Effectiveness of Treatment Accelerated Cross-Linking in Pediatric and Adult Age Groups

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ABSTRACT

Aim: To comparatively evaluate the efficacy of accelerated corneal collagen cross-linking (aCXL) treatment in patients under and over 18 years of age.

Material and Method: This study included 74 eyes of 55 patients diagnosed with progressive keratoconus who underwent aCXL treatment. Patients included in the study; were divided into two groups: those under the age of 18 (Group 1, n=25) and those aged 18 and over (Group 2, n=49). Preoperative and postoperative spherical/cylindrical refractive values, best-corrected visual acuity (BCVA), keratometric values, topographic astigmatism, topographic keratoconus indices, and aberrometric indices of the patients were evaluated separately and compared.

Results: While there was no significant change in spherical refraction value in group 1, there was a significant decrease in spherical refraction value in group 2 ($p=0.48$, $p<0.0001$, respectively). In both groups, the highest decrease was in the K max value. However, there was no significant difference in the decrease rates between the two groups. However, there was a significant increase in BCVA values obtained after CXL in both groups ($p=0.04$, $p<0.0001$, respectively). A significant decrease in both low- and high-order aberrations was found in both groups after aCXL. When the corneal curvature indices were evaluated, it was observed that there was a significant change in all indices except the IHA (height decentralization index) value.

Conclusions: Accelerated CXL treatment is a safe method that can stop the progression of keratoconus patients in the pediatric and adult age groups.

Keywords: Keratoconus, child, adult, cross-linking therapy, CXL.

INTRODUCTION

Keratoconus is bilateral, asymmetric, progressive thinning and ectasia of the cornea that results in decreased visual acuity from irregular astigmatism.[1] In the pediatric population, keratoconus is diagnosed at later stages, and the progression of keratoconus is faster.[2,3] Early diagnosis and timely treatment decisions are important in the paediatric population because keratoconus can lead to vision loss and the risk of amblyopia.[4]

The aim of keratoconus treatment is to improve the quality of life of patients by preventing the progression of the disease. Treatment options that can be used for the visual rehabilitation of keratoconus patients include the use of glasses, contact lenses, intracorneal ring application, and corneal transplantation. However, these treatment options do not affect keratoconus progression.

In 2003, the use of riboflavin and ultraviolet A (UV-A) light for corneal collagen cross-linking therapy (CXL) was

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first presented as an effective treatment method to stop keratoconus progression by Wollensak et al.[5] The method of corneal tissue improvement known as CXL with riboflavin and UVA involves the combination of riboflavin and UVA irradiation. The function of riboflavin is as a photosensitizer for the induction of cross-links between collagen fibrils and protection against UVA penetration into underlying tissues. It has been shown that corneal rigidity increases with this treatment, and the cornea becomes more resistant to enzymatic destruction.[6,7]

The progression of keratoconus is generally more aggressive in young patients, whereas treatment outcomes in adults may be less predictable; therefore, the efficacy of aCXL may differ between paediatric and adult patients.

This study aims to evaluate and compare the effectiveness of Acxl treatment in patients under 18 years of age and over 18 years of age.

MATERIALS AND METHODS

Ethical approval was obtained from the Mersin University Clinical Research Ethics Committee (2020/253), and the study was conducted in accordance with the Declaration of Helsinki. Both patients and their parents were informed about the study, and written consent forms were obtained. The study included 74 eyes of 55 patients who applied to the Mersin University Faculty of Medicine, Department of Ophthalmology and underwent aCXL treatment between January 2018 and August 2019 with the diagnosis of keratoconus.

Patients with clinically and topographically proven progressive keratoconus, clear corneas, no ocular or systemic disease other than keratoconus, and patients who had progressed within the last year were included in the study. In the last year, an increase of 1 D or more in Kmax value and a decrease of 1 line or more in best-corrected visual acuity (BCVA) were defined as progression criteria. Patients with severe dry eye, corneal scarring, history of refractive surgery, herpetic keratitis, active ocular infection, systemic connective tissue diseases, pregnancy or breastfeeding were excluded.

Patients underwent aCXL (9 mW/cm2 UV-A, 10 min) treatment under sterile conditions and topical anesthesia, adhering to the standard epi-off protocol previously described in the literature. While 0.1% riboflavin solution (medioCROSS M, Kiel, Germany) is used for patients with a corneal thickness over 400 µm, for patients with a corneal thickness below 400 µm, hypo-osmolar riboflavin solution (0.1% riboflavin-5-phosphate in NaCl) was used until the corneal thickness was 400 µm. At the end of the procedure, the eye was washed with a balanced salt solution, and a bandage contact lens was applied by adding one drop of 5% moxifloxacin (Vigamox®, Alcon Laboratories, Inc., USA). In the postoperative period, 4x1 topical antibiotic treatment and artificial tears were prescribed. After epithelialization was completed, the bandage contact lens was removed, and 4x1 0.5% loteprednol etabonate drops (Lotemax®, Bausch & Lomb, Rochester, New York) were added to the treatment. Patient checks were performed daily until the epithelial defect was closed, and then at 1st week, 2nd week, 1st month, 3rd month, 6th month, 12th month, and 1-year intervals thereafter.

Patients were divided into two groups based on age: under 18 (Group 1, n = 25) and 18 and over (Group 2, n = 49). Preoperative and postoperative 12th month spherical and cylindrical refractive values, BCVA (with Snellen chart), keratometric values with Pentacam (Oculus Optikgeräte GmbH, Wetzlar, Germany) of the patients; flat keratometric value (K1), steep keratometric value (K2), average keratometric value (K mean), maximum keratometric value (K max), topographic astigmatism, topographic keratoconus indices: ındex of surface variability (ISV), vertical asymmetry index (IVA), keratoconus index (KI), central keratoconus index (CKI), height decentralization index (IHA), vertical decentration index (IHD), radius of the flattest basic curve (Rmin), corneal aberrometric indices: Root mean square (RMS) TOTAL, low order aberration (RMS LOA), higher order aberration (RMS HOA), and biomicroscopic examination findings were evaluated separately and recorded.

Statistical analysis

Data analysis was done with the SPSS 25 package program. Shapiro-Wilk test was used to check whether the data had a normal distribution. As descriptive statistics mean and standard deviation were given for continuous parameters, and numbers and percentages were given for categorical structure. Paired sample t-test was used to test the differences between pre and post -mean values. Student t-test was used to compare two independent groups. $p<0.05$ was taken as statistical significance.

RESULTS

The minimum and maximum ages of the patients included in the study were 13 and 44 years, respectively. While the average age of the patients in group 1 was 17.76±1.67 years, it was 29.57±6.74 years in group 2. Of the patients in group 1, 9 (52%) were female and 8 (48%) were male, and in group 2, 16 (57.1%) were female and 22 (42%) were male. The average follow-up period after aCXL for patients in group 1 was 20.68 ± 6.52 months, and in group 2, this period was 21.43 ± 5.09 months. When all patients were evaluated, the average total follow-up period was 22.58±5.6 months, and the follow-up period after aCXL was 20.49±5.71 months. Keratometric and topographic astigmatism data of the two groups are summarized in Table 1, and there was a significant decrease in K1, K2, K mean, and K max values in both groups after aCXL. In both groups, the largest decrease was in the K max value. However, there was no significant difference in the decrease rates between the two groups. When postoperative mean topographic astigmatism values were examined, a decrease was observed in both groups compared to the preoperative period, but no statistically significant difference was found ($p = 0.64$, $p = 0.13$).

Table 2 summarizes the spherical and cylindrical refraction values and visual acuity data of both groups. While there was no significant change in the spherical refraction value in group 1, there was a significant decrease in the spherical refraction value in group 2. ($p = 0.48$, $p<0.0001$). There was no significant change in cylindrical refraction values in both groups ($p = 0.67$, $p = 0.31$). Additionally, no significant change was detected in the cylindrical axis after aCXL ($p = 0.11$, $p= 0,58$). However, there was a significant increase in BCVA values obtained after aCXL in both groups ($p = 0.04$, $p<0.0001$).

Table 3 summarizes the low- and high-order aberration data obtained before and after aCXL. After aCXL, a significant decrease in both low- and high-order aberrations was found in both groups. Similarly, corneal curvature indices are summarized in Table 4, and significant changes were observed in all indices except the IHA value.

No complications such as permanent stromal haze, infectious keratitis, or corneal endothelial damage that would reduce visual acuity were observed in any of the patients included in the study. None of the patients had any complications that would reduce visual acuity, such as permanent stromal clouding, infectious keratitis, or corneal endothelial damage. Corneal epithelialization delay and the presence of sterile infiltrates in the early postoperative period were observed in only one eye in group 1. Sterile infiltrates regressed with topical steroid drop treatment and healed completely (Figure-1). No progression was observed in both groups during the follow-up period. As a result, similar results were obtained in pediatric and adult patient groups after aCXL treatment.

Table 1 *Comparison of preoperative and postoperative keratometric values and topographic astigmatism values in the groups.*

(D)	Group 1			Group 2			All Patients		
	Preoperative	Postoperative	p	Preoperative	Postoperative	p	Preoperative	Postoperative	p
K1	46.15±3.53	44.87±3.36	0.007	45.35±3.03	43.8±2.84	<0.0001	45.62±3.2	44.16±3.05	<0.0001
K2	49.74± 3.3	48.72±3.33	<0.0001	49.33±3.24	47.63±3.06	<0.0001	49.47±3.24	48±3.17	<0.0001
K mean	47.68±2.96	46.7±3.24	<0.0001	47.23±2.94	45.61±2.73	<0.0001	47.38±2.93	45.98±2.94	<0.0001
K max	55.34±4.21	53.47±4.26	<0.0001	53.59±4.44	51.45±4.54	<0.0001	54.18±4.42	52.13±4.52	<0.0001
Topographic astigmatism	3.9±2.03	3.84±1.73	0.641	3.98± 2.14	3.83±2.2	0.138	3.95±2.09	3.83±2.04	0.131

Paired sample t-test was used to compare preoperative and postoperative values within each group. Student's t-test was used for comparisons between Group 1 and Group 2.

Table 2. *Comparison of preoperative and postoperative refraction and BCVA values.*

	Group 1			Group 2			All Patients		
	Preoperative	**Postoperative**	**p**	**Preoperative**	**Postoperative**	**p**	**Preoperative**	**Postoperative**	**p**
Spherical Refraction	-2.46±2.74	-2.49±3.28	0.48	-1.51±2.93	- 0.58±2.81	<0.0001	-1.81±2.89	-1.22±3.09	0.002
Cylindrical Refraction	-4.07±2.44	-4.25±1.97	0.67	-4.39±2.45	-4.05±2.66	0.31	-4.05±2.66	-4.29±2.43	0.27
Axis	90.45±67.6	102.4±71.79	0.11	78.51±60.82	76.73±59.4	0.58	82.32±62.81	85.41±64.5	0.36
BCVA	0.56±0.23	0.62±0.21	0.04	0.55±0.27	0.65±0.21	<0.0001	0.55±0.25	0.64±0.21	<0.0001
Paired sample t-test was used to compare preoperative and postoperative values within each group and in all patients									

Table 3. *Comparison of preoperative and postoperative corneal aberration values.*

(µ)	Group 1			Group 2			All Patients		
	Preoperative	**Postoperative**	**p**	**Preoperative**	**Postoperative**	**p**	**Preoperative**	**Postoperative**	**p**
RMS Total	9.97±3.4	8.97±3.44	0.001	9.39±3.72	8.49±4.08	0.002	9.59±3.6	8.65±3.86	p<0.0001
RMS LOA	9.66±3.3	8.69±3.33	0.001	9.1±3.61	8.21±3.94	0.002	9.29±3.49	8.38±3.73	p<0.0001
RMS HOA	2.44±0.85	2.19±0.92	0.0001	2.3±0.97	2.08±1.09	0.001	2.35±0.93	2.12±1.03	p<0.0001
Paired sample t-test was used to compare preoperative and postoperative values within each group and in all patients.									

Table 4. *Comparison of preoperative and postoperative corneal curvature indices.*

	Group 1			Group 2			All Patients		
	Preoperative	**Postoperative**	**p**	**Preoperative**	**Postoperative**	**p**	**Preoperative**	**Postoperative**	**p**
ISV	77.96±23.75	71.8±25.81	0.001	76.2±27.19	67.04±31.87	<0.0001	76.79±25.9	68.64±29.8	<0.0001
IVA	0.76±0.33	0.71±0.36	0.04	0.79±0.33	0.7±0.42	0.001	0.78±0.33	0.7±0.4	<0.0001
KI	1.19±0.08	1.17±0.09	0.03	1.19±0.09	1.15±0.11	<0.0001	1.19±0.09	1.16±0.1	<0.0001
CKI	1.06±0.04	1.05±0.04	0.001	1.05±0.03	1.02±0.03	<0.0001	1.05±0.04	1.03±0.04	<0.0001
IHA	30.9±21.05	34.27±20.31	0.35	29.21±24.23	25.59±21.92	0.26	29.78±23.0	28.52±21.6	0.61
IHD	0.1±0.04	0.08±0.04	0.003	0.1±0.04	0.09±0.05	<0.0001	0.1±0.04	0.08±0.05	<0.0001
R min	6.13±0.46	6.34±0.5	<0.0001	6.33±0.5	6.6±0.57	<0.0001	6.26±0.5	6.52±0.56	<0.0001
Paired sample t-test was used to compare preoperative and postoperative values within each group and in all patients.									

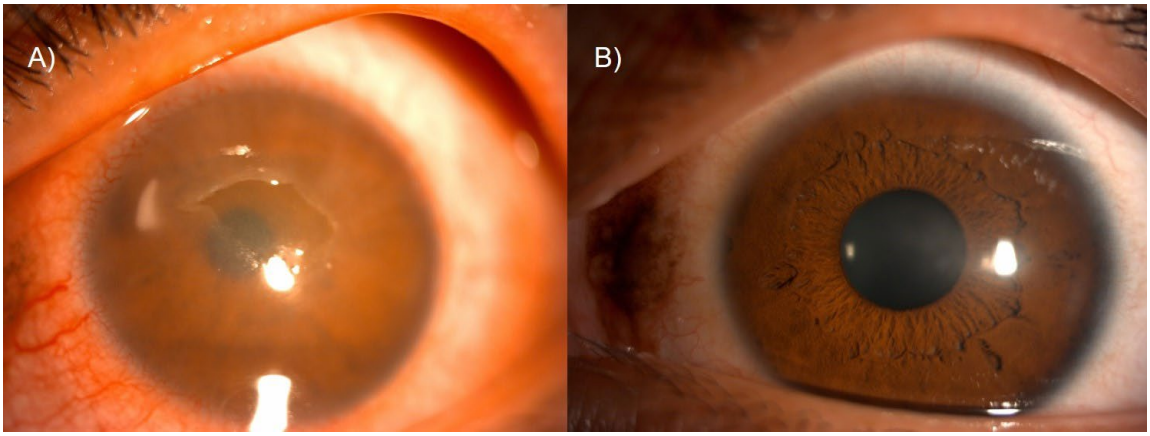

Figure-1. *re-treatment (A) and post-treatment (B) views of the patient with delayed sterile infiltrate and epithelial healing.*

DISCUSSION

Keratoconus usually starts in adolescence and progresses until around the 4th decade of life, but if it starts in childhood it can progress rapidly and be in the late stages at the time of diagnosis.[8,9]

Since keratoconus is a progressive disease and is more aggressive in the pediatric age group, it is very important to diagnose the disease at an early age and stop its progression. The sole treatment proven to halt keratoconus progression is CXL. An analysis of keratoconus progression after CXL in children involved the review of 23 studies, which revealed a progression rate of 9.9%.[10] Treatment for keratoconus in children should be initiated at the time of diagnosis, according to the Global Consensus on Keratoconus and Ecstatic Diseases.[11]

However, to prevent patient non-compliance and complications due to long procedure times, new CXL treatment protocols that shorten the procedure time have been developed as an alternative to the Standard/Dresden Protocol. Compliance with treatment is especially important for patients in the paediatric age group. Therefore, a short treatment duration should be considered an important advantage.[12] The first results of the accelerated protocol were published by Kanellopoulos in 2012 and it was shown that the data obtained was similar to the classical protocol.[13] In this study, the aCXL protocol was preferred due to its advantages, and very satisfactory results were obtained in both age groups. Many studies in the literature have reported a decrease in Kmax and a significant increase in BCVA after CXL treatment.[14-16] However, an important point to note here is that as the follow-up period increases, the K max value returns to the pre-procedure value, and visual acuity decreases. In a study by Chatsiz and Hafezi, it was reported that the K max value decreased in the first two years of follow-up but returned to the pre-procedure value in the third-year controls.[17] Similar results were observed in different studies.[14,18] However, there are studies in the literature showing that the increase in visual acuity can be maintained at a significant level along with the decrease in K max value in long-term follow-ups.[19] In the presented study, it was observed that there was a significant decrease in the K max values of the patients at the end of the 12th month, while visual acuity increased significantly in both groups. This result is short-term and is compatible with studies with similar follow-up periods in the literature. However, it would be appropriate to evaluate the long-term follow-up results of the patients.

In a study by Cummings et al., the results of patients treated with aCXL and standard CXL protocols were comparatively evaluated. When the results at 12 months were examined, no statistically significant differences were detected between the two groups in terms of changes in keratometry values, cylindrical refractive values, or cylindrical refraction axis values.[20] Conversely, Ucakhan et al.'s study revealed a significant decrease in all keratometry values, a non-significant decrease in spherical refraction and topographic astigmatism values, and a significant decrease in cylindrical refraction values following treatment with the standard CXL protocol.[19] In this study, postoperative average spherical refractive values were examined; while a statistically non-significant increase was observed in Group 1 compared to the preoperative period, a significant decrease

was observed in Group 2 compared to the preoperative period. When postoperative average cylindrical refractive values and postoperative average cylindrical refraction axis values were examined, no statistically significant change was observed in both groups compared to the preoperative period. This result seems to be compatible with the study conducted by Cummings et al.

Studies conducted on patients who received standard CXL treatment for keratoconus have shown a decrease in RMS HOA values after CXL. In the presented study, it was observed that there was a significant decrease in postoperative RMS TOTAL, RMS LOA, and RMS HOA values in both groups compared to the preoperative period.[21-22] Corneal curvature indices, especially ISV and IHD, have an important place in the progression and treatment follow-up of keratoconus.[23] A significant decrease was observed in the ISV, IVA, KI, CKI, IHD, and R min values in both groups compared to the preoperative period, while no statistically significant change was observed in the IHA value in our study. However, a similar analysis was conducted by Ucakhan et al., and while a significant decrease was found in ISV, IVA, and IHA, no statistically significant change was observed in IHD, CI, CKI, and R min values.[19] The main reason for the difference between the two studies may be the follow-up period. The follow-up period of the presented study is quite shorter compared to the follow-up period in the study conducted by Ucakhan et al. In another study of Uçakhan et al. At 3 years after surgery, compared with baseline, there was a statistically significant improvement in mean MAE, ISV, CKI, Rmin, IHA, IHD, minimum PI, average PI, maximum PI, vertical coma and spherical aberration in both the pediatric and adult age groups, with no difference between groups ($p>0.05$).[24]

Çerman et al. examined the CXL results of a total of 459 patients, 461 of whom were treated with the epi-off method and 127 of whom were treated with the epi-on method, to evaluate the possible risk factors that lead to sterile corneal infiltrates in patients receiving CXL treatment.[25] They observed that sterile infiltrate developed in a total of 19 patients (3.2%) after CXL, and all of these were in eyes that underwent CXL with the epi-off method. In the presented study, no serious complications such as permanent haze, infectious keratitis, or corneal endothelial damage that could negatively affect visual acuity were encountered after CXL. Delay in corneal epithelialization and the development of sterile infiltrate were observed in only 1 patient (1.35%).

In our study, the highest decrease was observed in K max value in both groups. However, there was a significant increase in BCVA values after aCXL in both groups. A significant decrease in both low- and high-order aberrations was observed in both groups following aCXL. When the corneal curvature indices were evaluated, it was observed that all indices except the IHA (height decentralisation index) value had changed significantly. No progression was observed in both groups during the follow-up period.

Previous studies have primarily compared the efficacy and safety of aCXL with standard CXL protocols. However, the present study specifically focused on the effect of age on the outcomes of aCXL treatment. Age has been shown to play a significant role in the progression of keratoconus and the response to CXL. It was reported that younger patients exhibited a higher risk of keratoconus progression and tended to respond differently to CXL compared to older patients.[26] Consistent with these findings, the current study emphasizes that evaluating patients according to age groups may provide additional insights into the clinical effectiveness of aCXL and help guide patient-specific treatment strategies.

As a result, aCXL treatment stands out as an effective and safe treatment method in preventing progression in patients under 18 years of age as well as in patients over 18 years of age. The results of the treatment were similar for both groups. The use of the aCXL method to shorten surgery duration is key to increasing patient compliance, especially in paediatric patients. It would be a good idea to do more studies with longer follow-up periods and novel cross-linking protocols.

REFERENCES

1. Davidson AE, Hayes S, Hardcastle AJ, Tuft SJ. The pathogenesis of keratoconus. Eye (Lond). 2014;28:189-195. doi:10.1038/eye.2013.278
2. Ertan A, Muftuoglu O. Keratoconus clinical findings according to different age and gender groups. Cornea 2008;27:1109-13.
3. Léoni-Mesplié S, Mortemousque B, Touboul D, et al. Scalability and severity of keratoconus in children. Am J Ophthalmol. 2012;154:56-62.
4. Sahin S, Palamar M, Egrilmez S, Yagci A, Selver OB. Comparison of Corneal Tomography Parameters in the Diagnosis of Keratoconus in Early and Late Pediatric Age Group. Middle

East Afr J Ophthalmol. 2024;30:241-245. Published 2024 Dec 2. doi:10.4103/meajo.meajo_105_23

5. Wollensak G, Spoerl E, Seiler T. Riboflavin/ultraviolet-a-induced collagen crosslinking for the treatment of keratoconus. Am J Ophthalmol. 2003;135: 620-7.
6. Kohlhaas M, Spoerl E, Schilde T, et al. Biomechanical evidence ofthe distribution of cross-links in corneas treated with riboflavin and ultraviolet A light. J Cataract Refract Surg 2006;32:279-83.
7. Wollensak G, Spoerl E, Seiler T. Stress-strain measurements of human and porcine corneas after riboflavin-ultraviolet-A-induced cross-linking. J Cataract Refract Surg. 2003;29:1780-5.
8. Mas Tur V, MacGregor C, Jayaswal R, O'Brart D, Maycock N. A review of keratoconus: Diagnosis, pathophysiology, and genetics. Surv Ophthalmol. 2017;62:770–83. doi: 10.1016/j.survophthal.2017.06.009.
9. Kankariya VP, Kymionis GD, Diakonis VF, Yoo SH. Management of pediatric keratoconus – Evolving role of corneal collagen cross-linking: An update. Indian J Ophthalmol. 2013;61:435–40. doi: 10.4103/0301-4738.116070.
10. Achiron A, El-Hadad O, Leadbetter D, et al. Progression of Pediatric Keratoconus After Corneal Cross-Linking: A Systematic Review and Pooled Analysis. Cornea. 2022;41:874-878. doi:10.1097/ICO.0000000000002808
11. Gomes JAP, Tan D, Rapuano CJ, et al. Global Consensus on keratoconus and ectatic diseases. Cornea. 2015;34:359–369.
12. Berhuni M. Öztürkmen C. Setge Tıskaoğlu N. Pediyatrik İlerleyici Keratokonus Tedavisinde Hızlandırılmış Korneal Çapraz Bağlama Tedavisinin 1 Yıllık Sonuçlarının Araştırılması. MN Oftalmoloji. 2023;30:207-211
13. Kanellopoulos AJ. Long term results of a prospective randomized bilateral eye comparison trial of higher fluence, shorter duration ultraviolet A radiation, and riboflavin collagen cross linking for progressive keratoconus. Clin Ophthalmol 2012;6:97-101.
14. Padmanabhan P, Rachapalle Reddi S, et al. Corneal Collagen Cross-Linking for Keratoconus in Pediatric Patients - Long-Term Results. Cornea 2017;36:138-43.
15. Zotta PG, Diakonis VF, Kymionis GD, et al. Long-term outcomes of corneal cross-linking for keratoconus in pediatric patients. J AAPOS 2017;21:397-401.
16. De Bernardo M, Capasso L, Lanza M, et al. Long-term results of corneal collagen crosslinking for progressive keratoconus. J Optom 2015;8:180-6.
17. Chatsiz N, Hafezi F. Progression of keratoconus and efficacy of pediatric [corrected] corneal collagen cross-linking in children and adolescents. J Refract Surg 2012;28:753-8.
18. Ozer MD, Batur M, Mesen S, et al. Long-Term Results of Accelerated Corneal Cross-Linking in Adolescent Patients With Keratoconus. Cornea 2019;38:992-7.
19. Uçakhan Ö, Bayraktutar B, Sağlık A. Pediatric Corneal Collagen Cross-Linking: Long-Term Follow-Up of Visual, Refractive, and Topographic Outcomes. Cornea 2016;35:162-8.
20. Cummings AB, McQuaid R, Naughton S, et al. Optimizing Corneal Cross-Linking in the Treatment of Keratoconus: A Comparison of Outcomes After Standard- and High-Intensity Protocols. Cornea 2016;35:814-22.
21. Schlegel Z, Lteif Y, Bains HS, et al. Total, corneal, and internal ocular optical aberrations in patients with keratoconus. J Refract Surg 2009;25:S951-7.
22. Vinciguerra P, Albe E, Trazza S, et al. Refractive, topographic, tomographic, and aberrometric analysis of keratoconic eyes undergoing corneal crosslinking. Ophthalmology. 2009;116:369-78.
23. Kanellopoulos AJ, Asimellis G. Revisiting keratoconus diagnosis and progression classification based on evaluation of corneal asymmetry indices, derived from Scheimpflug imaging in keratoconic and suspect cases. Clin Ophthalmol 2013;7:1539-48
24. Uçakhan ÖÖ, Celik Buyuktepe T, Yavuz Z, Asbell PA. Pediatric versus Adult Corneal Collagen Crosslinking: Long-term Visual, Refractive, Tomographic and Aberrometric Outcomes. *Curr Eye Res*. 2021;46:14-22. doi:10.1080/02713683.2020.1782940
25. Çerman E, Ozarslan Ozcan D, et al. Sterile corneal infiltrates after corneal collagen cross-linking: evaluation of risk factors. Acta Ophthalmolgy 2017;95:199-204.
26. Aslan L, Başkan AM, Yüksel E et al. Keratokonus Hastalarinin Korneal Çapraz Baglama Tedavisinde Yas Faktörünün Etkisi. Turk J Ophthalmol. 2012;42(6):450-453. doi:10.4274/tjo.42.02986

SYMBOLS AND ABBREVIATIONS

CKI: Central keratoconus index
aCXL: Accelerated corneal cross-linking
D: Diopter
BCVA: Best visual acuity corrected with glasses
IHA: Height decentralization index
IHD: Vertical decentration index
ISV: Index of surface variability
IVA: Vertical asymmetry index
K1: Flat keratometric value
K2: Vertical keratometric value
KI: Keratoconus index
K max: Maximum keratometric value
K mean: Average keratometric value
R min: Radius of the flattest basic curve
RMS: Root mean square
RMS HOA: Higher order RMS
RMS LOA: Low order RMS
UV-A: Ultraviolet-A