Egyptian Journal of Ophthalmology (MOC) 2022;*3:154-168*

Safety and Efficacy of Conventional Versus Accelerated Corneal Collagen Cross-Linking in Keratoconus and Corneal Ectatic Diseases

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Received: 24-11-2022, Accepted: 19-12-2022, Published online:16-3-2023

EJO(MOC) 2022;3:154-168.

Short title: Conventional verses Accelerated Crosslinking

Abstract

Purpose: This study compares the efficacy and safety of conventional versus accelerated corneal collagen cross linking in treatment of progressive keratoconus.

Methods: This randomized observational study was conducted on 79 eyes with keratoconus or corneal ectatic diseases. Patients' eyes were divided into two groups, group A (n=35 eyes) underwent conventional crosslinking (cCXL) and group B (n=44 eyes) underwent the accelerated (KXL) technique in the form of dextran-free riboflavin 0.1% solution every two minutes for a total of 10 minutes followed by UV illumination at 30 mW/cm^2 continuously for four minutes (total energy: 7.2J/cm^2).

Results: No eyes lost any lines of visual acuity and more than 80% gained 1-4 lines in both UCVA and BCVA in both groups. Comparing both groups after 6 months, a more significant decrease in ECD was seen in the accelerated group at 6months (p=0.011), the mean cylindrical error showed a more significant improvement in the accelerated group (p=0.044), less reduction of pachymetry at thinnest location in KXL (P=0.008), but the mean depth of the demarcation line was significantly better and more homogenous in the conventional group (363.57±46.92µm) than the accelerated group (319.56±36.50µm) (P<0.001). Both groups showed insignificant change in the coefficient of variation for specular microscopy (P=0.574 and 0.528). **Conclusion:** both types offer a significant improvement in UCVA and BCVA values, but cCXL offers a deeper demarcation line and less endothelial loss. KXL offers less reduction in pachymetry and better cylinder correction.

Keywords: Conventional cross-linking, accelerated cross-linking, depth of corneal demarcation, Endothelial cell count

INTRODUCTION:

Keratoconus (KC) is a non-inflammatory progressive ectatic disorder causing corneal thinning.[1, 2,3] Collagen cross-linking (CXL), a treatment for KC, stimulates physical cross-linking of collagen via Riboflavin absorbing UVA to stimulate the production of free radicals. Riboflavin acts as a shield that protects the deeper ocular tissues from UVA associated damage.[4] The oxidative reaction produces bonds within the corneal stroma collagen and limits corneal ectasia progression.[1,4]

CXL techniques include Dresden protocol and accelerated crosslinking. [4, 5] Accelerated transepithelial corneal collagen cross-linking preserves epithelium and shortens treatment duration via increasing the ultraviolet power.[6] Our study compares the efficacy of conventional (cCXL) versus accelerated crosslinking (KXL) in treatment of keratoconus.

SUBJECTS AND METHODS:

Study Design: Prospective randomized comparative observational study.

***Participants**:* This study was conducted on 79 eyes of patients suffering from corneal thinning disease, in the form of keratoconus (77 eyes) and post LASIK ectasia (2 eyes). The 79 eyes were subdivided into two groups:

1. Study group (A): 35 eyes were treated with conventional cross-linking.
2. Study group (B): 44 eyes were treated with accelerated cross-linking.

Prior to study enrollment, an informed written consent was taken from each patient. Ethics approval was obtained from the institutional review board of Faculty of Medicine, Cairo University. The study was conducted in accordance with the ethical standards of the institutional review board of the faculty of Medicine Cairo University.

Inclusion Criteria:

Patients with the following characteristics including evidence of progressive KC or keratectasia (determined using tomographic and topographic analysis), aged 18–35 years, a central corneal thickness >400, and a clear cornea free of any other disease were included in this study.

Exclusion Criteria:

A positive history of concurrent infection of the cornea including herpetic keratitis, autoimmune disorders, severe dry eye, keratoconus grade 3 or 4 (Krumeich classification), severe allergic conjunctivitis, acute hydrops, diffuse central corneal opacity, glaucoma, cataract, or other vitreoretinal disorders were excluded from this study. Any patient who was at the time of study pregnant or lactating was also excluded from the study.

Preoperative assessment:

A thorough patient history was taken. All patients underwent a complete ophthalmological workup that included uncorrected and best corrected visual acuity (UCVA, BCVA), slit lamp biomicroscopy, and fundus examination. Corneal parameters were assessed (corneal curvature and central corneal thickness (CCT)) using Scheimpflug imaging via the Sirius Scheimpflug Analyzer (CSO, Costruzione Strumenti Oftalmici, Florence, Italy). Corneal endothelial cell analysis was done using the noncontact specular microscope; Topcon SP 3000P (Japan).

Operative Technique:

Both the cCXL and KXL were performed under topical anesthesia using Benoxinate (oxybuprocaine 0.4%) under complete aseptic conditions, and an eyelid speculum was applied and the central 7-8mm of corneal epithelium was scraped using a spatula.

a. For the conventional treatment: One drop of a solution containing isotonic 0.1% riboflavin and 20% dextran (MedioCROSS D, Medio-Haus-Medizinprodukte GmbH, Kiel, Germany) was administered in each eye every two minutes for a total of 30 minutes (15 drops). The eye was placed directly below the UV illumination device (UV-X, Peschke Meditrade GmbH, Huenenberg, Switzerland), with special care to ensure that the beam diameter was within the treatment zone, while avoiding the limbal area, which was followed by additional administration of riboflavin solution every 2 minutes at an irradiance of $3mW/cm^2$ for 30 minutes (total energy: $5.4J/cm^2$).The distance between the patient's eye and the beam aperture was five centimeters.
b. For the accelerated treatment: One drop of dextran-free riboflavin 0.1% solution (VibeX Rapid, Avedro, Inc., Waltham, Massachusetts, MA, USA) was given every two minutes for a total of 10 minutes. Eyes were then thoroughly rinsed with a balanced salt solution and placed under the UV illumination system (KXL, Avedro, Inc., Waltham, Massachusetts, MA, USA), following which irradiation was conducted at 30 mW/cm^2 continuously for four minutes (total energy: $7.2J/cm^2$).

Following the operation, both patient groups had a contact lens bandage applied and topical antibiotics (moxifloxacin hydrochloride 0.5%) 3 times aday and steroids (prednisolone acetate 0.12%) were administered 3 times aday starting from 3rd day postoperatively, which were tapered at one month after complete epithelial healing. All patients were followed-up

postoperatively (day one, week one, one/ three/ six months after date of surgery).

Follow up:

A series of tests postoperatively were performed for each follow up visit, which included (1) evaluation (Day 3) included UCVA, BCVA, refractive, and topographic changes, (2) anterior Segment Optical Coherence Tomography (one month) was done one month postoperatively to assess the depth of the demarcation line, (3) Specular microscopy assessment (1 and 6 months), and (4) corneal parameters (six months) like corneal curvature, CCT, and biomechanics were measured.

Statistical analysis:

Data was analyzed using statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage. Independent sample T test was used to compare means, Mann Whitney U test was used to compare non-parametric data, and Chi square test was used to compare qualitative parameters. The confidence interval was set to 95%, the margin of error accepted was set to 5%, and significance was determined by a P-value of 0.05.

RESULTS:

I. Study population

Mean age of the patients in the accelerated group was 27.20 ± 8.62 and 25.74 ±8.40 in the conventional group (Table 1). There were no surgical or postoperative complications. The cornea re-epithelialized by one week after treatment. There was a minimal anterior stromal corneal haze that resolved approximately 1-3 months postoperatively. No eyes lost lines of the preoperative UCVA; 16.5% maintained the preoperative UCVA, and 83.5% gained one to four lines, Also, there was a significant improvement in BCVA, 83.6% experienced at least a gain of 1–4 lines of BCVA and 16.45% showed no change in BCVA. These results were comparable among both study groups.

Table 1: demographic data of accelerated crosslinking and conventional crosslinking groups

Demographic data	Accelerated CXL (n=24)	Conventional CXL (n=19)	t or #x^2	p-value
Age (years)				
Mean ±SD	27.20±8.62	25.74±8.40	0.646 (t)	0.521
Range	18-40	18-40		
Sex				
Male	15 (62.5%)	11 (57.9%)	1.226 (#x^2)	0.621
Female	9 (37.5%)	8 (42.1%)		
Laterality				
Bilateral	20 (83.3%)	16 (66.7%)	2.685 (#x^2)	0.195
Unilateral	4 (16.7%)	3 (12.5%)		

*t: Independent Sample t-test; #x^2: Chi-square test; *p-value <0.05 is significant; **p-value <0.001 is highly significant*

II. Conventional (cCXL) group results:

a. Tomographic results: Regarding K-MAX and K-AVG showed stable values, paired t test revealed an insignificant difference between pre and postoperative mean values (p=0.866; p=0.881) respectively. The mean cylinder recorded was significantly greater preoperatively (p=0.045) (Table 2). Pachymetry at the thinnest location was significantly reduced (p<0.001). (Figure 1)

Table 2: Comparison between pre-and postoperative specular microscopy values of endothelial cell density (ECD) and coefficient of variance (CV**)** and and topographic reading values for K-max, K average, thinnest location, and cylinder in conventional CXL group.

	Conventional CXL		**Paired Sample t-test**		
Specular	**Mean**	**+/- SD**	**Diff.**	**t-test**	**p-value**
			ECD		
Preop.	2736.13	251.19			
1 month postop.	2669.26	339.69	-66.87±56.57	1.213	0.237
6 months postop.	2654.24	419.29	-81.89±62.33	1.384	0.156
			CV		
Preop.	35.87	11.32			
1 month postop.	36.57	5.95	0.70±9.50	-0.351	0.729
6 months postop.	30.55	4.32	-5.32±5.97	-0.571	0.574
Topography	Mean	+/- SD	Diff.	t-test	p-value
			K-max		
Preoperative	58.10	10.11			
Postoperative (6 m)	58.26	8.03	0.16±5.45	-0.170	0.866
			K average		
Preoperative	49.13	2.71			
Postoperative (6 m)	49.15	3.05	0.02±0.89	-0.151	0.881
			Thinnest location		
Preoperative	460.42	39.59			
Postoperative (6 m)	441.45	47.49	-18.97±21.97	4.961	<0.001**
			Cylinder		
Preoperative	4.04	2.03			
Postoperative (6 m)	3.83	1.89	-0.21±0.58	2.082	0.045*

*Using: Paired Sample t-test*p-value <0.05 is significant; **p-value <0.001 is highly significant*

ECD: endothelial cell density; CV: coefficient of variance, 6 m = 6 months

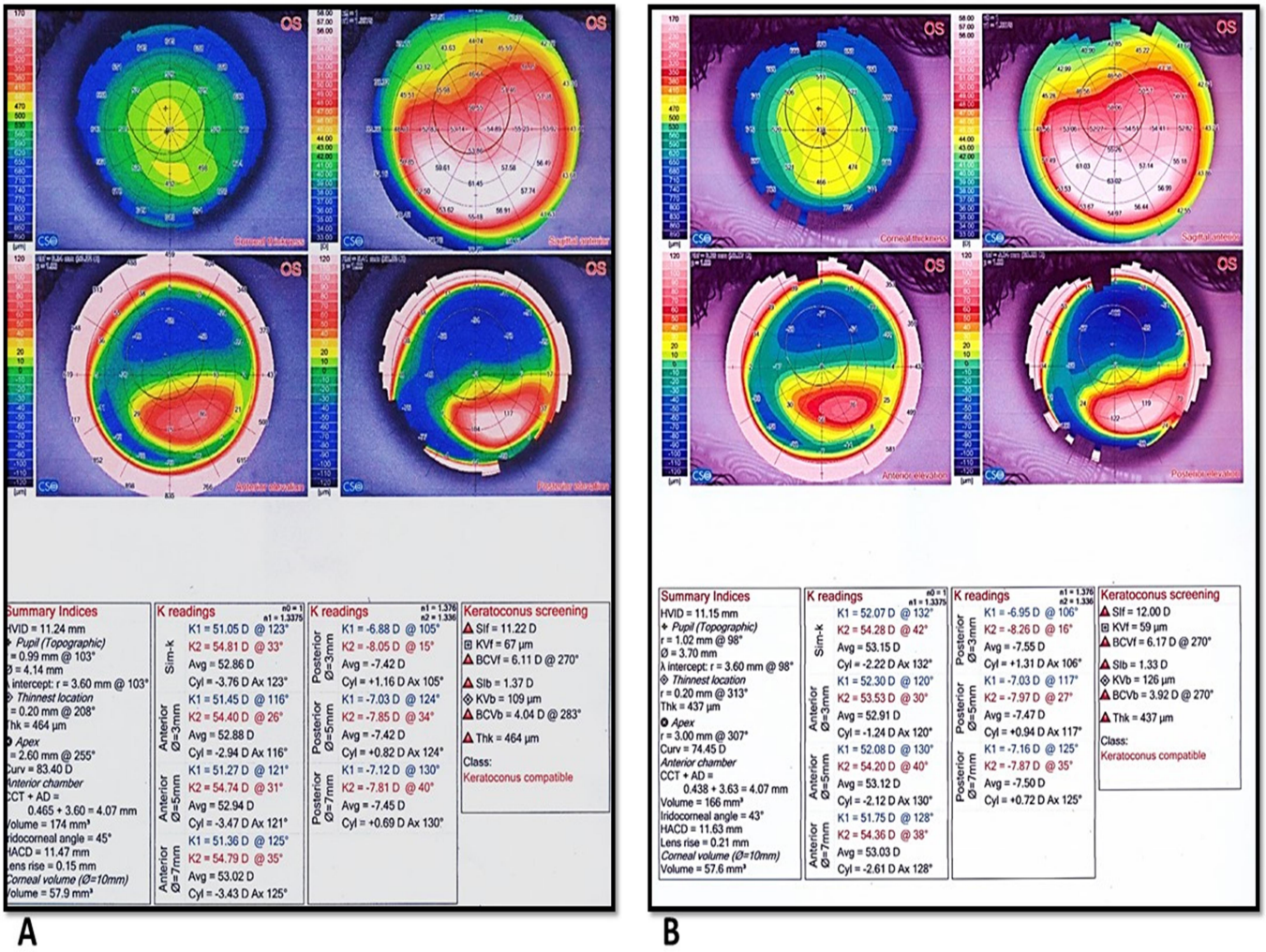

Figure 1: Corneal topography of left eye in patient X who had conventional CXL showing the following values K-MAX=54.81 D, KAVG=52.86 D, and thinnest location=464 µm preoperatively, which changed to 54.45 D, KAVG=53.15 D, and 437 µm respectively

b. Endothelial cell analysis: The mean baseline endothelial cell count was 2736.13± 251.19/ mm2 and decreased insignificantly to 2669.26± 339.69/ mm^2 after one month (P=0.237) and 2654.24± 419.29/ mm2 after six months postoperatively (P= 0.156). The coefficient of variance (CV) was 35.87/ mm^2 preoperative, then increased to 36.57/ mm^2 one month after CXL, followed by a decline (30.55/ mm2) after six months and the changes were insignificant (P=.0.729 and 0.574 respectively).

III. Accelerated (KXL) group results:

a. Tomographic results: K-MAX showed stable values and paired t test revealed an insignificant difference between pre and postoperative mean values (p=0.669), while K AVG showed insignificantly higher preoperative values than postoperative values (p=0.131) (Figure 2). Comparison of mean cylinder demonstrated significantly higher values preoperatively (p=0.023). Pachymetry at thinnest location showed minimal reduction. Comparison of K-MAX, K-AVG, cylinder and thinnest location thickness pre- and postoperative values are demonstrated in Table 3.

Table 3: Comparison between pre-and postoperative specular microscopy values of endothelial cell density (ECD) and coefficient of variance (CV) and topographic reading values for K-max, K average, thinnest location, and cylinder in accelerated CXL group.

	Accelerated CXL		Paired Sample t-test		
Specular microscopy	**Mean**	**+/- SD**	**Diff.**	**t-test**	**p-value**
		ECD			
• **Preoperative**	2806.08	391.16			
• **After one month**	2621.68	382.15	-184.40±357.23	2.732	0.011*
• **After 6 months**	2636.08	123.60	-170.00±222.78	2.666	0.013*
		CV			
• **Preoperative**	33.56	5.99			
• **After one month**	35.83	5.99	2.27±8.04	-1.493	0.147
• **After 6 months**	34.55	6.67	0.99±7.01	-0.640	0.528
Topography	**Mean**	**+/- SD**	**Diff.**	**t-test**	**p-value**
		K-max			
• **Preoperative**	54.54	5.45			
• **Postoperative**	54.86	6.85	0.32±3.22	-0.434	0.669
		K average			
• **Preoperative**	44.32	4.44			
• **Postoperative**	43.48	4.49	-0.85±2.70	1.564	0.131
		Thinnest location			
• **Preoperative**	443.16	40.78			
• **Postoperative**	438.28	38.44	-4.88±14.85	1.643	0.113
		Cylinder			
• **Preoperative**	3.33	2.10			
• **Postoperative**	3.01	2.47	-0.32±0.89	2.360	0.023*

*Using: Paired Sample t-test*p-value <0.05 is significant; **p-value <0.001 is highly significant*

ECD: endothelial cell density; CV: coefficient of variance

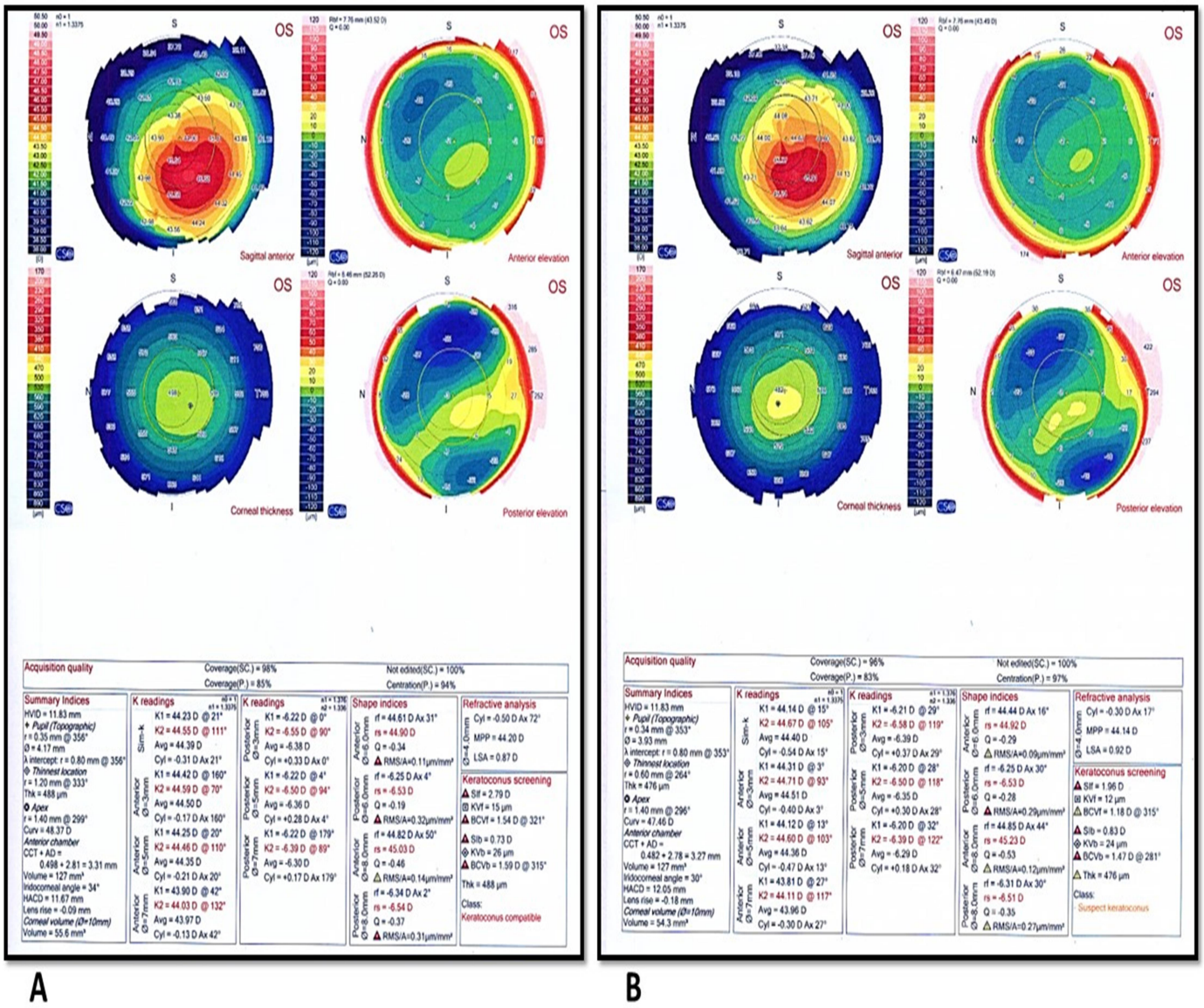

Figure 2: Corneal topography of left eye in patient Y who had accelerated CXL showing the following values: KMAX=48.37D, KAVG=44.39D, thinnest location=488µm preoperatively, which changed to 47.46 D, 44.40 D, and 476 µm respectively

IV. ***Endothelial cell analysis (ECD):***

The mean baseline ECD was 2806.08± 391.16/ mm2, then 2621.68± 382.15/ mm2 (p=0.011) and 2636.08± 123.60/ mm2 (p=0.013) after one and six months respectively. This demonstrates a statistically significant decrease in the mean post-operatively compared to the pre-operative values (P<0.001) (Figure 3). With regards to CV, it was 33.56/ mm2 preoperative then it increased to 35.83/ mm2 one month after KXL followed by a decline (34.55/ mm2) six months postoperatively. Comparison of pre- and postoperative ECD and CV values in patients who had KXL are demonstrated in Table 3.

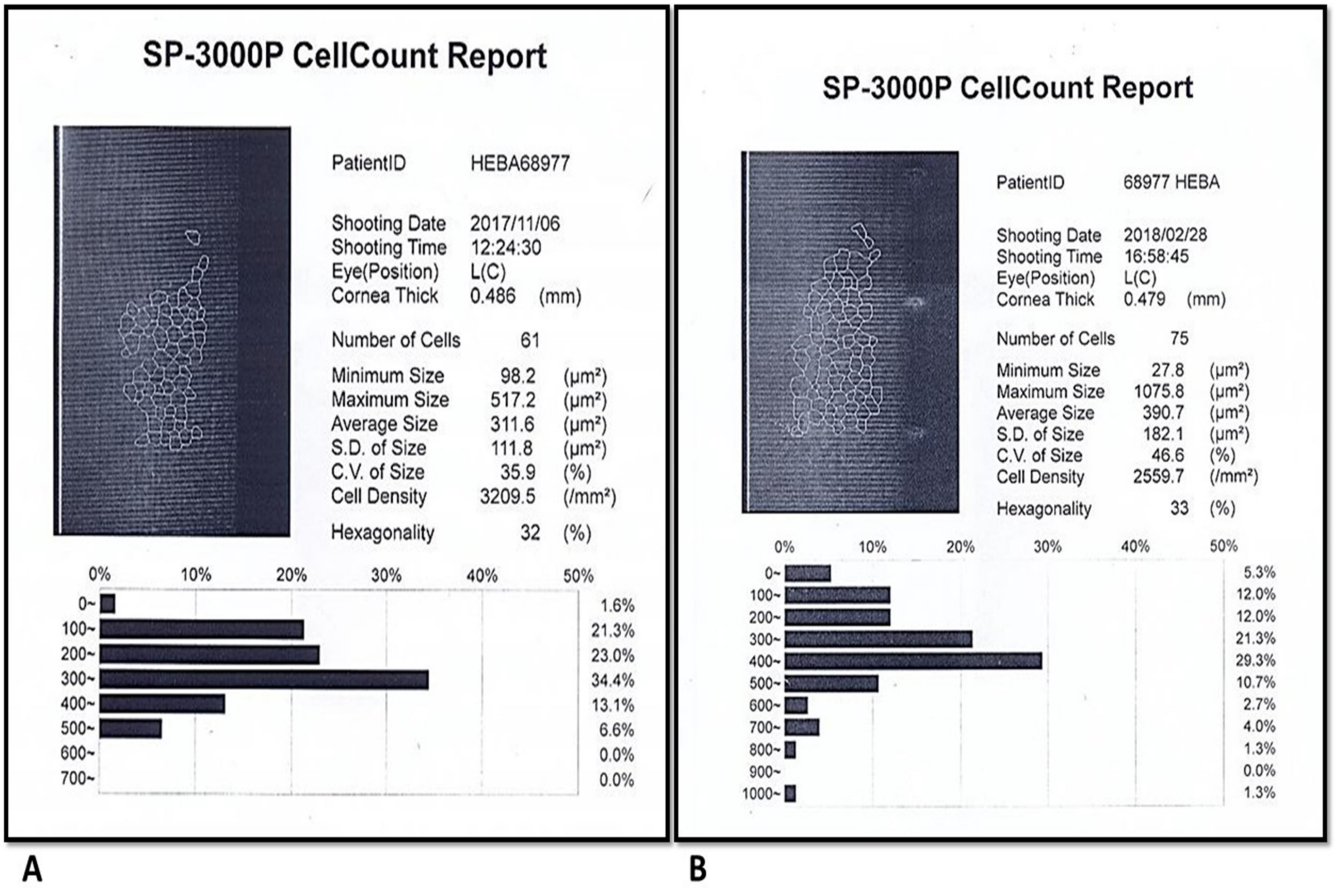

Figure 3: Preoperative left eye Endothelial Cell Analysis in a patient who had accelerated cross linking, showing the following values CD= 3209.5/ mm2, CV=35.9/ mm2, which changed to the following vales CD=2559.7/mm2, CV=46.6/ mm^2

V. Comparison of results for both the conventional and accelerated groups:

a. ECD and CV: ECD was higher preoperatively in both groups, which is more relevant in accelerated group. The difference between the baseline and one month postoperatively was significant (p=0.020) as well as at six months postoperatively (p=0.011) being better in cCXL (Table 4). With regards to CV values in both groups, it showed lower preoperative values then it significantly increased after one month (p=0.525) and then it decreased again after six months (close to preoperative values) with an insignificant change. (Table 4).

Table 4: Comparison between study groups according to their specular microscopy measurements; endothelial cell density (ECD) and coefficient of variance (CV).

	Accelerated CXL (n=44)	**Conventional CXL (n=35)**	**t-test**	**p-value**
		Specular CV		
• **Preoperative**				
Mean ±SD	32.81±6.10	34.00±10.22	-0.610	0.544
Range	19.2-46.6	27-72		
• **After one month**				
Mean ±SD	35.34±5.88	36.57±5.95	-0.752	0.455
Range	19.1-43.2	29-44		
• **After 6 months**				
Mean ±SD	34.55±6.67	32.83±8.78	0.792	0.432
Range	27.3-46.6	27-58		
• **Diff. Preop and one month**				
Mean ±SD	2.27±8.04	0.70±9.50	0.640	0.525
Range	-11.9_13.9	-28_15		
• **Diff. Preop and six months**				
Mean ±SD	0.99±7.01	-5.32±5.97	0.072	0.943
Range	-18.9_10.7	-5_11		
		Specular ECD		
• **Preoperative**				
Mean ±SD	2778.11±329.51	2738.13±224.81	0.579	0.565
Range	2033.2-3296.4	2188-3096		
• **After one month**				
Mean ±SD	2637.93±366.04	2671.26±472.19	0.874	0.372
Range	1963.5-3313	924-3067		
• **After 6 months**				
Mean ±SD	2636.08±123.60	2589.37±391.47	1.119	0.201
Range	2415.2-2855.4	1797-3049		
• **Diff. Preop and one month**				
Mean ±SD	-184.40±357.23	-66.87±56.57	2.252	0.020*
Range	-429.3_747.7	-286_824		
• **Diff. Preop and six months**				
Mean ±SD	-170.00±222.78	-81.89±62.33	2.572	0.011*
Range	-649.8_130.8	-1765_129		

*t-Independent Sample t-test *p-value <0.05 is significant; **p-value <0.001 is highly significant*

ECD: endothelial cell density; CV: coefficient of variance

b. K readings: Paired t test revealed that the difference between pre and postoperative mean K-MAX values between both groups was insignificant, but K-AVG was significantly reduced in the accelerated group (p=0.042). (Table 5)

Table 5: Comparison between the study groups according to their topographic data regarding K-max and K-average.

	Accelerated CXL (n=44)	**Conventional CXL (n=35)**	**t-test**	**p-value**
		K-max		
• **Preoperative**				
Mean ±SD	55.57±5.07	58.10±10.11	-1.384	0.171
• **Postoperative**				
Mean ±SD	55.12±6.34	58.26±8.03	-1.564	0.124
• **Difference**				
Mean ±SD	0.32±3.22	0.16±5.45	0.088	0.931
		K-average		
• **Preoperative**				
Mean ±SD	46.92±5.79	49.13±2.71	-2.013	0.048*
• **Postoperative**				
Mean ±SD	44.10±4.52	49.15±3.05	-5.209	<0.001**
• **Difference**				
Mean ±SD	-0.85±2.70	0.02±0.89	-1.714	0.042*

*t-Independent Sample t-test; *p-value <0.05 is significant; **p-value <0.001 is highly significant*

c. Corneal Demarcation line as demonstrated by corneal AS-OCT: The mean depth in the accelerated group was 319.56±36.50 and 363.57±46.92 (p<0.001) in the conventional group (P<0.001); it is not only the corneal demarcation line was deeper in cCXL but also more homogenous as compared to KXL where the line was less dense and less uniform.

d. Cylinder refractive error: The mean cylindrical refractive error was greater in both groups preoperatively than postoperatively, but a significantly greater reduction in mean cylinder refractive error was seen in the accelerated group (p=0.044). (Table 6)

e. Pachymetry: Postoperative pachymetry at thinnest location demonstrated a significantly higher reduction in corneal thickness in the conventional versus accelerated group (p=0.008). (Table 6).

Table 6: Preoperative and postoperative value comparison between study groups according to mean cylinder, topographic thinnest location, and AS-OCT findings measuring demarcation line depth**.**

	Accelerated CXL (n=44)	**Conventional CXL (n=35)**	**t-test**	**p-value**
		Topographic Cylinder		
• **Preoperative**				
Mean ±SD	3.33±2.10	4.04±2.03	-1.520	0.132
Range	0.31-7.14	2.2-7.7		
• **Postoperative (6 m)**				
Mean ±SD	3.01±2.47	3.83±1.89	-1.628	0.108
Range	0.23-7.41	1.01-7.36		
• **Difference**				
Mean ±SD	-0.32±0.89	-0.21±0.58	1.708	0.044*
Range	0.04-2.56	0.12-1.19		
		Topographic Thinnest location		
• **Preoperative**				
Mean ±SD	456.98±40.73	460.42±39.59	-0.365	0.716
Range	399-508	390-525		
• **Postoperative (6 m)**				
Mean ±SD	433.97±38.82	441.45±47.49	-0.674	0.503
Range	372-499	357-521		
• **Difference**				
Mean ±SD	-4.88±14.85	-18.97±21.97	2.761	0.008*
Range	-34_20	-87_13		
		AS-OCT CCT		
Mean ±SD	524.00±56.88	550.36±27.74	-2.278	0.026*
Range	401-598	480-580		
		Demarcation Line Depth		
Mean ±SD	319.56±36.50	363.57±46.92	-3.873	<0.001**
Range	260-387	310-460		

*t-Independent Sample t-test; *p-value <0.05 is significant; **p-value <0.001 is highly significant*

CCT: Central Corneal Thickness

DISCUSSION:

Collagen CXL is a technique that uses UVA light and riboflavin to enhance corneal stability via inducing additional cross-links between or within collagen fibers. [7] Recent studies have geared their focus to analyzing safety of this technique in KC patients.

Konstantopoulos et al reviewed the protocols of nine studies that compared conventional verses accelerated cross linking. The results of their study demonstrated no significant difference between both groups with regards to visual acuity, efficacy, and safety. [8] Cinar and Kanellopoulos et al both conducted studies comparing the accelerated and conventional cross-linking techniques, and both concluded that endothelial loss was negligible and that there was no difference in terms of endothelial safety for both groups. Till now, a consensus has not been reached for the efficacy and safety of the accelerated crosslinking technique compared to the conventional technique. [9,10]

In the present study, a significant improvement in UCVA was noticed. No eyes lost lines of the preoperative UCVA, 16.5% maintained the preoperative UCVA, and 83.5% gained one to four lines, which is comparable to the results of Arbelaez et al.[11] Also, there was a significant improvement in BCVA, 83.6% experienced at least a gained of 1–4 lines of BCVA and 16.45% showed no change in BCVA. These results were comparable among both study groups. Similarly, Wollensak et al [4], Arbelaez et al[12], Vinciguerra et al [13], and Caporossi et al [14]found an improvement in UCVA and BCVA in different degrees.

In contrast, El-Raggal et al [11] found that 6.67% lost one line of preoperative value and Hersh et al [15] found that 1.4% lost two or more Snellen lines of BCVA. The reasoning for BCVA loss in these patients is unclear. On other hand, the cause of the optical improvement in this study was unknown in some cases with a negative relation to keratometric or refractive changes. Hafezi et al [16] concluded a similar observation.

Shetty et al. (n=138 keratoconus eyes) noticed enhanced BCVA in all groups after 12 months following CXL treatment, although insignificant. [17]This was not demonstrated in our study. This study showed a statistically significant decrease of mean preoperative cylinder from (3.33±2.10D) to (3.01±2.47D) after six months in accelerated group, while in conventional group, the mean preoperative cylinder was (4.04±2.03D) and after six months was (3.83±1.89D). Several studies supported this significant reduction in mean cylindrical power. [4,10,12,14]

Like other studies, the results of our research did not observe any significant differences between the conventional and accelerated techniques regarding topographic changes. [9,14,18,19] However, Shetty et al. reported that a reduced CXL flattening effect with greater irradiation and shorter duration of treatment. [17] Brittingham et al., who studied 131 progressive KC eyes undergoing the same treatment protocol found a negative effect on topographic outcomes, with the mean change of -0.76D for the conventional protocol and a mean change of +0.72D in the accelerated group. [20]

In this study, the depth of the corneal stromal demarcation line was analyzed using a AS-OCT. The mean depth in the accelerated group was 319.56±36.50 and 363.57±46.92 ($p<0.001$) in the conventional therapy group.

Kymionis et al. analyzed corneal stromal demarcation line depth at two different illumination timings (10 versus 30 minutes) using a novel high-intensity UVA irradiation device and concluded that, the depth of the demarcation line was significantly deeper in the 30-minute (350.78 μm) CXL treatment group than the 10-minute (288.46 μm) CXL group. [21]

Various studies have reported significantly deeper corneal demarcation lines in the conventional CXL groups, [22,23] which coincide with the results of our study. It should be noted that, a greater riboflavin presoaking time may result in a deeper and greater intensity cross-linking depth. Also, the effect of CXL on stromal depth is dependent on the treatment duration (riboflavin application) and UVA light intensity.

A limitation associated with the accelerated CXL is the effect on corneal endothelium, which several studies have documented. [24–26] Results of our study were consistent with various studies including one conducted by Cing ü et al, who noticed significant changes in endothelium morphology (CV)

and density (ECD) after the accelerated treatment. Substantial endothelial cell changes were observed at week one and one month following the procedure. Corneal endothelial count was brought back to the baseline values at six months, and CV returned to the baseline values after three months. [27]

With regards to thinnest corneal thickness, we found that conventional CXL might lead to a greater reduction in thickness than the accelerated treatment. There was a significant reduction in pachymetry in conventional group at six months than the preoperative values ($P < 0.001$). It reduced from 460.42 ±39.59 µm pre-operatively to 441.45 ±47.49 µm at six months. Compared to accelerated group pachymetry value at thinnest location preoperatively was 443.16±40.78 µm at six months it was 438.28±38.44 µm with p-value at (0.113). This corresponds to the findings of Arbelaez et al and Vinciguerra et al. [12,13]

We did not encounter any complications in this study. However, several studies reported complications such as stromal haze to sight-threatening infectious keratitis and non-infectious corneal melting. Microbial keratitis after CXL occurs rarely. Herpes simplex was a documented cause of keratitis following CXL treatment.[28] Acanthamoeba[29] and several bacteria such as Escherichia coli, streptococcus species and staphylococcus. [30–32] Sterile keratitis may be another complication of CXL.[33]

CONCLUSION:

Corneal CXL with Riboflavin and UV-A irradiation stops progression of KC in all eyes with significant reduction in mean cylinder value in both groups. It is a minimal invasive technique that modifies corneal stromal structures and increases corneal stability and postpones the need of lamellar keratoplasty or PK. The use of CXL shows a significant improvement in UCVA and BCVA from the preoperative values in both groups. Pachymetry decreased six months postoperatively and showed gradual increase at the end of one year, but a significant reduction in pachymetry than preoperative values were more in conventional group. Accelerated Corneal crosslinking causes transient endothelial changes for 6 months follow- up. Stromal haze is the main complication which resolved within 4- 6 weeks. More clinical studies are needed to assess the safety, efficacy, and side effects of accelerated CXL. Studies that analyze the treatment over longer periods of time since the process of collagen turnover in the stroma may take several years.

Declarations:

Financial support and sponsorship: The authors of this manuscript declare that they did not receive any form of funding from any governmental/ private sector/ non-governmental institution.

Data availability: Data of this research is all available within the manuscript. Any additional details or information regarding this research may be provided upon request.

Ethics Declarations: This research was conducted based on the guidelines of the declaration of Helsinki. An informed consent was provided by each of the subjects prior to inclusion in the study. This study was approved by the International Eye Hospital in Cairo Egypt ethics committee.

Conflict of Interest: No conflicting relationship exists for any author. The authors state that they have no proprietary interest in the products named in this article.

Funding: None.

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