Excimer laser photorefractive keratectomy for patients with contact lens intolerance caused by dry eye

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Abstract

Aims/background—To evaluate epithelial wound healing and visual outcome of excimer laser photorefractive keratectomy (PRK) performed on high myopic eyes with contact lens intolerance due to dry eye.

Methods—PRK was performed on two groups of patients with non-Sjogren's dry eye: group A (−6 D to −9.5 D, 11 patients, 17 eyes) and group B (−11.5 D to −19.5 D, 11 patients, 16 eyes) in an attempt to eliminate the use of contact lenses (CL). The intended correction was full in group A and 10 D in group B.

Results—Uncorrected visual acuity in group A was better than 20/40 in 12 (80.0%) of 15 eyes at 6 months and in 10 (90.9%) of 11 eyes at 1 year. Fourteen (92.8%) of 17 eyes in group A and four (25.0%) of 16 eyes in group B achieved refraction within plus or minus 1 D of the intended correction at 6 months. Re-epithelialisation was complete in 4 days, and epithelial cell area and permeability returned to the preoperative level within 1 month in all cases. All patients in group A were able to eliminate CL, whereas in group B, one patient needed spectacles for residual myopia and two patients resumed CL use because of regression. One eye with severe subepithelial scar formation and one eye with macular haemorrhage were observed in group B.

Conclusion—Our results suggest that PRK is effective for patients with high myopia (−6 D to approximately −10 D) and CL intolerance due to dry eye. Further studies are required to improve predictability and to prevent complications in PRK for very high myopia (>−10 D).

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was found to be 80 times higher in CL wearers compared with non-CL wearers.³ Thus, especially for patients with dry eye, alternative ways of correcting myopia should be explored.

With excimer laser photorefractive keratectomy (PRK), developed during the past decade,⁴ the superficial cornea can be ablated with minimal damage to surrounding tissue creating a remodelled surface with new refraction. Although PRK has a potential to replace spectacles and CL in high myopic patients with dry eye, certain associated disadvantages may prevent its use as the first choice for refractive correction in these patients. PRK causes subepithelial haze in the visual axis, resulting in glare vision, regression, or a decrease in corrected visual acuity, which is more frequently observed in high myopic correction.⁵

Since the success of PRK depends on proper wound healing, this procedure has been thought to be contraindicated in patients with dry eye who have a potential risk of postoperative epithelial problems. In one case, re-epithelialisation was delayed more than 2 weeks after PRK, possibly associated with dry eye (McDonald *et al*, American Academy of Ophthalmology annual meeting, Dallas, 1992). Despite the anticipation of compromised wound healing after PRK, there has been no study on the relation between preoperative tear functions and postoperative epithelial wound healing.

Two types of dry eye are defined by tear dynamics.⁶ One type, often seen in Sjogren's syndrome (SS dry eye), is associated with a decrease in both basic and reflex tear secretion. Wound healing after PRK may be suppressed by an absolute shortage of tear components caused by a destruction of lacrimal gland in SS dry eye. In the other type of dry eye (non-SS dry eye), reflex tears are not affected, suggesting that proper wound healing could be expected after PRK. In the present study we performed PRK in an attempt to eliminate CL use in patients with high myopia and CL intolerance due to non-SS dry eye. The safety, especially in terms of epithelial wound healing, and the efficacy of PRK were evaluated.

Materials and methods

PATIENT SELECTION

Twenty two Japanese patients (33 eyes, nine men, 13 women, aged 34.3 (SD 11.3) years) participated in the study. All patients had high myopia (>−6.0 D with spherical equivalent), low astigmatism (<2.0 D), and dry eye

Although spectacles provide safe and accurate correction of myopia, an aberration, or prism effect, may cause distorted peripheral vision and poorly corrected visual acuity,¹ which patients with high myopia may not be able to tolerate. Contact lenses (CL) are free of these optical problems and are preferable for individuals with high myopia, but patients with dry eye often suffer pain and discomfort with CL wear.² The incidence of CL related problems, such as corneal erosion and ulcer, is higher in patients with dry eye than in those with normal tear dynamics.² The risk of ulcerative keratitis

symptoms related to CL wear, and found spectacles inconvenient because of aberration. CL intolerance was manifested by recurrent corneal erosion in six patients and by symptoms such as pain, discomfort, and red eye in 16 patients. Dry eye was diagnosed if patients had chronic dry eye symptoms and one or more of the following findings⁷: vital staining of the ocular surface (rose bengal score ≥ 3 or fluorescein score ≥ 1), or abnormal tear dynamics (Schirmer test with anaesthesia ≤ 5 mm, phenol red thread tear test⁸ ≤ 10 mm, tear break up time (BUT) ≤ 5 seconds, or tear clearance test⁹ ≤ 1.4).

Patients with a negative reflex tears as determined by a Schirmer test with nasal stimulation¹⁰ < 10 mm, the absence of palisades of Vogt,¹¹ or the presence of infection or active inflammation of the eye were excluded. All patients were evaluated with a specular microscope, and those with morphological abnormalities in corneal epithelium and endothelium, except for slight changes associated with long term CL use¹² or with dry eye^{13 14} were also excluded.

The barrier function of corneal epithelium after PRK was evaluated in an additional nine patients with dry eye (nine eyes, two men, seven women, aged 27.4 (5.1) years) who met the above selection criteria.

PREOPERATIVE REFRACTION AND INTENDED CORRECTION

Eyes were divided into two groups according to preoperative refraction of ≤ -10 D or > -10 D of spherical equivalent: group A ($n=17$, -6.0 D to -9.5 D, mean -7.5 (1.0) D), group B ($n=16$, -11.75 D to -19.75 D, mean -14.8 (2.6) D). All eyes in group A and 11 eyes (68.7%) in group B achieved a corrected visual acuity (CVA) $\geq 20/20$ with spectacles and with CL, but five eyes (31.3%) of group B achieved a best CVA only with CL. One eye of group B had a best CVA of 20/25 owing to macular degeneration associated with high myopia.

The intended refractive correction was the entire preoperative refraction in group A and 10 D in group B, which is the maximum obtainable with the Summit excimer laser.

INFORMED CONSENT

Patients were provided oral and written explanations of the experimental nature of the procedure and possible complications of PRK for high myopia. They were told that the goal of PRK was to eliminate the need for CL, but not for spectacles. For group B patients, the possibility of second PRK was explained and agreed, because deeper ablation may cause unexpected side effects so that full correction was not attempted in the first PRK. Informed written consent for the study and for the surgery was obtained from all patients.

PRK PROCEDURE AND POSTOPERATIVE MANAGEMENT

PRK was performed with ExciMed UA200LA (Summit Technology, Waltham, MA, USA). After a 6 mm diameter section of the epithelium was removed with a spatula, photo-

ablation was performed at a repetition rate of 10 Hz, energy 180 mJ/cm², ablation depth 0.25 μ m/pulse, and diameter 4.5 mm. To minimise the thermal effect of PRK, the cornea was cooled with 4°C BSS Plus (Alcon, Osaka, Japan) for 3 minutes before and after epithelial removal and for 1 minute after photoablation.¹⁵

After PRK a bandage soft contact lens (Breath-O, Toray, Tokyo, Japan; Dk=64 $\times 10^{-11}$ ml O₂ cm/cm²/s mm Hg, central thickness=0.22 mm, water content=78%) was applied until re-epithelialisation was complete. Topical ofloxacin (Tarivid, Santen, Osaka, Japan) and 0.1% betamethasone (Sanbethason, Santen, Osaka, Japan) were used five times a day for 3 months, three times a day during the fourth month, and then discontinued. Oral diclofenac sodium (Voltarene, 25 mg) was prescribed three times a day for 2 days to minimise postoperative pain. The mean follow up period was 10.2 (SD 2.3) months and two eyes in group A failed to be checked at 6 months.

PRE- AND POSTOPERATIVE EVALUATION

Subjective score

Dry eye symptoms were evaluated using a questionnaire⁷ that covers 12 symptoms including ocular fatigue, dryness, foreign body sensation, pain, blurred vision, brightness, red eye, discharge, heavy sensation, discomfort, difficulty in opening eyes in the morning, and excess tearing. Each symptom was scored on a scale of 0–5; the total for 12 symptoms constituted the total subjective score (maximum score 60). Mean subjective scores before PRK (with CL wear) and 3 months after PRK were compared.

Visual acuity and refraction

Uncorrected (UCVA) and corrected (CVA) visual acuity and manifest refraction were measured preoperatively, 1 week postoperatively, and monthly thereafter.

Epithelial wound healing

Epithelial wound healing was assessed by vital staining of the ocular surface, examination of corneal sensitivity, specular microscopic observation of the corneal epithelium, and examination of epithelial barrier function. Vital staining of the ocular surface was performed using double vital staining¹⁶ with rose bengal and fluorescein at 1, 2, 4, 7, 14 days, and monthly thereafter. Corneal sensitivity was measured at the centre of the cornea using a Cochet and Bonnet anaesthesiometer at the same time points. Specular microscopy was performed using a CSP580 specular microscope (Konan Medical, Osaka, Japan) and a special lens for epithelial observation.¹⁷ Results were analysed with a cell analyser (Konan Medical, Osaka, Japan).

Epithelial barrier function was examined in an additional nine patients. Corneal epithelial uptake of fluorescein was measured using a slit-lamp fluorophotometer¹⁸ (Laser Flare Meter KM-500, Kowa, Tokyo) before and 10 days and 1 month after PRK. After measurement of background fluorescein, 3 μ l of 0.5% fluorescein (5 mg/ml, Fluorocyte, Alcon,

Figure 1 Mean total subjective score of dry eye symptoms before and 3 months after photorefractive keratectomy (PRK). * $p < 0.01$.

Osaka, Japan) was instilled into the eye; 10 minutes later the fluorescein was washed out with 20 ml of BSS Plus (Alcon, Osaka). Fluorescein uptake in the central cornea was measured 20 minutes after washing. Background fluorescein intensity was subtracted from the total uptake. Fluorescein permeability (ng/ml) of the corneal epithelium was determined from the average of 10 measurements in each eye.

Subepithelial haze

Subepithelial haze formation was examined with a slit-lamp and graded¹⁹: 0, clear cornea; trace, barely perceptible haze apparent only to a trained observer; 1+, mild reticulated haze that does not affect refraction; 2+, moderate haze, refraction possible but difficult; 3+, opacity prevents refraction, anterior chamber easily viewed; 4+, opacity impairs view of anterior chamber and iris detail; 5+, totally opaque scar, anterior chamber not visible.

Intraocular pressure

Intraocular pressure was measured with the T12 Non Contact Tonometer (Canon, Tokyo, Japan).

STATISTICAL ANALYSIS

Student's *t* test was used for the statistical analyses.

Results

All patients in group A were able to eliminate CL use and spectacles 1 year after PRK. In group B one patient needed spectacles for

Figure 2 Uncorrected visual acuity $\geq 20/40$ and $< 20/40$ at 3, 6, and 12 months after photorefractive keratectomy in eyes in group A (A) and group B (B).

residual myopia, two patients resumed CL use because of regression, and one patient needed a second PRK because of regression as well as decreased UCVA related to severe subepithelial haze. The mean total subjective score was 23.3 (1.0) preoperatively and significantly reduced to 6.5 (3.8) 3 months after PRK ($p < 0.01$) (Fig 1).

VISUAL ACUITY

In group A, UCVA of $\geq 20/40$ was achieved in 14 (82.4%) of 17 eyes at 3 months, 14 (93.3%) of 15 eyes at 6 months, and 10 (90.9%) of 11 eyes at 1 year (Fig 2). Sixteen eyes at 3 and 6 months and 12 eyes at 1 year were examined UCVA in group B. These eyes, whose correction was 10 D against the preoperative refraction of -11.75 D to -19.75 D, showed unexpectedly good UCVA at 3 months as a result of overcorrection and then exhibited decreased UCVA because of residual myopia.

Best CVA was maintained at 1 year in all group A eyes. In contrast, two (12.5%) of 16 group B eyes lost more than two lines at 1 year. One of these two eyes had macular degeneration preoperatively, and CVA dropped to 20/100 at 6 months because of a macular haemorrhage 1 month postoperatively. The other eye developed severe subepithelial haze and resulting in CVA of 20/80.

REFRACTION

The mean refraction in group A eyes was $+0.33$ (1.6) D at 3 months and was stable until 1 year (-0.59 (1.1) D) except for two eyes (one patient) who showed regression (Fig 3). In group B eyes, overcorrection was remarkable at 3 months (13.2 (1.7) D), which was 3.2 diop-

Figure 3 Change of manifest refraction in eyes in group A (A) and correction in eyes in group B (B). The broken lines indicate the intended refraction or correction. SE=spherical equivalent.

Table 1 Corneal sensitivity: recovery to preoperative level

Time after PRK	Group A (n=17)	Group B (n=16)
<1 Week	12 (70.6%)	3 (18.8%)
<1 Month	17 (100%)	6 (37.5%)
<3 Months		10 (62.5%)
<6 Months		11 (68.8%)
<9 Months		16 (100%)

tre overshoot to the intended correction, and following regression was observed at 6 months (10.95 (4.5) D) and 1 year (8.03 (4.8) D).

Fourteen (93.3%) of 15 eyes and eight (72.7%) of 11 eyes in group A achieved within plus or minus 1.0 D at 6 and 12 months, respectively, as did four (25.0%) of 16 eyes and five (41.7%) of 12 eyes in group B.

WOUND HEALING OF CORNEAL EPITHELIUM
Re-epithelialisation as determined by vital staining was complete within 4 days after surgery in all eyes. There was no recurrent erosion or persistent epithelial defect.

Corneal sensitivity had returned to the preoperative level by 1 month in all group A eyes, whereas it took more than 1 month in 10 group B eyes (62.5%) (Table 1).

Figure 4 Specular microscopic observation of corneal epithelium in a representative case in group A before (A), 4 days (B), and 1 month (C) after photorefractive keratectomy (PRK). The preoperative refraction was -7.75D. Spindle-shaped cells were seen at 4 days after PRK. Normal hexagonal cells and no spindle-shaped cells were observed at 1 month. Bar=100 μm.

Table 2 Subepithelial haze after photorefractive keratectomy

Score	Group A		Group B	
	3 months (n=16)	6 months (n=15)	3 months (n=16)	6 months (n=16)
0	4 (23.5%)	6 (40.0%)	4 (25.0%)	8 (50.0%)
Trace	5 (29.4%)	4 (26.7%)	3 (18.8%)	2 (12.5%)
1+	6 (35.3%)	2 (13.3%)	7 (43.8%)	1 (6.23%)
2+	2 (11.8%)	3 (20.0%)	2 (12.5%)	3 (18.8%)
≥3+	0 (0%)	0 (0%)	0 (0%)	2 (12.5%)

Figure 5 Epithelial barrier function determined by mean fluorescein permeability before and 10 days and 1 month after photorefractive keratectomy (PRK) in nine eyes. *p<0.05

Specular microscopy of the corneal epithelium revealed a normal wound healing pattern. Spindle-shaped cells were dominant at 4 days after PRK. These cells had disappeared and normal hexagonal cells reappeared at 1 month (Fig 4). There was no morphological difference before and 3 months after PRK. The mean cell area was 521.2 (49.4) μm² before PRK and 503.4 (68.2) μm² 3 months after PRK in group A eyes (p>0.05), and 572.9 (56.7) μm² before PRK and 575.2 (51.9) μm² 3 months after PRK in group B eyes (p>0.05).

The coefficient of variation of mean cell area before and 3 months after PRK was 0.34 (0.06) and 0.38 (0.33), respectively, in group A eyes (p>0.05), and 0.38 (0.07) and 0.33 (0.05), respectively, in group B eyes (p>0.05).

In nine additional eyes, epithelial barrier function determined by fluorescein permeability returned to the preoperative level within 1 month after PRK (Fig 5). The mean permeability of the epithelium was 11.0 (5.98) ng/ml before PRK and significantly increased at 10 days postoperatively (59.8 (63.0) ng/ml, p<0.05). At 1 month, the permeability was 17.9 (12.5) ng/ml, not significantly different from preoperative status.

SUBEPITHELIAL HAZE

Subepithelial haze formation at 3 months was less than 2+ in all eyes. There was no significant difference between the two groups in the severity of haze formation (Table 2). In most cases, haze decreased or disappeared after 3 months. However, two eyes in group B showed increased haze 6 months after PRK and one of these eyes required a second PRK at 10 months.

INTRAOCULAR PRESSURE

Intraocular pressure increased in three (13.6%) of all 22 patients after PRK. After topical steroid was discontinued, intraocular pressure decreased to normal level.

Discussion

The success of PRK, which removes the epithelium, Bowman's layer, and stroma of central cornea, depends on proper wound healing, which requires an adequate supply of tear components. In dry eye patients, compromised tear production may impair corneal wound healing, especially in the epithelium. In

the present study, re-epithelialisation was complete within 4 days in all eyes. No epithelial problems, such as recurrent erosion or persistent epithelial defect were observed during the 1 year follow up period. Specular microscopic observation of the epithelium showed no morphological changes 1 month postoperatively. Abnormal cells which are often observed in diseased epithelium, such as elongated cells, giant cells, or nucleated cells were not found.¹² The mean cell area and coefficient variation in any observation period were not significantly different from normal average, which are 623 (121) μm^2 and 0.40 (0.14), respectively.²⁰ Epithelial permeability 1 month after PRK was 17.9 (12.5) ng/ml. Since the normal level of permeability has been reported as 28 (17) ng/ml,¹⁸ post PRK epithelium can be functionally recovered within 1 month after surgery. These findings suggest that proper wound healing of corneal epithelium can be expected after PRK in non-SS dry eye patients.

Although the patients had a short BUT and/or decreased Schirmer value, reflex tearing, determined preoperatively by Schirmer test with nasal stimulation,¹⁰ was not decreased, indicating that tear components such as EGF²¹ and vitamin A,²² which are crucial for wound healing, were available. Although PRK has been thought to be contraindicated for dry eye patients, there has been no report on preoperative tear functions. One study showed that re-epithelialisation took over 2 weeks in a dry eye patient with rheumatoid arthritis who underwent PRK (McDonald *et al*, American Academy of Ophthalmology annual meeting, Dallas, 1992). We speculate that the patient had a SS dry eye with no reflex tears. It may be useful to check the presence of reflex tears before PRK to ensure that proper wound healing will occur.

The cooling technique can reduce postoperative pain and subepithelial haze and enhance recovery of corneal sensitivity.¹⁵ Corneal sensitivity in group A eyes returned to the preoperative level more quickly in our study than in that of Campos *et al*.²³ Also a recent report suggests that adequate hydration of cornea by humidified gas promotes a smooth ablated surface and facilitates removal of the ejected debris.²⁴ Our cooling technique may provide proper hydration of cornea during PRK, because cornea can be desiccated during epithelial scraping or laser ablation, which takes longer in high myopic correction. On the other hand, irrigation with BSS may also cause overhydration of cornea, which can change the ablation rate and induce undercorrection of PRK.^{25, 26} Even though the mean refraction in group A was -0.59 D at 1 year, which was similar with the result (-0.80D) without cooling of Caeson *et al*, it is difficult to determine whether our patients were more undercorrected or not compared with their large series study.²⁷ More studies, including basic experiments, are needed to investigate how our cooling method affects the hydration of cornea in order to obtain accurate ablation rate. Alternatively, we could improve our method, such as using cold humidified gas²⁵ to maintain the normal hydration of cornea.

When PRK was performed in eyes with mild to moderate myopia, more than 80% of eyes achieved within plus or minus 1.0 D of attempted refraction 6 months after PRK.^{28, 29} However, less than 50% of high myopic eyes achieved this range.³⁰⁻³³ In the present study, refraction within plus or minus 1 D at 1 year was 72.7% in group A eyes and 41.6% in group B eyes indicating that the deeper ablation had less predictability of outcome. We believe that this outcome in group A is reasonably acceptable, because all patients achieved the goal of eliminating CL. If these patients could tolerate CL and their expectation was complete elimination of both spectacles and CL, our results may not be satisfactory. In this regard, patients with CL intolerance are good candidates for PRK.

In contrast with the good results of group A, regression and severe haze formation were observed in some group B eyes. Wu *et al*³⁴ reported that active collagen synthesis continued for more than 6 months after PRK, and Seiler *et al*³⁵ found that the significant refractive change occurred 1 to 2 years after PRK in high myopic patients. Our data, even with a small scale and short follow up period, suggest that refraction after high myopic correction is unstable and less predictable. Moreover, in our study, macular haemorrhage was observed in one patient who had preoperative macular degeneration. Although this incidence of a single case may be coincidental, the mechanism of haemorrhage could be related to a shock wave of laser, which may induce or break the subretinal new vessels in high myopic maculopathy. Thus, careful follow up of maculopathy is needed after PRK in high myopic patients.

In conclusion, although CL provide excellent correction of high myopia, many patients with dry eye can not tolerate CL wear.² PRK is useful as an alternative way to correct myopia for these patients if the correction is less than 10 D. However, PRK for very high myopia (>10 D) requires further studies to improve outcome predictability and prevent complications.

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