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ORIGINAL RESEARCH ARTICLE

Accelerated corneal crosslinking for treatment of progressive keratoconus in pediatric patients

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ABSTRACT

Purpose: To evaluate the safety and efficacy of accelerated corneal crosslinking (CXL) in patients with progressive keratoconus aged 18 years or less.

Methods: A total of 28 eyes from 19 patients with progressive keratoconus aged 18 years or less were enrolled. We divided participants into 2 groups according to corneal thickness (CT). Group 1 included 13 eyes of 8 patients with CT ≥450 µm; group 2 included 15 eyes of 11 patients with CT <450 µm. Each participant underwent accelerated CXL using 10-minute ultraviolet A irradiance at 9 mW/cm^2 for a total energy dose of 5.4 J/cm^2. The efficacy and safety of the procedure were assessed postoperatively at 1, 3, 6, and 12 months with Pentacam and visual acuity.

Results: In uncorrected visual acuity, group 1 showed a statistically significant +0.12 logMAR improvement at 3 months postoperatively (p = 0.003), and in group 2, there was a statistically significant +0.3 logMAR improvement at 1 month postoperatively (p = 0.005). In best-corrected visual acuity, there was a +0.15 logMAR (p<0.001) and +0.22 logMAR (p = 0.005) improvement in group 1 and group 2, respectively, at 12 months postoperatively. All mean keratometric values including K1 and K2 dropped by at least 1 D or remained stable (< ± 1 D) in both groups after accelerated CXL treatment.

Conclusions: The findings showed that accelerated CXL treatment seems to be effective in slowing or halting the progression of keratoconus and that no permanent apparent complications are noted 6 months after accelerated CXL.

Keywords: Accelerated collagen crosslinking, Crosslinking, Keratoconus, Pediatric keratoconus, Pentacam

Introduction

Keratoconus is a noninflammatory, progressive, asymmetric, bilateral degenerative corneal disease associated with the thinning and conical protrusion of the corneal apex (1, 2). Although the etiology of keratoconus remains unclear, proposed causes include microtrauma due to atopy, eye-scratching, and the use of rigid gas-permeable contact lenses, as well as oxidative damage and genetic factors, including familial predisposition and associations with other genetic diseases, as studies of monozygotic and dizygotic twins have shown.

The onset of keratoconus generally occurs during puberty. As Reeves et al (3) have demonstrated, younger patients with keratoconus tend to exhibit a more aggressive progression of the disease. Accordingly, early treatment of keratoconus in children is crucial. Among treatments currently available to manage progressive keratoconus in the pediatric population, corneal collagen crosslinking (CXL) has been found to be effective (4). By inducing photopolymerization, CXL increases the formation of strong covalent bonds between stromal collagen fibrils, namely via the combined action of a photosensitizing substance (i.e., riboflavin or vitamin B_2) and ultraviolet A (UVA) irradiation (5, 6). As a result, the biomechanical rigidity of the cornea becomes stiffer, thereby allowing CXL to decelerate, if not block, the progression of keratoconus.

In the standard CXL treatment procedure defined by Wollensak et al (5), UVA light with 3-mW/cm^2 radiation is used for 30 minutes, for a total energy dose of 5.4 J/cm^2. However, that procedure disadvantageously requires a longer period for the completion of surgery. Yet, as the Bunsen-Roscoe law of reciprocity suggests, if a higher-irradiance UVA light source is used, then the same total UVA energy dose can be produced in a briefer period. Therefore, for shorter treatment periods and higher throughput of patients, an accelerated CXL procedure for keratoconus would be more desirable, especially for pediatric patients. We designed the present study to objectively evaluate the safety and efficacy of accelerated CXL in patients with progressive keratoconus aged 18 years or less, specifically by using a Pentacam Scheimpflug camera (Oculus, Wetzlar, Germany).

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Methods

Study sample and design

We performed this cross-sectional study at the Ophthalmology Department of Kayseri Training and Research Hospital. Our sample included 28 eyes of 19 patients with keratoconus aged 18 years or less, in whom we detected clinical and instrumental progression of the disease in the preceding 3 months. We verified the progression of keratoconus in all eyes by using consecutive corneal topography and optical pachymetry measurements. We based evidence of progression of keratoconus on at least one of the following criteria: at least a 3.0 D increase in myopic or astigmatic refractive error in the previous 3 months, a steepening of at least 1.5 D in average central keratometry between 2 consecutive topographies, or at least a 5% decrease in average central corneal thickness (CT) among 3 consecutive topographies. We used Amsler-Krumeich keratoconus classification for grading.

We divided participants into 2 groups according to CT. Group 1 included 13 eyes of 8 patients (grades 1 and 2) with CT ≥450 µm and group 2 included 15 eyes of 11 patients (grades 3 and 4) with CT <450 µm. Exclusion criteria were CT <350 µm at the thinnest point, herpetic keratitis, severe dry eye, corneal infection, concomitant autoimmune disease, and previous ocular surgery. Contact lens wear among participants, if any, stopped at least 4 weeks before baseline examination. The study followed the tenets of the Declaration of Helsinki and received approval from the local ethics committee. Each participant received oral and written information about the study and provided written informed consent.

Examination protocol and study measurements

We recorded preoperative uncorrected visual acuity (UCVA) converted to the logarithm of the minimum angle of resolution (logMAR) for statistical analysis, as well as best-corrected visual acuity (BCVA) (logMAR), manifest spherical and cylindrical values, and endothelial cell density (ECD), by noncontact endothelial specular microscopy (SP3000P; Topcon, Tokyo, Japan). All participants also received a detailed ophthalmologic examination, performed by the same ophthalmologist, who also took corneal topography measurements by using a Pentacam Scheimpflug camera. Two independent ophthalmologists evaluated and assessed measurements, and an experienced clinician (D.M.U.) assessed all images. We recorded measurements at 1, 3, 6, and 12 months postoperatively as well.

Pentacam Scheimpflug camera measurements

The Pentacam system uses rotating Scheimpflug imaging for noninvasive and 3D anterior segment evaluation. In this study, 3D anterior chamber analysis modules were used. Pentacam Scheimpflug camera measurements were made in darkness to standardize all measurements for each patient. After the placement of the head in the appropriate position, the patient was asked to look at the blue fixation light. To avoid miscalculations due to poor imaging quality, each patient underwent 3 measurements, and only 1 measurement defined as acceptable for examination quality specification by the unit was selected for the study. Anterior chamber depth (ACD), anterior chamber volume (ACV), apical CT (ACT), thinnest CT (TCT), corneal volume (CV), anterior elevation (AE), posterior elevation (PE), and K1 and K2 measurements were obtained in each Pentacam image.

Surgical technique

A single ophthalmologist (D.M.U.) applied the operation protocol to all patients. Following topical anesthesia (proparacaine hydrochloride 0.5%, Alcaine; Alcon, Fort Worth, TX, USA), cleaning with antiseptic solution, and the placement of drape and the lid speculum, the ophthalmologist removed the corneal epithelium with a blunt spatula 9 mm in diameter. The ophthalmologist dropped a 20% dextran-1% riboflavin (Ricrolin; Sooft, Montegiorgio, Italy) solution into the epithelial region and removed it every 2 minutes for 30 minutes. In most eyes, an iso-osmolar riboflavin solution was used; however, in eyes with a denuded CT less than 400 µm, a hypo-osmolar riboflavin solution was administered. After 30 minutes, ultrasound pachymetry was performed on the de-epithelialized cornea. If a thinnest point of CT less than 400 µm was found, the hypo-osmolar riboflavin solution was applied every 20 seconds for 5 more minutes and the CT was checked again by ultrasound pachymetry. The ophthalmologist continued in the same way until the thinnest point of CT reached 400 µm. After observing riboflavin fluorescence in the anterior chamber, the ophthalmologist exposed the cornea to an ultraviolet wavelength of 365-370 nm with 9 mW/cm^2 irradiance (Apollon Crosslinking System, Meran Tıp, Turkey). Exposure to the area 7 millimeters in diameter 4-5 centimeters away from the corneal surface lasted for 10 minutes, during which the ophthalmologist applied riboflavin solution once every 2 minutes. The procedure ended with application of a soft contact lens.

During the postoperative period, we prescribed a topical antibiotic (4 × 1, ofloxacin 0.3%, Exocin; Allergan, Irvine, CA, USA) and artificial tears (4 × 1, hiyalüronikasit 0.5%, Eyestil; Teka, Zug, Switzerland). After re-epithelization, participants ceased contact lens use, and we added topical fluorometholone (4 × 1, 0.1%, Flarex; Alcon). The treatment period lasted 1 month, after which we performed examinations at 1 week and 1, 3, 6, and 12 months postoperatively.

Statistical analyses

Shapiro-Wilk test, q-q, and histogram plots were examined to assess data normality, and Levene test was applied for variance homogeneity. Pearson chi-square analysis was used to compare the differences among categorical variables. Independent samples *t* test, Mann-Whitney *U* test, repeated measures analysis of variance, and Friedman test were used to compare the differences among continuous variables. Bonferroni test was applied to multiple comparisons. Values are expressed as frequencies and percentages, mean and standard deviation, or median and interquartile range. Analysis was conducted using R 3.1.1 (www.r-project.org). A $p<0.05$ was considered as statistically significant.

Results

Of the 19 patients with keratoconus involved in the study, 8 were in group 1 and 11 were in group 2. The demographics of patients with an average 17 (12-19) months follow-up appear in Table I. We assessed the findings of patients by group.

Visual acuity

In our assessment of average UCVA values, group 1 showed no difference in postoperative measurements at 1 month compared to preoperative measurements, though there was a statistically significant +0.12 logMAR improvement at 3 months postoperatively (p = 0.003). Remaining unchanged, these values demonstrated stabilization. In group 2, there was a statistically significant +0.3 logMAR improvement in measurements 1 month postoperatively compared to preoperative measurements (p = 0.005). Remaining unchanged, these values demonstrated stabilization, as shown in Figure 1 and Table II.

Regarding BCVA values, there was a +0.08 logMAR improvement in group 1 and a +0.12 logMAR improvement in group 2 at 1 month postoperatively compared to preoperative measurements (group 1, p<0.001; group 2, p = 0.005). These improvements continued at 3 months postoperatively, and at 6 months postoperatively, there was an additional +0.07 logMAR improvement in group 1 and a +0.1 logMAR improvement in group 2, though none of these values was statistically significant. It was established that these values show stabilization remaining unchanged at the 12-month control, as also shown in Figure 1 and Table II.

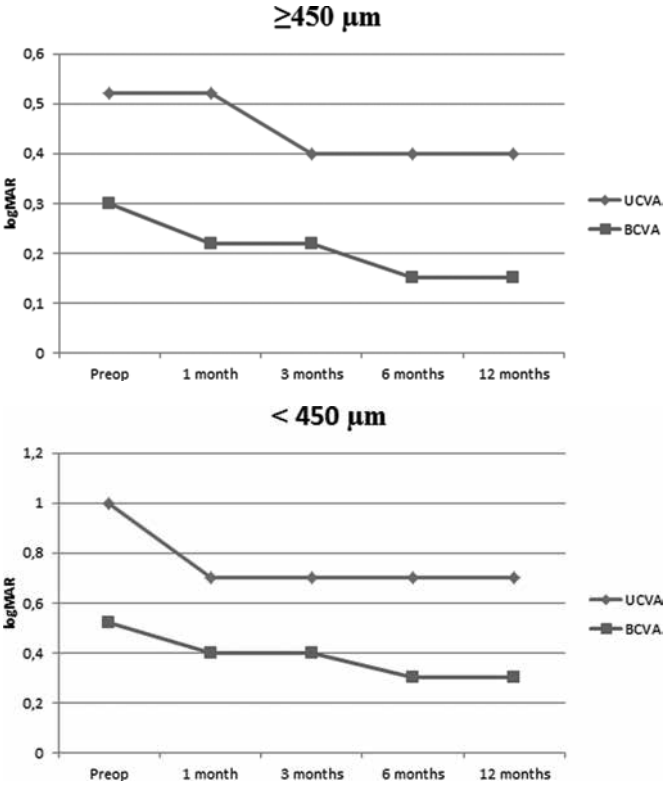

Fig. 1 - Alteration in uncorrected visual acuity (UCVA) and best-corrected visual acuity (BCVA) between preoperatively and 12 months postoperatively.

Refraction

As Table II shows, there was no statistically significant difference between preoperative and postoperative spherical values between the groups (group 1, p = 0.406; group 2, p = 0.055). Though there was a statistically significant improvement of +0.90 D in group 1's cylindrical values according to the last postoperative control, there was an improvement of +0.02 D in the last postoperative control compared with preoperative values. However, these values were not statistically significant (group 1, p = 0.082; group 2, p = 0.021).

Keratometry

Average preoperative K1 values of groups 1 and 2 were 45.13 ± 1.75 D and 49.21 ± 5.94 D; K1 values at 1, 3, 6, and 12 months postoperatively for group 1 were 45.02 ± 1.58 D, 44.82 ± 1.55 D, 44.74 ± 1.64 D, and 44.56 ± 1.12 D, respectively, and for group 2 were 49.46 ± 5.51 D, 49.03 ± 5.64 D, 48.85 ± 5.7 D, and 48.34 ± 5.1 D, respectively. Preoperative K2 values were 49.85 ± 2.34 D for group 1 and 54.41 ± 6.77 D for group 2. K2 values at 1, 3, 6, and 12 months postoperatively were 49.8 ± 2.23 D, 49.6 ± 2.12 D, 49.37 ± 2.17 D, and 48.92 ± 2.12 D for group 1, respectively, and 53.73 ± 6.48 D, 53.72 ± 6.56 D, 53.70 ± 6.64 D, and 53.48 ± 6.16 D in group 2, respectively. These values indicate a flattening effect on the keratoconic cornea in both groups (K1: group 1, p = 0.001; group 2, p = 0.004; K2: both groups; p<0.001), as shown in Figure 2.

TABLE I - Patient demographics and characteristics

Variables	Corneal thickness		p
	≥450 µm (n = 8)	<450 µm (n = 11)	
Age, y, mean ± SD	14.69 ± 2.53	12.93 ± 2.82	0.064
M:F	4:4	8:3	0.142
R:L	6:7	9:6	0.464

Pachymetry mapping

Statistically significant thinning in ACT and TCT was noted at 1 month postoperatively compared to preoperative values in both groups (p<0.001 for both groups), and returned to baseline values at 12 months, as shown in Table III.

Anterior and posterior elevations

There was no significant difference in AE and PE values between preoperative and postoperative periods in group 1 (p = 0.115 and p = 0.265, respectively). There was also no significant difference in average PE values between the preoperative and postoperative periods in group 2 (p = 0.049); for AE, these values were 7.2 ± 0.47 mm and 7.32 ± 0.44 mm,

TABLE II - Mean uncorrected visual acuity, best-corrected visual acuity, spherical and cylindrical refraction preoperatively and last visit postoperatively

Groups	UCVA (logMAR)	BCVA (logMAR)	Spherical refraction	Cylindrical refraction
1 (≥450 µm) (n = 13)				
Preoperative	0.52 (0.3/1)[a]	0.3 (0.1/0.3)[a]	-1.5 (-3/-0.75)	-4.5 ± 1.53[a]
1 mo	0.52 (0.3/1)[a]	0.22 (0.1/0.3)[b]	-2 (-2.5/-0.75)	-4.52 ± 1.9[a]
3 mo	0.4 (0.22/0.7)[b]	0.22 (0.05/0.22)[b]	-1.5 (-2.5/0)	-4.04 ± 1.42[a,b]
6 mo	0.4 (0.22/0.7)[b]	0.15 (0.05/0.3)[b]	-1.5 (-2.5/0)	-3.85 ± 1.32[b]
12 mo	0.4 (0.22/0.7)[b]	0.15 (0.05/0.3)[b]	-1.5 (-2.5/-0.5)	-3.60 ± 0.77[b]
p	0.003	<0.001	0.406	0.082
2 (<450 µm) (n = 15)				
Preoperative	1 (0.52/1)[a]	0.52 (0.3/1)[a]	-3.5 (-5/-1)	-4.15 ± 2.09[a]
1 mo	0.7 (0.52/1)[b]	0.4 (0.22/0.7)[b]	-4 (-5/-1)	-4.37 ± 2.22[b]
3 mo	0.7 (0.4/1)[b]	0.4 (0.22/0.7)[b]	-3.5 (-5/-1)	-4.13 ± 2.18[a]
6 mo	0.7 (0.4/1)[b]	0.3 (0.22/0.7)[b]	-3.5 (-5/-1)	-4.13 ± 2.16[a]
12 mo	0.7 (0.4/1)[b]	0.3 (0.22/0.6)[b]	-3.5 (-5/-1)	-4.13 ± 2.16[a]
p	0.005	0.005	0.055	0.021

BCVA = best-corrected visual acuity; UCVA = uncorrected visual acuity.
Values are expressed as mean ± SD or median (1st/3rd quartiles).
Different superscripts in a row indicate statistically significant difference.

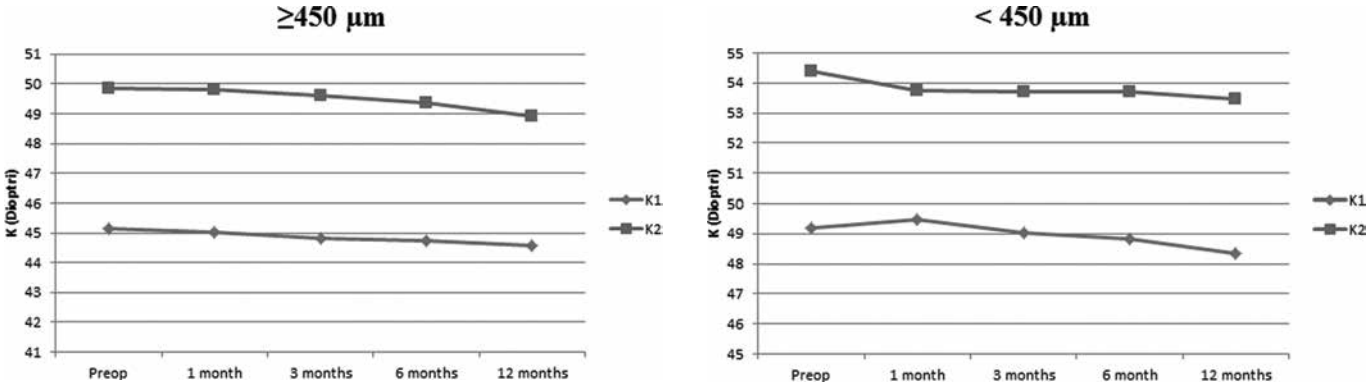

Fig. 2 - Change in keratometric values in 2 groups with progressive keratoconus after accelerated crosslinking.

respectively, and thus statistically significant (p = 0.005), as shown in Table III.

Other topographic results

There was no statistically significant difference in ACD and ACV between preoperative and postoperative periods in the groups (group 1, p = 0.31 and p = 0.44; group 2, p = 0.025 and p = 0.454). In group 1, CV values were 59.36 ± 2.45 mm^3 and 58.85 ± 2.21 mm^3 in preoperative examinations and examinations at 3 months postoperatively, respectively, which marked a statistically significant decrease (p = 0.003). In group 2, CV values were 54.84 ± 5.28 mm^3 and 54.11 ± 5.71 mm^3 in preoperative examinations and examinations at 1 month postoperatively, respectively, which also marked a statistically significant decrease (p = 0.002), as shown in Table III.

Endothelial cell density

Average preoperative ECD was 2,947 ± 86 cells/mm^2 and 2,941 ± 33 cells/mm^2 in group 1 and group 2, respectively. Average ECD at 12 months was 2,939 ± 93 cells/mm^2 and 2,929 ± 38 cells/mm^2 in group 1 and group 2, respectively. The difference between baseline and 12 months was not statistically significant (group 1, p = 0.529; group 2, p = 0.165), indicating that CXL did not induce endothelial cell damage in the 1-year follow-up period.

There were no complications noted after CXL in any of the patients. Postoperatively, the mean time for epithelial healing was 3.12 ± 1.08 days. Mild haze was noticed in most patients by way of slit-lamp examination, though that condition did not affect visual acuity and had subsided completely by 8 weeks after surgery. In no patient was there any evidence

TABLE III - Topographic outcomes before and after accelerated crosslinking in pediatric keratoconus

Groups	Apical corneal thickness	Thinnest corneal thickness	Anterior chamber volume	Corneal volume	Anterior chamber depth	Anterior elevation	Posterior elevation
1 (≥450 µm) (n = 13)							
Preoperative	492.92 ± 25.9[a]	481 (460/501)[a]	215 (192/222)	59.36 ± 2.45[a]	3.42 ± 0.21	7.52 ± 0.25	6.11 ± 0.18
1 mo	467.62 ± 33.65[b]	457 (436/482)[b]	214 (194/222)	58.98 ± 2.29[a,b]	3.43 ± 0.24	7.54 ± 0.22	6.07 ± 0.18
3 mo	469.92 ± 30.87[b]	460 (432/484)[b]	215 (194/221)	58.85 ± 2.21[b]	3.41 ± 0.21	7.54 ± 0.22	6.07 ± 0.18
6 mo	469.46 ± 31.3[b]	459 (431/477)[b]	214 (190/220)	58.88 ± 2.3[b]	3.45 ± 0.19	7.55 ± 0.22	6.06 ± 0.19
12 mo	483.25 ± 29.42[a]	472 (456/496)[a]	215 (192/220)	58.86 ± 2.27[b]	3.43 ± 0.2	7.58 ± 0.28	6.19 ± 0.22
p	<0.001	<0.001	0.44	0.003	0.31	0.115	0.265
2 (<450 µm) (n = 15)							
Preoperative	421.4 ± 33.2[a]	412 (389/435)[a]	226 (181/261)	54.84 ± 5.28[a]	3.56 ± 0.29	7.2 ± 0.47	5.94 ± 0.44
1 mo	396.07 ± 33.49[b]	395 (365/407)[b]	234 (180/254)	54.11 ± 5.71[b]	3.6 ± 0.33	7.24 ± 0.47	5.91 ± 0.43
3 mo	393.73 ± 35.06[b]	392 (351/406)[b]	230 (180/258)	54.49 ± 5.43[a,b]	3.58 ± 0.3	7.23 ± 0.48	5.89 ± 0.43
6 mo	395.07 ± 35.28[b]	396 (352/409)[b]	227 (185/260)	54.37 ± 5.54[b]	3.55 ± 0.31	7.23 ± 0.46	5.92 ± 0.45
12 mo	408.38 ± 38.25[a]	402 (388/426)[a]	231 (184/262)	54.34 ± 5.48[b]	3.56 ± 0.28	7.32 ± 0.44	5.98 ± 0.42
p	<0.001	<0.001	0.454	0.002	0.25	0.005	0.049

Values are expressed as mean ± SD or median (1^{st}/3^{rd} quartiles).
Different superscripts in a row indicate statistically significant difference.

of delayed wound healing, ocular surface damage, or uveitis after CXL.

Discussion

Corneal collagen crosslinking is an effective treatment in stopping the progression of keratoconus, especially in the pediatric population. Among children, the course and progression of keratoconus are reported to be more aggressive and may not subside on their own (4, 7-9). For that reason, patients with keratoconus should be treated at an earlier age. Since CXL can successfully and safely slow, if not also halt, the progression of keratoconus, CXL is widely used in the treatment of keratoconus in children. Currently, 2 treatment modalities involving CXL can be used to halt the progression of keratoconus: the standard (Dresden) or accelerated CXL treatment. The accelerated CXL treatment is preferred over the standard protocol in the pediatric population since briefer treatments can offer advantages to children. A greater UVA irradiance intensity and lower total exposure time are used in accelerated CXL treatment than in the standard protocol (10-12).

Though the superiority of accelerated CXL treatment over the Dresden protocol is not entirely clear, previous studies on the topic have painted a promising picture for accelerated CXL treatment (10, 11, 13-18). In recent research on accelerated CXL, researchers have treated keratoconus with various irradiances between 3 and 90 mW/cm^2 and illumination times of 30 to 1 minutes (11, 19). Wernli et al (12) reported that illumination intensities of 40-50 mW/cm^2 produced significantly stiffer corneas in porcine eyes, though intensities >50 mW/cm^2 did not show significantly greater stiffness. In our study, accelerated CXL treatments were performed using a10-minute UVA irradiance at 9 mW/cm^2 for a total energy dose of 5.4 J/cm^2. According to our data, accelerated CXL treatment exerts an important effect in terms of efficiently treating, if not also halting, the progression of pediatric keratoconus in all treated eyes by follow-up at 12 months. To our knowledge, ours is the first study to compare moderate and advanced keratoconus in pediatric patients after accelerated CXL treatment.

Increased UCVA and BCVA after CXL has been previously reported for pediatric keratoconus (14, 18, 20, 21). Arora et al (18) performed epithelium-off CXL using the standard protocol in pediatric keratoconus and found that mean UCVA improved significantly, from 20/200 to 20/100 (p = 0.035), and that mean BCVA also improved, from 20/70 to 20/40 (p = 0.003), both at 12 months postoperatively. Similarly, Vinciguerra et al (21) reported that the progression of keratoconus in pediatric patients after standard CXL was halted at 24 months postoperatively and that there was a statistically significant improvement in both UCVA and BCVA. The results of Chatzis and Hafezi's (4) study also demonstrated increased BCVA and stopped keratoconus progression in 22 of 23 (96%) eyes at 24 months postoperatively and in 21 of 21 (100%) eyes at 36 months postoperatively. Kodavoor et al (22) found that UCVA and BCVA improved or remained stable in 41 (93.1%) and 44 (100%) eyes, respectively, at 24 months follow-up after accelerated CXL treatment. Ozgurhan et al (23) additionally performed accelerated CXL treatment using 4 minutes of continuous UVA at an irradiance of 30 mW/cm^2 (7.2 J/cm^2) in pediatric keratoconus and reported that both UCVA and BCVA improved significantly, from 0.52 to 0.39 logMAR (p = 0.002) and from 0.38 to 0.30 logMAR (p<0.001), respectively.

In our study of accelerated CXL treatment, we found parallel results, for UCVA and BCVA improved significantly from 0.52 to 0.4 logMAR (p = 0.003) and from 0.3 to 0.15 logMAR (p<0.001), respectively, in group 1 at 12 months postoperatively.

Similarly, UCVA improved significantly, by approximately +0.3 logMAR ($p = 0.005$), in group 2 at 12 months postoperatively. At the same time, BCVA increased significantly from 0.52 to 0.3 logMAR ($p = 0.005$) in group 2. Our study of the treatment of patients with advanced keratoconus thus attained its goal, for as preoperative levels indicate, all keratometric values and values of visual acuity in both groups remained stable or even improved after accelerated CXL. The improved visual acuity in pediatric patients could explain the reduction of K1, K2, and cylindrical refraction. Though other studies have demonstrated that the improvement of corneal aberrations is important for better visual acuity, we could not perform corneal surface aberrometric analysis in our patients (21, 23).

Keratometric values—in our study, K1 and K2—are important for the diagnosis, staging, and monitoring of keratoconus. As a treatment that aims to decrease the progression of keratoconus, CXL may have several effects on keratometry. Previous studies have found controversial results concerning the corneal flattening effect of conventional CXL in pediatric patients. For instance, Caporossi et al (24) have reported topographic results showing statistically significant improvements in keratometric readings in pediatric patients. Similarly, Kodavoor et al (22) and Magli et al (14) detected a significant reduction in keratometric values with a follow-up ranging from 12 to 36 months. Vinciguerra et al (21) also described that the both K1 and K2 values showed a slow but continuous improvement during the 24 months after surgery. Likewise, in our study, all mean keratometric values including K1 and K2 dropped by at least 1 D or remained stable ($< \pm 1$ D) in both groups after accelerated CXL treatment. On the contrary, Soeters et al (16) and Arora et al (18) found no significant changes in either K1 or K2 values at 12 months after treatment. In fact, Buzzonetti and Petrocelli's (20) results regarding keratometric readings showed statistically significant worsening at 18 months after transepithelial CXL in young patients. As such, more clinical studies are needed that address accelerated CXL, namely to demonstrate its effect upon keratometric values.

A reduction of CT during and early after CXL treatment was previously reported, which the authors attributed to the effects of treatment, largely from increased endothelial pump activity caused by hypoxic stress or UVA exposure-related corneal dehydration and changes in epithelial healing and distribution (25-27). The CT increases after approximately the first 12 months following CXL treatment (18, 21, 27, 28). In another study, Ozgurhan et al (23) reported that CT returned to its baseline value at 6 months after accelerated CXL treatment in pediatric patients. In our study, CT in both groups was significantly reduced at 6 months after accelerated CXL and returned to approximately preoperatively values at 12-month follow-up. Similarly, in another study, Vinciguerra et al (21) investigated CT in patients younger than 18 years, after conventional CXL using the Oculus Pentacam HR, and found significantly greater corneal thinning after months than detected preoperatively. They also showed the continuous improvement of postoperative values 6-12 months after CXL treatment compared with preoperative values, though no statistically significant difference in CT at 12 or 24 months following treatment was noted.

Since keratoconus can affect all anterior segment parameters, some studies researching effect of CXL on anterior segment parameters have been designed, though with controversial results. Vinciguerra et al (21, 29) found that total CV and ACD were significantly decreased at 12 months after CXL treatment, whereas another study reported that total CV increased by 24 months, though ACV and ACD remained stable. In our study, we demonstrated that CV was significantly reduced in groups 1 and 2 after CXL treatment, though ACD and ACV were similar preoperatively and postoperatively. The reason for decreased CV is that the cornea stiffens after CXL treatment.

Over the last decade, many studies have demonstrated that accelerated CXL is a safe procedure (21-24). Complications rarely occur, including sterile infiltrates, infectious keratitis, corneal scarring, persistent epithelial defects, corneal edema, and endothelial damage (30-32). Ultraviolet A irradiation can potentially damage corneal endothelial cells (33). The CT without epithelium must be thicker than 400 µm for CXL to be safely performed (34). This is a main problem in corneal CXL procedures because in many patients with progressive keratoconus, the CT is less than 400 µm. Hafezi et al (34) used hypo-osmolar riboflavin solution to solve this problem. They saturated the stroma with iso-osmolar riboflavin solution before and during the UVA irradiation and they did not observe any complication after CXL. In addition, previous studies did not find any endothelial damage in accelerated corneal CXL on corneas thicker than 400 µm (13, 35, 36). Similarly, Ozgurhan et al (37) reported that patients with thin corneas can be treated successfully with accelerated corneal CXL, without ECD loss. In our study, we did not note any serious complications. The corneal ECD was unchanged throughout the follow-up at 12 months in both groups.

Our study has a limitation. Anterior segment optical coherence tomography is a fast, noncontact procedure that has been shown to be useful in the analysis of postoperative corneal stromal demarcation line depth. However, we could not evaluate demarcation line depth.

In summary, our study has demonstrated that accelerated CXL treatment seems to be effective in slowing or halting the progression of keratoconus and that no permanent apparent complications are noted 12 months after accelerated CXL treatment. Visual acuity and keratometric values also improved in pediatric patients with progressive keratoconus due to the accelerated CXL treatment. Among other implications, young patients need longer follow-up periods, for keratoconus is more aggressive in the pediatric population than among adults. Children with keratoconus can be effectively treated with accelerated CXL.

Disclosures

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