The Comparison of Accelerated Corneal Crosslinking Treatment for Progressive Keratoconus in the Pediatric and Adult Age Groups: One-Year Results

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Abstract

Purpose: To investigate the short-term results of accelerated crosslinking (A-CXL) treatment for progressive keratoconus in the pediatric and adult age groups.

Materials and methods: The records of the 62 eyes of 40 patients who had undergone the A-CXL procedure (9 mV/cm², 10 min) for progressive keratoconus between January 2015 and January 2019 were evaluated retrospectively. The patients were divided into 2 groups as the pediatric group (aged 17 years or less) and the adult group (aged 18 years or more) for statistical analysis. Pre- and post- 12th month A-CXL best-corrected visual acuity (BCVA), maximum keratometry (Kmax), sim K1, sim K2, corneal thickness at the thinnest point (thCT), and corneal astigmatism (CA) values of the patient groups were recorded.

Results: The 29 eyes of 16 patients were included in the pediatric group and the 33 eyes of 24 patients were included in the adult group. The mean age was 13.50 ± 3.05 years in the pediatric group and 23.58 ± 4.37 years in the adult group. A significant improvement in BCVA and a significant decrease in thCT values were present in both groups 12 months after the surgery compared to the preoperative period. A decrease was present in the Kmax, sim K1, sim K2 and CA values in the pediatric group, but was not statistically significant. The decrease in Kmax, sim K1 and sim K2 values compared to the preoperative period was significant in the adult group, but the decrease in CA values was not significant. When the two groups were compared at the end of 12 months, only the sim K1 value was significantly lower in the adult group, and there was no significant difference between the other measurements.

Conclusions: Better visual acuity improvement, a higher flattening rate, and less progression occur after 12 months with A-CXL treatment for progressive keratoconus in the adult age group compared to the pediatric age group.

Introduction

Keratoconus is a bilateral, progressive, and non-inflammatory corneal degenerative disease that causes irregular astigmatism and visual impairment as a result of the steepening and thinning of the cornea. The disease is usually asymmetrical. It begins at puberty and can be progressive until the age of 35–40 years. The incidence of the disease has been reported as 1 in 2000 in some studies and 1 in 7500 in some others [1, 2]. The incidence has been reported to be higher in the Asian population compared to the Caucasian population [3, 4]. Keratoconus has a more serious and progressive course in the pediatric age group than in the advanced age group [5, 6]. It is one of the most common keratoplasty indications in the pediatric age group, with a rate of 15–20% [7]. Therefore, slowing or stopping the progression of the disease in the pediatric age group is of great importance. Although the etiology and pathophysiology of the disease are not fully understood, a genetic predisposition being triggered by environmental factors is most commonly considered. Keratoconus has a strong association with allergic eye diseases and eye rubbing [1, 8]. It may be associated with ocular diseases such as vernal conjunctivitis, Leber's congenital

amaurosis, and retinitis pigmentosa, as well as systemic diseases such as Down syndrome, Turner syndrome, Ehlers-Danlos syndrome, atopy, and osteogenesis imperfecta. High K values in the paracentral cornea and irregular astigmatism with Placido disk-based scheimpflug corneal topography, in addition to Vogt lines, Fletcher ring, and the Munson and Rizzoti signs in the cornea on biomicroscopic examination have an important place in the diagnosis. Progression has been defined as an increase of 0.75 D after 6 months and 1 D after 12 months in Kmax values as measured by Placido disk-based Scheimpflug corneal topography and a decrease of 2 lines after 12 months in the best-corrected visual acuity (BCVA) [9].

Corneal Crosslinking (CXL) was first defined by Wollensak et al. in 2003 in order to slow or stop the progression or decrease the need for keratoplasty in keratoconus treatment [10]. The aim of CXL treatment is to slow or stop the progression of keratoconus by strengthening the covalent bonds between the collagen fibrils in the corneal stroma and increasing the resilience and rigidity of the cornea by using riboflavin (vitamin B2) and ultraviolet A [11]. When compared with 30-minute exposure to 3 mW/cm² UVA in the standard CXL treatment (Dresden protocol), the shorter exposure to higher-intensity UVA in the accelerated CXL treatment protocol may be an advantage in the pediatric age group who may have treatment compliance problems. There are many studies showing that standard CXL and Accelerated CXL (ACXL) treatments are effective and safe in stopping the progression of keratoconus [12–15]. According to the Bunsen-Roscoe reciprocity law, it is theoretically possible to achieve the same energy dose by setting a higher UVA power at a shorter exposure time and provide a proportional biological effect with the accelerated CXL procedure [16–18]. It has been predicted that a shorter exposure duration could be ensured with higher irradiation intensity, and results similar to those obtained with the standard CXL treatment have been seen with different irradiation intensities and durations in the ACXL procedure, as defined based on this assumption [19–20]. A shorter treatment period provides advantages in terms of preventing adverse conditions such as preventing perioperative corneal dehydration and thinning and postoperative infection [15].

We aimed to reveal the results of ACXL treatment used for the treatment of progressive keratoconus in the pediatric and young adult age groups in the current study by comparing the postoperative 12th month topographical characteristics and disease progression.

Material And Method

The 62 eyes of 40 patients treated with crosslinking (CXL) for progressive keratoconus between January 2015 and January 2019 at the Gaziantep Göznuru Hospital were included in this retrospective study. Ethics committee approval was obtained from the Gaziantep Sani Konukoğlu University Ethics Committee. The study was conducted in accordance with the Helsinki Declaration principles. The patients were divided into two groups as the pediatric group (age 8–17 years) and the adult group (age 18–35 years). All patients underwent a comprehensive ophthalmological examination. Visual acuity was measured with a Snellen chart and converted into logmar.

The diagnosis of keratoconus was made with by observing the Munson and Rizotti signs, a Fletcher ring and Vogt striae with slit lamp biomicroscopy, and the typical topographic findings obtained with the scheimpflug imaging system (Sirius, CSO, Italy). Keratoconus progression was confirmed by corneal topographic and pachymetric analyses and the best-corrected visual acuity. Progression was defined as a 1 D increase in the maximum keratometry value in 1 year.

All patients were examined preoperatively and 12 months after the surgery. Examinations included best-corrected visual acuity measurement with the Snellen chart, slit lamp biomicroscopy, maximum keratometry value as measured by corneal topography (Sirius, CSO, Italy), sim K1, sim K2, corneal thickness at the thinnest point, and corneal astigmatism values. The patients were divided into stages based on the Amsler-Krumeich keratoconus staging system [21]. The presence of 5D or lower induced myopia and/or astigmatism, 48 D or lower keratometric value, Vogt lines, and a typical topographic appearance was identified as stage 1. The presence of induced myopia or astigmatism above 5 D and below 8 D, 53 D or lower keratometric value, and 400 μm or lower corneal thickness at the thinnest point was identified as stage 2. The presence of induced myopia and/or astigmatism above 8 D and below 10 D, a keratometric value above 53 D, and a corneal thickness of 200–400 μm at the thinnest point was stage 3. Refractive values that could not be measured, keratometric value above 55 D, a corneal thickness of 200 μm or less at the thinnest point, and scarring on the cornea indicated stage 4. Patients at stage 1, 2 and 3 were included in the study.

Patients at the age of 8 to 35, who were diagnosed with progressive keratoconus based on the the progression criteria and received corneal crosslinking treatment, had a follow-up of at least 1 year, had a corneal thickness of 350 μm and above at the thinnest point, had not undergone previous corneal crosslinking surgery or another eye surgery, and had no other systemic disease were included in the study. Patients with stage 4 keratoconus, corneal thickness less than 350 μm at the thinnest point, herpetic keratitis scar on the cornea, any disease that causes scarring in the cornea, an additional systemic disease, a history of continuous drug use, and those who were pregnant or breastfeeding were not included in the study.

Surgical Procedure

The surgery was performed under sterile conditions. After instillation of topical anesthetic (0.5% proparacaine), the central 9 mm area of the epithelium was mechanically separated. Afterwards, 0.1% riboflavin (MedioCross, Kiel, Germany) was administered to the cornea every 2 minutes for 30 minutes. The cornea was exposed to an Ultraviolet A beam of 370 nm (9 mV/cm²) for 10 minutes by using the CCL-VARIO (Peschke Ltd, Borsigstrabe, Germany) device. After the procedure, the surgery was concluded by placing a therapeutic bandage contact lens on the eye. The patients were prescribed topical antibiotics (moxifloxacin, Vigamox, Alcon Laboratories, Inc., Fort Worth, Texas, USA) to be used four times a day. Postoperative follow-up took place on the 1st and 4th days. The contact lens was removed on the 4th day if the corneal epithelium was completely healed and the drops were continued for one month.

Statistical Method

The IBM SPSS Statistics 23 software program was used in the analysis of the data. Mean and standard deviation values are provided for the measurable continuous variables, and frequency and percentage values for the qualitative variables as descriptive statistics. The compliance of the continuous variables with a normal distribution was evaluated with the Kolmogorov-Smirnov test. When comparing two independent groups, the t-test for independent groups was used for continuous variables, and the Pearson chi-square or chi-square test with continuity correction was used based on the relevance of the data for the qualitative variables. The paired groups t-test was used for the comparison of two dependent measures. A p value < 0.05 was considered statistically significant in all evaluations.

Results

The 62 eyes of 40 patients treated with A-CXL for progressive keratoconus were included in the study. The mean age of the patients was 18.74 ± 6.27 (range 8–35) years. The patients were divided into two groups based on their age as pediatric and adult groups. The 29 eyes of 16 patients in the pediatric group (aged 17 years and under) and the 33 eyes of 24 patients in the adult group (aged 18 years and over) were included. Table 1 shows the patients' demographic data, flattening and progression rates and the ratio of the eyes included according to the stage of keratoconus. The pediatric patient group included 9 males (56.3%) and 7 females (43.8%), and the adult patient group included 13 males (54.2%) and 11 females (45.8%). The mean age was 13.50 ± 3.05 years in the pediatric group patients and 23.58 ± 4.37 years in the adult group patients. In the pediatric group, Stage 1 keratoconus (31%) was present in 9 eyes, stage 2 (37.9%) in 11 eyes, and stage 3 (31%) in 9 eyes while the respective percentages in the adult group were stage 1 in 12 eyes (36.4%), stage 2 in 12 eyes (36.4%), and stage 3 in 9 eyes (27.3%). No significant difference was present between the two groups in terms of the keratoconus stage (p:0.898). Intragroup and intergroup comparisons were performed for the preoperative and postoperative 12th month BCVA, Kmax, sim K1, sim K2, thCT, and CA measurements (Table 2).

Table 1
Demographic characteristics of patient groups, distribution according to keratoconus stages, progression and flattening rates

		Pediatric group	Adult group	p value
Age (mean $\pm$ SD)		13,50 $\pm$ 3,05	23,58 $\pm$ 4,37	<0,05 ^a
Gender [M(%) / F(%)]		9(56,3) / 7(43,8)	13(54,2) / 11(45,8)	$\approx$ 0,05 ^a
Stage	stage 1 (n/%)	9/31,0	12/36,4	0,898 ^a
	stage 2 (n/%)	11/37,9	12/36,4	
	stage 3 (n/%)	9/31,0	9/27,3	
Progression rate (%)		24,1	12,1	0,367 ^a
Flattening rate (%)		48,2	51,5	$\approx$ 0,05 ^a
SD standard deviation, M male, F female				
^a Pearson Chi-square test with continuity correction				

Table 2
Preoperative and postoperative BCVA and topography values of the patients

Variables		Pediatric group	Adult group	p value
BCVA (logmar)	Preoperatif (mean ± SD)	0,59 ± 0,40	0,49 ± 0,34	0,285 ^b
	Postoperatif 12. month (mean ± SD)	0,54 ± 0,39	0,39 ± 0,29	0,091 ^b
	p value	0,033^a	0,001^a	-
Kmax (diopters)	Preoperatif (mean ± SD)	56,7 ± 6,66	54,2 ± 6,08	0,120 ^b
	Postoperatif 12. month (mean ± SD)	56,4 ± 6,63	53,4 ± 6,40	0,073 ^b
	p value	0,306 ^a	0,005^a	-
sim K1 (diopters)	Preoperatif (mean ± SD)	47,05 ± 3,65	45,85 ± 3,42	0,185 ^b
	Postoperatif 12. month (mean ± SD)	46,96 ± 4,06	44,90 ± 2,82	0,022^b
	p value	0,609 ^a	0,025^a	-
sim K2 (diopters)	Preoperatif (mean ± SD)	51,33 ± 4,90	50,96 ± 3,51	0,131 ^b
	Postoperatif 12. month (mean ± SD)	51,11 ± 4,98	50,12 ± 3,25	0,096 ^b
	p value	0,282 ^a	0,011^a	-
thCT (µm)	Preoperatif (mean ± SD)	449,5 ± 49,1	452,5 ± 43,5	0,800 ^b
	Postoperatif 12. month (mean ± SD)	422,9 ± 45,4	425,8 ± 46,8	0,809 ^b
	p value	<0,001^a	<0,001^a	-
CA (diopters)	Preoperatif (mean ± SD)	-4,28 ± 1,80	-4,20 ± 1,49	0,112 ^b

Statistical significance is highlighted in bold

BCVA best-corrected visual acuity, Kmax maximum keratometry, simK1 simulated K1, simK2 simulated K2, thCT corneal thickness at thinnest point, CA corneal astigmatism, SD standard deviation

^a Paired sample t test

^b Independent sample t test

Variables	Pediatric group	Adult group	p value
Postoperatif 12. month (mean $\pm$ SD)	-4,14 $\pm$ 1,62	-4,22 $\pm$ 1,50	0,125 ^b
p value	0,345 ^a	0,856 ^a	-
Statistical significance is highlighted in bold			
BCVA best-corrected visual acuity, Kmax maximum keratometry, simK1 simulated K1, simK2 simulated K2, thCT corneal thickness at thinnest point, CA corneal astigmatism, SD standard deviation			
^a Paired sample t test			
^b Independent sample t test			

In the pediatric group patients, the preoperative mean BCVA measurement was 0.59 ± 0.40 and the postoperative 12th month mean BCVA measurement was 0.54 ± 0.39 with a statistically significant postoperative improvement ($p:0.033$). Preoperative and postoperative 12th month thCT measurements were 449.5 ± 49.1 and 422.9 ± 45.4 , respectively, and thCT was statistically significantly lower postoperatively than in the preoperative period ($p < 0.001$). The mean Kmax, sim K1, sim K2 and CA measurements were 56.7 ± 6.66 , 47.05 ± 3.65 , 51.33 ± 4.90 , and -4.28 ± 1.80 , respectively in the preoperative period and 56.4 ± 6.63 , 46.96 ± 4.06 , 51.11 ± 4.98 and -4.14 ± 1.62 at the postoperative 12th month; the difference was not statistically significant ($p:0.306$, $p:0.609$, $p:0.282$, $p:0.345$)(Table 2).

In the adult group patients, preoperative mean BCVA measurement was 0.49 ± 0.34 and the postoperative 12th month mean BCVA measurement was 0.39 ± 0.29 with a statistically significant postoperative improvement ($p:0.001$). The mean Kmax, sim K1, sim K2 and thCT measurements were 54.2 ± 6.08 , 45.85 ± 3.42 , 50.96 ± 3.51 and 452.5 ± 43.5 , respectively, in the preoperative period and 53.4 ± 6.40 , 44.90 ± 2.82 , 50.12 ± 3.25 and 425.8 ± 46.8 , respectively, in the postoperative 12th month; all measurements were statistically significantly lower postoperatively ($p:0.005$, $p:0.025$, $p:0.011$, $p < 0.001$)(Table 2). The mean preoperative and postoperative 12th month CA measurements were 4.20 ± 1.49 and -4.22 ± 1.50 , respectively, and the difference was not statistically significant ($p:0.856$).

All pre- and post-CXL data were compared between the two groups. No statistically significant difference was present between the two groups in terms of the preoperative BCVA, Kmax, sim K1, sim K2, thCT and CA measurements ($p:0.285$, $p:0.120$, $p:0.185$, $p:0.131$, $p:0.800$, $p:0.112$). No significant difference was present between the two groups at the postoperative 12th month in terms of the BCVA, Kmax, sim K2, thCT and CA measurements ($p:0.091$, $p:0.073$, $p:0.096$, $p:0.809$, $p:0.125$). Postoperative sim K1 measurements were significantly lower in group 2 patients ($p:0.022$).

An increase of more than 1 diopter in the Kmax value at the postoperative 12th month was defined as progression. The progression rate was 24.1% in the pediatric group patients and 12.1% in the adult group

patients, with no statistically significant difference ($p:0.367$). Postoperative flattening was defined as more than 1 diopter decrease in Kmax value 12 months after the CX surgery. The flattening rates were 48.2% ($\pm 1D$) and 20.6% ($\pm 2D$) in the pediatric group and 51.5% ($\pm 1D$) and 24.2% ($\pm 2D$) in the adult group with higher rates observed in the adult group.

No postoperative complication was found in any of the patients.

Discussion

Keratoconus has different characteristics in the pediatric and adult age group in terms of the progression and severity of the disease. Keratoconus has a more progressive and severe course in pediatric patients [22]. Stabilization of the disorder as soon as possible is of great importance in this age group in terms of providing better visual function and decreasing the need for keratoplasty. The standard corneal crosslinking procedure (S-CXL, Dresden protocol) has been used for years to stop the progression of keratoconus, after being defined by Wollensak et al [10]. There are many studies reporting that the procedure (30-minute exposure to 3 mW/cm² UVA rays) is an effective and reliable treatment for the stabilization of pediatric and adult progressive keratoconus [23–27]. The accelerated cross linking (A-CXL) procedure is based on the Bunsen-Roscoe reciprocity law using the principle that shorter exposure to higher intensity UVA rays has similar photochemical effects on the cornea. A short procedure time has advantages such as higher compliance with treatment in the pediatric age group, less corneal dehydration, and less intraoperative corneal thinning. S-CXL and A-CXL procedures have been reported in many studies to have similar efficiency and reliability in the stabilization of progressive keratoconus in the pediatric and adult age groups [28–33]. The 1-year results of accelerated CXL (9 mW/cm² UVA, 10 min) treatment for progressive keratoconus in the pediatric and adult age groups were compared in the current study.

Flattening after the CXL procedure was first defined as a decrease of $\pm 1D$ in the Kmax value by Koller et al. in their 2011 study [34]. The ratio of the eyes with a Kmax decrease of more than 1D was reported as 37.7% while the ratio of a Kmax decrease of more than 2D was 13% at the 12th month following the CXL surgery performed on 103 eyes with keratoconus and 32 with pellucid marginal degeneration. Uçakhan et al. have found a flattening rate of 32.5% ($\pm 1D$) and 17.5% ($\pm 2D$) 4 years after CXL treatment in the pediatric age group [23]. Sloot et al. have noted the flattening rate at the 12th month after CXL surgery performed in the keratoconus patient group with the mean age of 21.5 years as 59% [35]. Soeters et al. have divided their patients who had undergone standard CXL into 3 groups as a pediatric group [mean age 15 (range 12–17) years], an adolescent group [mean age 22 (range 18–26) years], and an adult group [mean age 33 (range 26–49) years] and found the postoperative 12th month flattening rates to be 52%, 43%, and 50%, respectively [25]. They have attributed the high flattening rate in the pediatric patients to their high corneal collagen plasticity. Unlike the study of Soeters et al., the flattening rates in the current study were 48.2% ($\pm 1D$) and 20.6% ($\pm 2D$) in the pediatric age group, and 51.5% ($\pm 1D$) and 24.2% ($\pm 2D$) in the adult age group, with the flattening rates found to be higher in the adult group.

The progression rate after corneal CXL has been the subject of a multitude of studies. Keratoconus has been found to be more progressive and more aggressive in the pediatric age group in many of these [22, 36–39]. Barbisan et al. have divided their progressive keratoconus patients treated with CXL using the standard Dresden protocol into 2 groups as a pediatric group aged 16 years or under and an adult group aged 17 years or over. The postoperative 12th month progression rates of the groups were reported as 19.2% and 20.7%, respectively [26]. Toker et al. have reported the postoperative 12th month progression rate of their patients treated with accelerated CXL using a value of 9 mW/cm² and with a mean age of 22.4 years as 7% in their study where they compared the efficacy of various CXL procedures in patients with progressive keratoconus [40]. Mazzotta et al. have found a progression rate of 24% in their study where they investigated the 10-year results on 62 pediatric age group eyes with a mean age of 14.1 years who had received standard CXL treatment [41]. Uçakhan et al. have found no progression at the postoperative 24th month in the standard CXL group with a mean age of 23.13 years while the progression rate in the group receiving accelerated CXL with a value of 9 mW/cm² and with a mean age of 24.69 years was 11.1% in their study where they compared the standard CXL and 9 mW/cm² accelerated CXL procedures [42]. The postoperative 12th month progression rate was 24.1% in the pediatric patient group and 12.1% in the adult group in the current study where the accelerated CXL procedure was performed with a value of 9 mW/cm² for progressive keratoconus, and the difference between the two groups was not statistically significant (p:0.367).

Best-corrected visual acuity (BCVA) is the most important indicator of functional recovery in keratoconus. Henriquez et al. have reported a statistically significant improvement in the postoperative 3rd year BCVA of the pediatric group patients treated with standard CXL (p:0.01) [43]. Padmanabhan et al. have reported a 38.7% improvement rate in the postoperative 1st year BCVAs of the pediatric group patients treated with standard CXL [44]. Sadoughi et al. have found an improvement compared to the preoperative period in the postoperative 12th month BCVA of their patients with mean age of 19.4 (range 13–30) years treated with 9 mW/cm² accelerated CXL but this was not statistically significant (p:0.058) [45]. Soeters et al. have observed a significant BCVA improvement in all groups at the postoperative 1st year, but this improvement was more pronounced in the pediatric group in their study where they divided the 119 eyes of 95 patients treated with standard CXL into pediatric (aged ≤18 years), adolescent (aged 18–26 years) and adult (aged ≥26 years) age groups [25]. We also found a significant BCVA improvement in the postoperative 12th month compared to the preoperative period in both the pediatric and adult patient groups, but the improvement was more significant in the adult group, unlike the Soeters et al. study (p:0.033, p:0.001). This can be explained by the fact that keratoconus is more progressive and aggressive in the pediatric patients. The difference between the BCVAs of the groups after 12 months was not statistically significant in our study (p: 0.091). Similarly, the BCVA difference between the two groups at the postoperative 12th month was reported not to be significant in the Barbisan et al. study where the 1-year results of standard CXL for the treatment of progressive keratoconus was compared in the pediatric group aged 16 years or less and the adult group aged 17 years or more (p:0.941) [26]. Uçakhan et al. have also reported no statistically significant BCVA difference between their two groups at the end of the 3rd

year in their recent study where the 192 eyes of 122 patients treated with standard CXL were divided into two groups as pediatric (aged ≤ 18 years) and adult (aged ≥ 18 years) [27].

Comparison of the preoperative and postoperative keratometry values revealed that the postoperative 12th month Kmax, K1 and K2 values showed a decrease compared to the preoperative values in the pediatric group patients but the difference was not statistically significant (p: 0.306, p: 0.609, p: 0.282). Similarly, Barbisan et al. have reported no significant difference between the preoperative and postoperative 1st year Kmax, K1 and K2 values in the pediatric group with a mean age of 13.8 (range 10–16) years treated with standard CXL treatment for progressive keratoconus [26]. Tian et al. have found lower postoperative 1st year Kmax, K1 and K2 values compared to the preoperative period in their pediatric patients treated with A-CXL but the difference was not statistically significant [46]. Uçakhan et al. have also reported lower postoperative 1st year Kmax, K1 and K2 values than the preoperative period but the difference was again not statistically significant in the study where they investigated the 4-year results of S-CXL in pediatric age group [23]. However, the 4th year results were lower than in the preoperative period. Soeters et al. have reported significantly lower postoperative 1st year Kmax values in the pediatric age group compared to the adolescent and adult groups while the lower K1 and K2 values were not significant in the study they conducted with S-CXL [25].

In the current study, the 12th month Kmax, K1 and K2 values in the adult group were statistically significantly lower (p: 0.005, p: 0.025, p: 0.011). Similarly, Belviranlı et al. have found the 2nd year Kmax, K1 and K2 values after A-CXL treatment in their patient group with a mean age of 22.7 (14–38) years to be statistically significantly lower compared to our results [47]. Uysal et al. have also reported that the Kmax, K1 and K2 values were statistically significantly lower at the postoperative 12th month compared to preoperative period in their keratoconus patients treated with S-CXL with a mean age of 22.9 years [48]. Barbisan has reported that the postoperative 12th month Kmax, K1 and K2 values of the patients over the age of 17 who underwent S-CXL treatment were lower than in the preoperative period, but the difference was not significant [26]. Soeters et al. have found significantly lower Kmax and K2 values at the 12th month after S-CXL in their adolescent (aged 18–26 years) patients but the concurrent decrease in the K1 was not significant; they also found a significant decrease in the Kmax value in the adult (aged ≥ 26 years) group patients while the decrease in K1 and K2 was not significant in this group [25]. Tomita et al. have reported decreased Kmax, K1 and K2 values at the 1st year compared to the preoperative period, but these were again not significant, in the study where they compared the 1-year results of A-CXL and S-CXL treatments in the adult patient group [33].

In the current study, no significant difference was present between the preoperative Kmax, K1 and K2 values of the adult and pediatric groups. Postoperative 12th month K1 values were statistically significantly lower in the adult patients (p: 0.022), while the Kmax and K2 values were also lower in the adult patients but without statistical significance (p: 0.073, p: 0.096). Similarly, other studies where pediatric and adult age groups who underwent S-CXL were compared have reported no significant difference between the two groups in terms of postoperative 1st year keratometry values [25–27].

The mean thCT values were statistically significantly lower at the postoperative 12th month than in preoperative period ($p < 0.001$, $p < 0.001$) in both groups in the current study. Similarly, Soeters et al. have reported a statistically significant decrease in the thCT values at the 12th month after S-CXL treatment in the pediatric, adolescent and adult groups [25]. Barbisan et al. have measured statistically significantly lower postoperative 12th month CCT values in pediatric and adult patients treated with S-CXL when compared to our study [26]. In contrast, Tian et al. and Henriques et al. have found the postoperative 1st year CCT of the pediatric group patients treated with A-CXL to be lower when compared to our study, but this difference was not statistically significant [30, 46].

When the two groups were compared, there was no significant difference between the postoperative 12th month mean thCT values ($p: 0.809$). Similarly, no significant difference was found between 1st year thCT results after CXL treatment of the pediatric and adult patients in other studies [25, 26].

Although a decrease was present in the mean CA values of the pediatric group patients at the 12th month compared to the preoperative period, the difference was not statistically significant ($p: 0.345$). Similarly, the difference between the postoperative 1st year CA values and the preoperative ones was not found to be significant for either procedure in the study by Nicula et al. comparing S-CXL and A-CXL treatments [49]. However, postoperative 2nd year CA values were found to be significantly lower in the study of Padmanabhan et al. where the S-CXL results in pediatric patients were investigated [44]. Although there was an increase in the mean CA values of adult patients at the postoperative 12th month compared to the preoperative period, the difference was not statistically significant ($p: 0.856$). In contrast, two recent studies have found a significant decrease in CA values in adult patients 1 year after S-CXL treatment [45, 48].

Comparison of the pediatric and adult groups revealed no significant difference between the postoperative 12th month mean CA values ($p: 0.125$). We did not find any study investigating the pre and post CXL CA values in the pediatric and adult age groups.

Only a limited number of studies have compared the results of CXL treatment in pediatric and adult patients with progressive keratoconus [25–27]. The S-CXL protocol has been used in all these studies. In contrast, we have compared the 1st year results of A-CXL (9 mV/cm² for 10 minutes) treatment between two groups in our study. As far as we know, our study is a first in this field.

The limitations of our study can be listed as its retrospective nature, the small number of patients, not including optic aberrations, and not providing spherical equivalent information.

In conclusion, the A-CXL (9 mV/cm² for 10 minutes) procedure is an effective and reliable method for the treatment of pediatric and adult progressive keratoconus patients. Better visual acuity improvement, a higher flattening rate, and less progression occur with A-CXL treatment after 12 months in adult progressive keratoconus patients compared to the pediatric age group. Besides, there was a greater decrease in Kmax, simK1 and simK2 values in the adult group. Further studies with larger participation and longer follow-up are required for results with greater impact.

Declarations

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Conflicts of interest/Competing interests All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or nonfinancial interest in the subject matter or materials discussed in this manuscript

Availability of data and material The data supporting the findings of the study are available from the corresponding author upon request.

Ethical approval The study protocol was approved by the Institutional Review Board of Sani Konukoglu University School of Medicine Hospital.

Informed consent The study was performed in accordance with the Declaration of Helsinki principles, and written informed consent about having their medical information used in the study analysis was routinely provided from all of the patients at their first presentation to our clinic.

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