated with improved postoperative visual acuity, and longer application of MMC is associated with lower recurrence rates of MCD.

Keywords:

Macular dystrophy, mitomycin C, phototherapeutic keratectomy

Introduction

Corneal dystrophies are a group of inherited disorders that are bilateral, progressive, and not associated with an underlying systemic disease.[1] Macular corneal dystrophy (MCD) is an autosomal recessive condition that is caused by a mutation in carbohydrate sulfotransferase gene which leads to the accumulation of a nonresolvable substance in the stroma, Descemet membrane, and endothelium.[1] The defective sulfation of keratan sulfate, which is the major glycosaminoglycan in the corneal stroma, is responsible for the accumulation of deposits in the stroma in MCD.[2] Based on the distribution and reactivity of keratan sulfate in serum and corneal tissue, MCD is divided into three subtypes, type I is the most common type which is characterized by the absence of antigenic activity of keratan sulfate in the patient's serum and cornea, type II has low levels of keratan sulfate in both serum and corneal stroma, and the third immunophenotype, MCD IA was initially identified in Saudi Arabia; in this variant, there are undetectable levels of keratan sulfate in the serum; however, the stromal keratocytes are immunoreactive to keratan sulfate antibodies.[2-4]

MCD is considered the most common corneal stromal dystrophy requiring keratoplasty in Saudi Arabia.[5,6] A single-center study from

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Saudi Arabia reported that more than 90% of stromal corneal dystrophy patients undergoing keratoplasty were diagnosed with MCD.[5] In contrast, MCD is considered a rare stromal dystrophy in the Western nations. For example, a study from the United States reported the prevalence of MCD was <1%.[7] This vast disparity in the prevalence of MCD could be attributed to the high rate of consanguinity in the Saudi population.[8]

Patients with MCD often experience visual impairment, glare, and pain from recurrent corneal erosion which can cause significant distress in patient-related quality of life.[9] Surgical modalities to treat MCD include penetrating keratoplasty (PK), deep anterior lamellar keratoplasty (DALK), and phototherapeutic keratectomy (PTK).[1,10-12] PTK is considered a reasonable option in cases where the corneal opacities are condensed anteriorly or in patients where more definite surgical intervention is not possible and a temporizing measure is required.

Previously published reports on the outcomes of PTK in corneal dystrophies are limited, and those investigating MCD are even less frequent.[9,13] In addition, reports of MCD report on a small number of patients.[9,13] This study aims to evaluate the visual outcomes and recurrence rate of patients who have undergone PTK for MCD.

Methods

This retrospective was performed at King Khaled Eye Specialist Hospital, Riyadh, Saudi Arabia. A standard consent form was signed by all patients. The study adhered to the Declaration of Helsinki and was approved by the Institutional Research Board (KKESH, RP 21020-R) at King Khaled Eye Specialist Hospital. A chart review was performed of all patients diagnosed with MCD who had undergone PTK with 193-nm excimer laser from 2000 to 2020. The surgical technique has been previously described.[9] All patients enrolled before 2017 underwent PTK with the Nidek EC-500 (Nidek, Tokyo, Japan), and patients enrolled from the year 2017 onward underwent PTK using the Schwind Amaris 500E (Kleinostheim, Germany). Patients with a clinical diagnosis of MCD who had undergone PTK with a 193-nm excimer laser were included in this study. Patients with postoperative follow-up <24 months, and patients who had previously undergone corneal surgery or excimer laser treatment were excluded from the study.

Data were collected on patient demographics and preoperative, operative, and postoperative parameters including, uncorrected and best-corrected visual acuity (UCVA and BCVA, respectively), spherical equivalent (SE), topographic data, method of epithelial removal, ablation depth (stromal ablation depth excluding the epithelium), optical zone, duration of mitomycin C (MMC) application in seconds, postoperative complications, recurrence of MCD, and the need for subsequent surgery.

The primary outcome measure was postoperative BCVA. Other outcome measures included UCVA, SE, central keratometric power, keratometric astigmatism, recurrence rate, and necessity for subsequent surgery. Success was defined as an improvement of two lines or more in postoperative visual acuity compared to preoperative visual acuity. Failure was defined as no improvement or worsening of postoperative visual acuity compared to preoperative visual acuity. After PTK, the recurrence of the dystrophy was considered present whenever visual acuity decreased, and the recurrence of corneal deposits was observed by slit-lamp microscopy examination.

Descriptive and comparative analysis of the data was performed using SPSS statistical software (version 19.0; SPSS Science, Chicago, IL, USA). We reported demographic information including age, gender, and operated eye as percentages for categorical variables and means (or medians) for continuous variables. The Fisher's exact test (2-tailed) was used to compare proportions, and the Student's *t*-test was used to compare means. The postoperative visual acuity and the frequency of postoperative complications were examined. For all analyses, $P \leq 0.05$ was considered statistically significant.

Results

Forty-two eyes of 29 patients met the inclusion criteria for this study (24 right eyes and 18 left eyes). The average duration of postoperative follow-up was 41.7 months. The average age of patients at the time of surgery was 23.1 years, ranging from 13 to 35 years of age. Out of 29 patients, 51.7% were males and 48.3% were females. The most common type of preoperative refractive error was compound myopic astigmatism (59%), followed by simple myopic astigmatism (20.5%), mixed astigmatism (13%), compound hyperopic astigmatism (5%), and simple hyperopic astigmatism (2.5%). Following PTK, the most prevalent type of refractive error was compound myopic astigmatism (58%).

The average UCVA improved from 0.57 (±0.43) preoperatively to 0.50 (±0.35) at the last postoperative visit. Average BCVA improved from 0.41 (±0.17) preoperatively to 0.30 (±0.16) at the last postoperative visit. SE almost remained the same, whereas keratometry readings and pachymetry measurements were reduced postoperatively [Table 1].

Thirty-one eyes (74%) underwent transepithelial PTK, seven eyes (17%) had alcohol-assisted epithelial removal followed by PTK, and four eyes (9%) had mechanical debridement of the epithelium using a surgical blade before PTK. Optical zones ranged from 6 to 8 mm (average: 7.3 mm), ablation depth ranged from 30 to 150 μ (average of 80 μ), and topical MMC was applied in 27 of 42 eyes (64%) with an average time of application of 22.8 s (range: 20–60 s).

There were no cases of postoperative infection or persistent epithelial defect. Two out of 42 eyes (4.7%) had visually significant postoperative haze that persisted despite medical treatment. Those two eyes underwent transepithelial PTK, but topical MMC was not used. The recurrence of macular dystrophy deposits within the stroma was noted in 16 of 42 eyes (38%). The average time from PTK to recurrence was 37 months (range: 5.5–115.4 months). The overall success rate of PTK at 2 years was 44.8%. Eleven eyes (26%) required subsequent surgery after PTK at an average of 43.4 months postoperatively (range: 8.7–121.6 months), of which one eye (3%) underwent repeat PTK due to the recurrence of macular dystrophy, 2 eyes (5%) underwent DALK, and 8 eyes (19%) underwent PK following PTK.

Table 2 compares the different variables among successful treatments and failed treatments. Ablation depth was an average of 96.3 μ in successful treatments and 72.8 μ in failed PTK treatment ($P < 0.05$). MMC application was similar in successful and failed treatments with no statistical significance between the two. However, the duration of topical MMC application averaged 26.6 s in successful treatments compared to 15 s in failed treatments ($P < 0.05$). The method of epithelial removal was not significantly different between successful and failed treatments ($P = 0.87$).

Table 3 presents the differences in variables among eyes with no recurrence of MCD during the follow-up period compared to eyes that had a recurrence following PTK. There was no recurrence observed during the study period in 70% of eyes that had MMC application at the end of the procedure, whereas 53% of eyes with no MMC application had a documented recurrence of macular deposits after PTK ($P = 0.130$). The duration of MMC application was longer in eyes that had no recurrence compared to eyes that had the recurrence of MCD (26.6 vs. 15.4 s, respectively, $P < 0.05$).

Table 1: Comparison between pre- and post-operative findings in eyes with macular corneal dystrophy

	Preoperative	Postoperative (last FU)	*P*
UCVA (LogMar)	0.57 (0.43)	0.50 (0.35)	0.454
BCVA (LogMar)	0.41 (0.17)	0.30 (0.16)	0.063
Sphere (D)	−1.6 (2.7)	−1.2 (3.1)	0.284
Spherical equivalent (D)	−2.7 (2.5)	−2.4 (3.2)	0.075
K1 (D)	43.2 (3.6)	42.6 (3.2)	0.010*
K2 (D)	46.7 (2.9)	45.8 (3.9)	<0.0001*
Kmax (D)	49.1 (4.2)	48.3 (10.7)	0.092
Keratometric astigmatism (D)	3.2 (1.6)	4.7 (8.4)	0.674
Pachymetry (microns)	552.7 (142.2)	427.3 (161.5)	<0.0001*
HOA (RMS)	1.6 (0.9)	1.9 (1.3)	0.481

*P<0.05 is statistically significant, FU: Follow-up, UCVA: Uncorrected visual acuity, BCVA: Best-corrected visual acuity, LogMar: Logarithm of the minimum angle of resolution, Kmax: Maximal corneal curvature, HOA: High order abberations, RMS: Root mean square

Table 2: Comparison of different variables among eyes with success and failure after phototherapeutic keratectomy

Variable	Category	Success, *n* (%)	Failure, *n* (%)	*P*
Ablation depth	Mean±SD	96.3±30.9	72.8±23.0	0.034*
MMC application	Yes	10 (37)	17 (63)	0.233
	No	6 (40)	9 (60)	
MMC duration	Mean±SD	26.6±18.3	15±13.8	0.045*
Epithelial removal method	Mechanical	1 (7.7)	2 (12.5)	0.872
	Alcohol	2 (15.4)	3 (18.8)	
	Trans-PTK	10 (76.9)	11 (68.8)	

*P<0.05 is statistically significant, PTK: Phototherapeutic keratectomy, MMC: Mitomycin C, SD: Standard deviation

Table 3: Comparison of different variables among eyes with and without recurrence following phototherapeutic keratectomy

Variable	Category	No recurrence, *n* (%)	Recurrence, *n* (%)	*P*
Ablation depth	Mean±SD	82.9±25.1	76.5±30.6	0.216
MMC application	Yes	19 (70)	8 (30)	0.130
	No	7 (47)	8 (53)	
MMC duration	Mean±SD	26.6±18.3	15.4±13.3	0.035*
Epithelial removal method	Mechanical	1 (3.8)	3 (18.8)	0.107
	Alcohol	3 (11.5)	4 (25)	
	Trans-PTK	22 (84.6)	9 (56.3)	

*P<0.05 is statistically significant, PTK: Phototherapeutic keratectomy, MMC: Mitomycin C, SD: Standard deviation

Discussion

The result of this study confirms that PTK is a safe, effective, and minimally invasive procedure for the treatment of corneal opacities caused by MCD. In this study, 44.8% of eyes had an improvement of two or more lines in postoperative visual acuity compared to preoperative visual acuity, and this improvement was maintained for at least 2 years. This finding concurs with previous literature.[9,13-16] In this study, BCVA improved from 0.41 (±0.17) preoperatively to 0.30 (±0.16) at the last follow-up visit. This outcome is comparable to Yuksel *et al*.'s study which reported an increase in BCVA from 0.70 (±0.34) to 0.45 (±0.3) postoperatively.[15] A Turkish study that enrolled 14 eyes with MCD that underwent PTK, reported a significant improvement in BCVA from 0.61 (±0.31) preoperatively to 0.37 (±0.20) postoperatively at 24 months.[13] Previous literature confirms that PTK can restore an adequate vision of approximately 20/40 Snellen acuity with the advantage of repeatability of the procedure and negligible complications.[13-16]

Although PK is considered the traditional treatment for MCD, it carries the attendant risks of increased intra- and post-operative complications compared to less invasive and more affordable procedure such as PTK. After PK for MCD, Karimian *et al*. reported an improvement of BCVA from 1.4 (±0.4) preoperatively to 0.2 (±0.3) postoperatively; however, 19.4% of eyes had an episode of graft rejection.[17]

As confirmed by our results, PTK has the advantage of being minimally invasive, effective and has limited complications compared to PK. PTK also requires fewer follow-up visits postoperatively compared to PK. However, it is important to highlight that one of the advantages of PKP in macular dystrophy is the reduced rate of recurrence of the macular deposits within the stroma compared to PTK.[17] PTK can be offered to patients initially before proceeding with major intraocular surgery such as PK. In fact, studies have shown that the outcomes of subsequent PK is not affected by a prior PTK.[18] Our results showed that only 11 out of 42 eyes required subsequent keratoplasty surgery or repeat PTK over an average of 3½ years. This outcome suggests that PTK can delay or even avoid proceeding to keratoplasty in most cases.

PTK causes corneal flattening with subsequent hyperopia. However, a large optical zone, shallow ablation depth, and a transition zone can mitigate the magnitude of postoperative hyperopia.[19] Kemer Atik *et al*. reported a mean hyperopic shift of 1.48 (±0.73 D) following PTK; however, they used a small optical zone (6.72 ± 0.27 mm).[13] Similarly, Yuksel *et al*. reported high levels of postoperative hyperopia (2.8 ± 3 D), which can be explained by the small optical zone used (6.5 mm) and deep ablation depth (117.8 ± 24.4).[15] In this study, the SE almost remained the same with a minimal hyperopic shift of 0.3 D (from −2.7 D preoperatively to −2.4 D postoperatively). This outcome is likely due to the use of larger optical zones (7.3 mm) and the shallow ablation depth. In addition, most eyes included in this study had myopic preoperative refraction which reduced the risk of induced postoperative hyperopia, and PTK in such cases can be curative for both myopia and corneal opacification.

Transepithelial photorefractive keratectomy (PRK) is safe and effective for treating low-to-moderate myopia, and compared with alcohol-assisted PRK, it is associated with less postoperative pain, faster reepithelialization and visual recovery, less tissue removal, less haze, and shorter surgical times.[20,21] Another advantage of transepithelial PTK in treating surface irregularities is that the epithelium works as a natural masking agent which enhances the outcomes of surface smoothing following PTK.[22] In our study, around 74% of eyes (n = 31) underwent transepithelial PTK, all 31 eyes had timely healing of epithelial defects with no delay. Further analysis revealed that the method of epithelial removal did not influence the success of the procedure or the recurrence rate [Tables 2 and 3].

In our series, the overall recurrence following PTK was 38% at an average of approximately 3 years. Hafner *et al*. reported an unusually high rate of recurrence of 90% at an average of 3.4 years.[9] The high recurrence rate in Hafner *et al*.'s study can be explained by the fact that PTK was performed without the application of MMC at the end of the procedure.[9] Studies have shown that the application of topical MMC along with PTK for the treatment of corneal dystrophy decreases the recurrence rate.[15,23] In our series, 27–42 eyes (64%) received 0.02% of topical MMC with a cellulose sponge at the end of procedure for an average of 22.8 s. In the current literature, the duration of the application of MMC is not standardized.[13,15] For example, Yuksel recommends an application time of 30 s, whereas Kemer Atik *et al*. recommend applying MMC for 20 s if the ablation depth is below 85 μ and 30 s if the ablation depth is above 85 μ.[13,15]

Our analysis of variables in successful versus failed procedures indicated that both ablation depth and duration of MMC application were significant factors. As expected, deeper ablations are associated with better postoperatively vision, as MCD deposits involve deeper layers of the cornea. Some surgeons advocate a stepwise approach to PTK, where small increments in the depth of PTK are applied in multiple steps until most opacities are cleared as assessed intraoperatively.[15] Although the application of MMC did not seem to influence the success of the procedure in the current study, which might be attributed to the small sample size of this study, the duration of MMC application, however, was significantly longer (26 s) in eyes with a successful outcome. Despite the lack of standardization in the duration of MMC application, the results of our study indicate longer applications of MMC confer a greater chance of success following PTK. Furthermore, further analysis revealed that the longer the duration of MMC application the less chance of recurrence, and this finding is supported by other studies as well.[15,23] It is important to highlight that the severity and the depth of the macular deposits within the stroma are important factor that might influence the recurrence rate following PTK; however, this factor was not explored in our study.

There are some limitations of our study including the retrospective nature of the chart review, and the inclusion of multiple surgeons with different surgical techniques precluded the standardization of the PTK procedure. The exact depth of the macular deposits was not investigated in this study as anterior segment optical coherence tomography (OCT) was not done preoperatively for most eyes included. Further studies investigating the outcomes of OCT-assisted PTK in macular dystrophy patients are recommended. Furthermore, studies with larger sample size are required to further clarify the role of MMC application on the outcomes of PTK in macular dystrophy.

Conclusion

PTK is a reasonably effective tool to improve vision, reduce glare, and provide faster visual recovery in MCD. PTK can moderately improve BCVA even if deep stromal opacities were not completely removed. A major hyperopic shift can be avoided using larger optical zones, shallow ablation depths, and a transition zone. The application of MMC at the end of surgery reduces the risk of postoperative recurrence. PTK should be considered a first-line treatment modality in patients with MCD before proceeding with keratoplasty.

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Conflicts of interest

There are no conflicts of interest.

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