Simultaneous Conventional Photorefractive Keratectomy and Corneal Collagen Cross-linking for Pellucid Marginal Corneal Degeneration

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ABSTRACT

PURPOSE: To present the results after simultaneous conventional photorefractive keratectomy combined with corneal collagen cross-linking for pellucid marginal corneal degeneration.

METHODS: In this prospective, interventional case series, 6 patients (8 eyes) with pellucid marginal corneal degeneration were enrolled. All patients underwent simultaneous conventional photorefractive keratectomy combined with corneal collagen cross-linking; corneal epithelium was removed by transepithelial phototherapeutic keratectomy during treatment (Cretan protocol plus conventional photorefractive keratectomy). Visual and refractive outcomes were evaluated along with endothelial cell density preoperatively and at 1, 3, 6, and 12 months postoperatively.

RESULTS: No intraoperative or postoperative complications were observed in any of the patients. LogMAR mean uncorrected distance visual acuity improved significantly from 1.05 ± 0.33 preoperatively to 0.41 ± 0.27 (P = .018) at 12 months postoperatively. Mean corrected distance visual acuity did not change significantly (P > .05) postoperatively. Mean spherical equivalent improved significantly from -3.52 ± 2.29 diopters preoperatively to -1.57 ± 1.76 diopters (P = .028) at last follow-up. Mean corneal astigmatism was significantly reduced from -6.83 ± 2.33 diopters preoperatively to -4.71 ± 1.89 diopters (P = .018) at the last follow-up. No endothelial cell density alterations were observed throughout the follow-up period (P > .05).

CONCLUSIONS: Simultaneous conventional photorefractive keratectomy combined with corneal collagen cross-linking seems to be an effective, safe, and promising treatment for the management of pellucid marginal corneal degeneration.

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Pellucid marginal corneal degeneration (PMD) is a progressive non-inflammatory ectatic corneal disorder that leads to gradual visual decrease.[1] Treatment options for ectatic corneas include spectacles, contact lenses, and intracorneal ring segments.[2] In advanced cases, lamellar or penetrating keratoplasty is the last treatment option.[3] Corneal collagen cross-linking (CXL) is a minimally invasive surgical treatment used to strengthen the corneal tissue and stabilize the ectatic cornea.[4-9]

CXL is used to strengthen and stabilize the ectatic cornea, but visual outcomes are only slightly improved in most of the cases; the majority of these patients cannot achieve functional vision. To improve the visual outcome after CXL, several adjuvant procedures in combination with CXL have been proposed, such as intracorneal ring segments implantation and topography-guided photorefractive keratectomy (PRK).[10-17]

In this case series, we present the visual and refractive outcomes of simultaneous conventional PRK combined with CXL treatment in patients with progressive PMD. To the best of our knowledge, this is the first study regarding this combined treatment in patients with PMD.

PATIENTS AND METHODS

Patient Population

In this prospective, interventional case series, 6 patients (2 males and 4 females; 8 eyes) with progressive PMD were enrolled. None of the patients could tolerate spectacles (due to anisometropia and/or high astigmatism). The diagnosis of PMD was based on the presence of corneal thinning with

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ectasia of the cornea above or below the area of thinning with no evidence of scarring, vascularization, or lipid deposition and typical topographic features.[1] Inclusion criteria were progressive PMD, corneal thickness greater than 450 µm, no other corneal or anterior segment pathological signs, no pregnancy or lactation, and no prior ocular or systemic disease. All patients underwent simultaneous conventional PRK combined with CXL treatment.

Institutional review board committee approval was obtained and all patients were appropriately informed before their participation in the study about the possible outcomes and the current clinical experience, and provided written informed consent in accordance with the tenets of the Declaration of Helsinki.

Clinical Evaluation

Preoperative and postoperative evaluation consisted of ocular and general health history assessment; autorefractometry and autokeratometry (Canon autorefractor; Canon USA, Inc., Lake Success, NY), corneal topography (Technomed C-Scan; Technomed GmbH, Baesweiler, Germany and/or iTrace; Tracey Technologies, Houston, TX), uncorrected distance visual acuity (UDVA), corrected distance visual acuity (CDVA), manifest refraction, slit-lamp examination of the anterior and posterior ocular segments, and endothelial cell density.

Surgical Technique

All procedures were performed in our institute by the same surgeon (GDK) under sterile conditions. After topical anesthesia with proxymetacaine hydrochloride 0.5% eyedrops (Alcaine; Alcon Laboratories, Inc., Fort Worth, TX), corneal epithelium was removed by transepithelial phototherapeutic keratectomy using the Allegretto Wavelight excimer laser (Wavelight Technologies, Erlangen, Germany). Transepithelial phototherapeutic keratectomy ablation was performed at a 6.5-mm zone in an intended depth of 50 µm and then the de-epithelialized area was enlarged mechanically by scraping the epithelium with a spatula (Tutton double ended flat oval spatula/elevator; Duckworth & Kent Ltd., Hertfordshire, England) at an intended 8.0- to 9.0-mm zone. After epithelial removal, conventional PRK was performed using the Allegretto Wavelight excimer laser (Cretan protocol plus conventional PRK). Maximum ablation was up to 50 µm in depth and at a 5.5-mm zone to minimize the possibility of an iatrogenic weakening of the cornea. After PRK, riboflavin (0.1% solution of 10 mg riboflavin-5-phosfate in 10 mL dextran-T-500 20% solution; Medicross, Medio-Haus, Behrensbrook, Neudorf, Germany) was instilled on the center of the cornea every 3 minutes for approximately 30 minutes. Saturation of the corneal stroma and presence of riboflavin in the anterior chamber (riboflavin shielding) was monitored by the surgeon using the blue light of the slit lamp. Ultraviolet-A (UVA) irradiation was performed using a commercially available UVA optical system (UV-X illumination system, version 1000; IROC, Zurich, Switzerland) with a light source consisting of an array of UV diodes (370 nm) with a potentiometer in series to allow regulation of voltage. Before treatment, an intended irradiance of 3.0 mW/cm^2 was calibrated using the UVA light meter YK-34UV (Lutron Electronic Enterprise Co., Ltd., Taipei, Taiwan), which is supplied with the UV-X device. Irradiance was performed for 30 minutes, corresponding to a total surface dose of 5.4 J/cm^2. During UVA irradiation, riboflavin solution was applied every 3 minutes to maintain corneal saturation with riboflavin. At the end of the procedure, a silicon-hydrogel (Lotrafilcon B, Air Optix, Ciba Vision, Duluth, GA; 14.0-mm diameter, 8.6-base curvature) bandage contact lens was applied until full re-epithelialization.

Postoperative medication included nepafenac suspension 0.1% (Nevanac; Alcon Laboratories, Inc., Hertfordshire, UK) for 2 days and chloramphenicol/dexamethasone drops (Dispersadron; Thea Laboratories, Inc., Clermont-Ferrand, France) four times daily until the removal of the bandage contact lens. After removal of the contact lens, patients received corticosteroid drops (fluorometholone 0.1%; Falcon Pharmaceuticals, Fort Worth, TX) tapering for the next 2 weeks. Patients were encouraged to use artificial tears at least six times per day for 3 months postoperatively.

Statistical Analysis

All data were collected in an Excel spreadsheet (Microsoft Corporation, Redmond, WA). Stata software version 12.0 (StataCorp LP, Lakeway Drive, TX) was used for statistical analysis of the results. Continuous variables are presented as mean ± standard deviation (minimum, maximum). Wilcoxon signed rank test appropriate for non-parametric data was used for the analysis because of the small sample size. A *P* value less than .05 was considered statistically significant. Visual acuity is expressed as logMAR.

RESULTS

Follow-up was 12 months. Mean patient age was 41.38 ± 9.8 years (range: 26 to 48 years). No intraoperative or postoperative complications were observed in any of the patients during follow-up. Mean preoperative central corneal thickness using ultra-

TABLE 1

Patient Preoperative and Postoperative Data[a]

Parameter	Preoperative (n = 8)	1 Month (n = 6)	3 Months (n = 8)	6 Months (n = 7)	12 Months (n = 7)
SE (D)	-3.52 ± 2.29 (-6 to 1.5)	-2.56 ± 1.86 (-4.375 to 0.25)	-1.72 ± 1.61 (-4 to 0.375)	-1.92 ± 1.63 (-3.875 to 0)	-1.57 ± 1.76 (-3.875 to 1.25)
P	–	.53	.067	.15	.028
UDVA (logMAR)	1.05 ± 0.33 (1.3 to 0.5)	0.53 ± 0.20 (0.8 to 0.3)	0.53 ± 0.30 (1.2 to 0.3)	0.46 ± 0.26 (1 to 0.2)	0.41 ± 0.27 (1 to 0.2)
P	–	.046	.036	.018	.018
CDVA (logMAR)	0.225 ± 0.16 (0.5 to 0.1)	0.23 ± 0.15 (0.5 to 0.1)	0.19 ± 0.08 (0.3 to 0.1)	0.2 ± 0.08 (0.3 to 0.1)	0.2 ± 0.1 (0.3 to 0.1)
P	–	.916	.466	.721	.446
K steep (D)	48.28 ± 3.04 (43.98 to 52)	45.47 ± 4.13 (40.76 to 53.2)	45.26 ± 3.17 (41.93 to 50.51)	45.78 ± 3.09 (42.74 to 51.26)	45.38 ± 2.00 (42.62 to 47.84)
P	–	.063	.012	.028	.018
K flat (D)	41.45 ± 1.24 (39.13 to 42.75)	41.73 ± 3.16 (39.19 to 47.99)	40.73 ± 1.98 (38.91 to 44.87)	40.94 ± 2.04 (38.26 to 44.75)	40.69 ± 1.88 (37.48 to 43.73)
P	–	.87	.16	.4	.612
Corneal astigmatism (D)	6.83 ± 2.33 (3.06 to 9.67)	3.74 ± 2.16 (0.75 to 6.29)	4.53 ± 1.80 (2.01 to 6.61)	4.86 ± 2.16 (0.95 to 7.11)	4.71 ± 1.89 (2.3 to 7.5)
P	–	.018	.017	.018	.018

SE = spherical equivalent; D = diopters; UDVA = uncorrected distance visual acuity; K = keratometric value; CDVA = corrected distance visual acuity; SD = standard deviation

[a]Data are given as mean ± standard deviation with range in parenthesis.

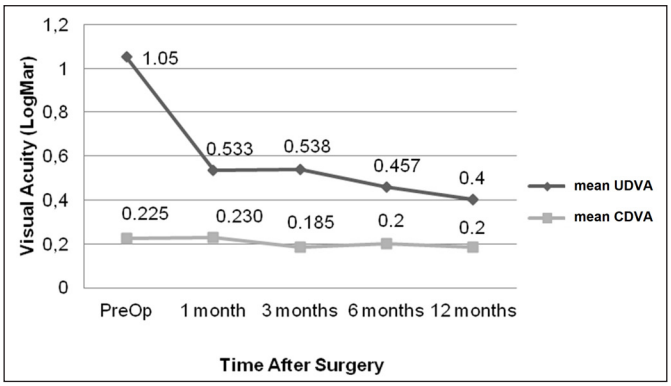

Figure 1. Stability of uncorrected distance visual acuity (UDVA) and corrected distance visual acuity (CDVA).

sound pachymetry (Corneo-Gage Plus; Sonogage, Inc., Cleveland, OH) was 518 ± 38 µm (range: 476 to 589 µm). **Table 1** shows the parameters evaluated preoperatively and at each postoperative interval (1, 3, 6, and 12 months postoperatively).

Mean UDVA improved significantly ($P < .05$) at all postoperative intervals, whereas mean CDVA did not change significantly ($P > .05$) at any postoperative interval (**Table 1**, **Figure 1**). Furthermore, at 12 months postoperatively, 28.56% of eyes gained one line or more of CDVA (14.28% gained two lines and 14.28% gained one line), 57.16% neither gained nor lost any line of CDVA, and 14.28% lost one line of CDVA (**Figure 2**). Regarding the method's efficacy, 12.5% of eyes had UDVA of 20/63 or better (Snellen) preoperatively, whereas 85.74% of eyes had UDVA of 20/63 or better (Snellen) at the last follow-up (**Figure 3**). Mean spherical equivalent improved postoperatively, attaining significance 12 months postoperatively ($P = .028$) (**Table 1**). Mean corneal astigmatism decreased significantly at all postoperative intervals ($P < .05$) (**Table 1**). Mean steep keratometry readings improved postoperatively, attaining significance at 3 months ($P = .012$), and improvement remained significant at 6 and 12 months postoperatively ($P < .05$) (**Table 1**). Mean flat keratometry readings did not change significantly ($P > .05$) at any postoperative interval (**Table 1**). **Figure 4** shows a patient's topographic improvement using the iTrace technology.

Endothelial cell density did not change significantly ($P > .05$) at any postoperative interval. Endothelial cell density was 2,598 ± 23 cells/mm^2 preoperatively and 2,642 ± 35 cells/mm^2 at 12 months postoperatively. No significant difference was revealed at any postoperative interval ($P > .05$) compared with preoperative values with respect to endothelial cell density.

Twelve months postoperatively, 3 patients were independent of spectacles, whereas the other three could tolerate spectacles.

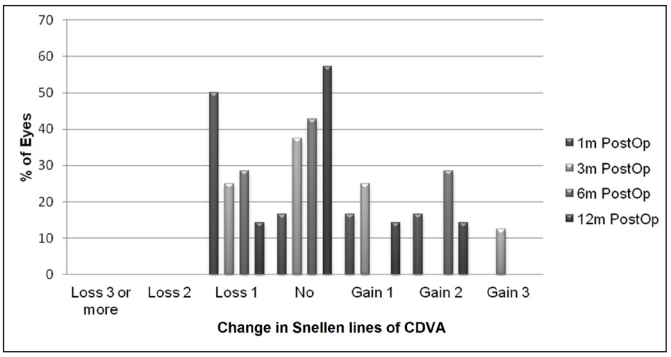

Figure 2. Change in corrected distance visual acuity (CDVA) bar graph (safety). Postop = postoperatively

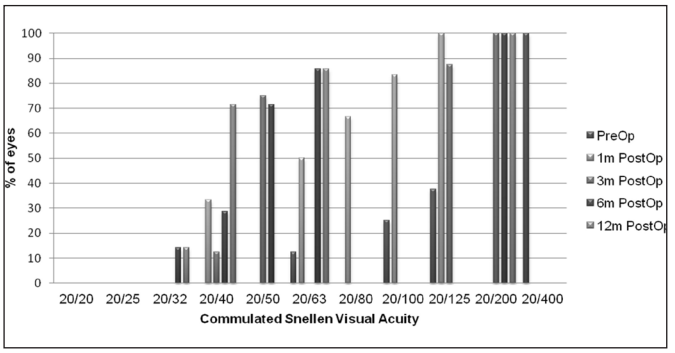

Figure 3. Change in uncorrected visual acuity (UCVA) bar graph (efficacy); Pre = preoperatively; Postop = postoperatively

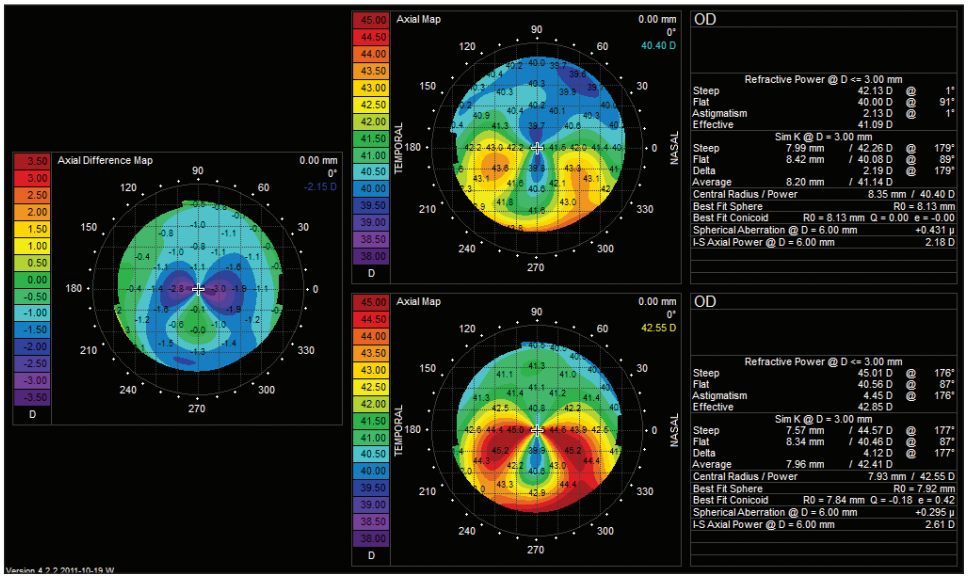

Figure 4. Comparative topographic map (bottom right) before and (upper right) after simultaneous conventional photorefractive keratectomy combined with corneal collagen cross-linking treatment for pellucid marginal corneal degeneration showing (difference topographic map left) significant improvement.

DISCUSSION

In this study, we present a series of patients with PMD that underwent simultaneous conventional PRK combined with CXL; corneal epithelium was removed by transepithelial phototherapeutic keratectomy during treatment (Cretan protocol plus conventional PRK). We chose to perform conventional PRK instead of topography-guided PRK for the following reasons. First, preoperative CDVA of our PMD group was adequate to provide functional vision; none of the patients could tolerate spectacles (due to anisometropia or high astigmatism) preoperatively, whereas all patients were spectacles tolerant postoperatively. Moreover, 3 patients were independent of spectacles postoperatively. On the contrary, topography-guided PRK is usually performed in patients with irregular astigmatism and decreased CDVA. Second, topography-guided PRK ablates more stromal tissue in thinner areas of the cornea in an attempt to normalize corneal topographic irregularities; therefore, we performed conventional PRK to avoid removing a significant amount of stromal tissue in these corneal areas. Furthermore, the final refractive outcome after topography-guided PRK could not be as predictable as conventional PRK.

There are some limitations regarding our study, including the small number of patients enrolled and the lack of a control group that could facilitate the comparison between this combined treatment and CXL alone. Another possible limitation of our study could be the decrease of stromal tissue by the conventional PRK procedure. Conventional PRK might trigger the progression of the ectatic disorder and induce corneal damage or endothelial cell toxicity from UVA irradiation. However, maximum ablation of conventional PRK was up to 50 µm in depth and at a 5.5-mm zone to avoid removing a significant amount of stromal tissue at the thinner corneal areas and minimize the possibility of an iatrogenic weakening of the cornea that would trigger the progression of the ectatic disorder. In our case series, endothelial cell density remained unchanged postoperatively, whereas no intraoperative or postoperative complications were observed in any of the patients.

Simultaneous conventional PRK combined with CXL seems to be an effective, safe, and promising treatment for the management of PMD. Larger patient series with a longer follow-up are necessary to evaluate the outcomes of this combined treatment.

AUTHOR CONTRIBUTIONS

Study concept and design (IGP, GDK); data collection (ADP, KIT, MAG); analysis and interpretation of data (ADP, KIT, MAG, MMS, VPK); writing the manuscript (ADP, GDK, KIT, MAG, MMS, VPK); critical revision of the manuscript (IGP, GDK, MAG); statistical expertise (ADP); supervision (IGP, GDK)

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