THE ROLE OF CORNEAL COLLAGEN CROSS-LINKING IN KERATOCONUS MANAGEMENT: BASED ON ONE-CENTER EXPERIENCE IN SULAIMANI CITY, KURDISTAN REGION-IRAQ

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ABSTRACT

Background

Corneal Collagen Cross-Linking has a major role in the management of keratoconus.

Objectives

Determining the effectiveness of Corneal Cross-linking, using Corneal Topography and tomography, with progressive Keratoconus.

Materials and Methods

The study conducted at Soma Eye Center, Sulaimani City, Kurdistan-Iraq, six months from September 2018 to March 2019. A total of 34 eyes of 20 patients with progressive bilateral Keratoconus. Each patient sought written informed consent, which was accompanied by corneal cross-linking with the riboflavin topical eye drops. Patients were followed up the for 6 months and corneal topography and tomography was replicated and recorded.

Results

The patients ' age was between 12 and 35 years. There were 12 females and 8 males. The change in post procedure K1 was statistically significant at the significant level of 0.05 as the p-value was 0.029. For the post procedure K2 the same can be noticed as the p value was 0.0. In addition post procedure central corneal thickness change was remarkable, the mean change in central corneal thickness was about 10.14µ, and this change was significant at the statistical level of 0.05, because the P value was 0.00. Changes in keratometry, was more significant for female than male both for K1 and K2, mean K1 change for males was 0.05 and for females was 0.2, the same result can be viewed for the post procedure change in K2, mean change for males was 0.6 while for females was 0.8. These changes were more significant in female than in male. P values were 0.01 and 0.00 respectively.

Conclusion

In patients with progressive Keratoconus within six months of follow-up it has been demonstrated that corneal cross-linking is effective for inducing regression or halting progression of disease, while the effectiveness of the corneal cross-linking has been affected by patients' gender but not by age.

Keywords: *Corneal Cross-linking; Thinnest location of cornea, K1; Fattest meridian, K2; Steepest meridian D; Diopter; Efficacy; Keratoconus.*

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INTRODUCTION

Keratoconus is a disease of the eye that affects approximately one person in 2000. The disease leads to a gradual increase in corneal curvature and reduced visual acuity, thereby decreasing quality of life. It is a younger-age disease in which progressive thinning of the cornea occurs and the cornea takes an abnormal conical shape of the curvature. This adjustment frequently results in irregular astigmatism and myopia. [1] Corneal topography Figure (I) is a higher tool in diagnosing keratoconus, since it is noninvasive and it is able to detect early stages of keratoconus that allow for prompt intervention and also assist in the monitoring of treatment progression. [2,3] Ultraviolet-A (370 nm) corneal irradiation is performed after penetration with the photosensitizer riboflavin. The standard CXL protocol recommends a minimum de- epithelized corneal thickness of 400 µ to avoid possible corneal endothelial irradiation damage. Corneal cross-linking (CXL) is the only treatment to stop or decrease Keratoconus progression.[4] It is a technique that uses Ultraviolet A (UVA) light in combination with riboflavin as a photo mediator to add additional polymer bands between collagen fibers, thereby increasing the biomechanical resistance of the cornea [5,6].

The peak K value is decreasing by average 2.47D for 55 percent and remained stable in 38 percent of treated eyes.[7]

In the past few years, CXL has been used in many corneal disorders other than keratoconus, for instance, non-healing corneal ulcer and Fuchs endothelial dystrophy. [8,9] However, there is no proof of the efficacy of the CXL in these conditions. Some authors claim its usefulness in the case of non-cure ulcer and some consider the treatment ineffective. The use of corneal topography is the ratio of some researchers to show the efficacy of CXL in progressive keratoconus at six months after the procedure [10, 11].

METHODS

This is an interventional study conducted from September 2018 to March 2019 at the Soma eye center. 34 eyes of 20 patients with progressive keratoconus who met the inclusion criteria were reported by means of unusual consecutive sampling after seeking permission from the Hospital Ethical Committee. Prior to the procedure written consent was given to all patients. Determined history and ophthalmic examination have been performed and six months after surgery corneal tomography was performed CXL had been done the final result, was tested after surgery. Fig.I. Corneal cross-linking with isotonic riboflavin was carried out under standard protocol on selected eyes.

During this study ethical consideration regulated by the ministry of Health, related to the patient's safety and rights were observed.

Procedure

All patients were undergoing corneal topography before treatment. CXL was performed as a day-care procedure under sterile conditions. After topical anesthesia a sterile, blunt spatula was used to remove the central corneal epithelium, and 30 minutes (one drop each two minutes) of riboflavin drops were instilated, then UVA radiation has been transmitted for 30 minutes at a power setting of 3mW / cm^2 (Standard Dresden Protocol). At the end, bandage contact lenses have been applied and topical moxifloxacin, and dexamethasone eye drops for 2 weeks, and an artificial tear drop for 1 month from the day the operation was carried out were prescribed to the patients. Patients were examined on day one after 2 weeks, 4 weeks, 3 months and then 6 months.

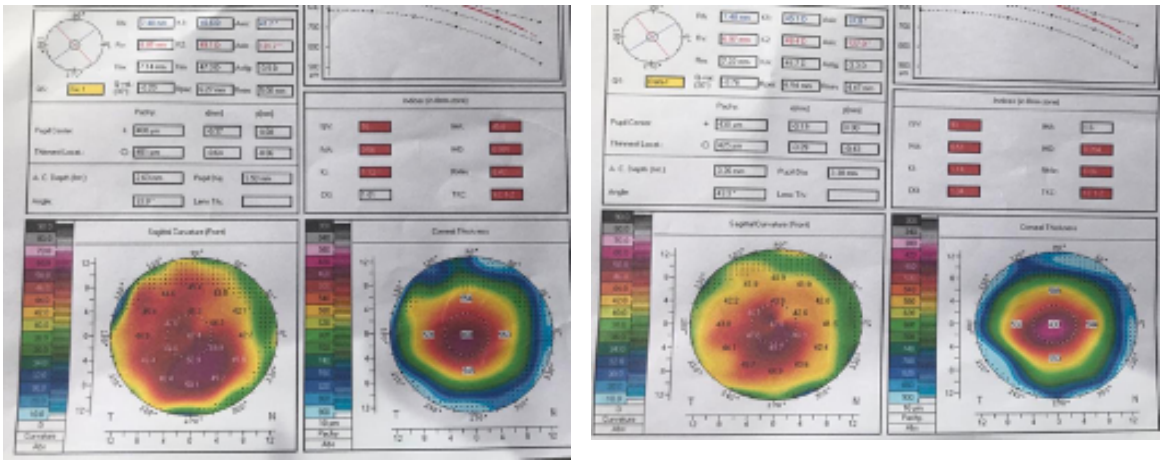


Figure 1. Corneal tomography of one of the patients before and after cross-linking.

RESULTS

Twenty patients underwent surgery with a median age of 29.5 years. There were twelve women and eight men. At the beginning of the study, the mean K 1 was 45.9 D, the mean K2 was 48.55 D, the mean thinnest corneal location at the start of the study was 468 microns. The mean K1 was 45.85D, mean K2 was 46.85 D, and the mean thinnest corneal location was 455 microns six months later. The mean K2 value was considerably lower by 1.7D and 11.7% remain stable and the thinnest corneal location was declined.

By running t-test, the change in post procedure K1 was statistically significant at the significant level of 0.05 as the p-value is 0.029. For the post procedure K2 the same can be noticed as the p value is 0.0. In addition post procedure central corneal thickness change is remarkable, the mean change in central corneal thickness is about 10.14µ, this change is significant at the statistical level of 0.05, because the P value is 0.00.

Table 3 shows the changes in keratometry, it can be seen that this change is more significant for female than male as the mean changes in K1 for males is 0.05µ and mean change for females is 0.2µ, the same result can be viewed for the post procedure change in K2, mean change in keratometry for males 0.6µ is while for females is 0.8µ. This change is more significant in female than in male. P values are 0.01 and 0.00 respectively

In analysis of the effect of age on the changes in all three parameters including K1, K2 and CCT; it can be seen that this effect is not significant. Using chi square test p values for post procedure change in K1, K2 and CCT were 03, 0.5 and 0.5 respectively.

Table 1. Paired Samples Test to analyze change in K1 and K2

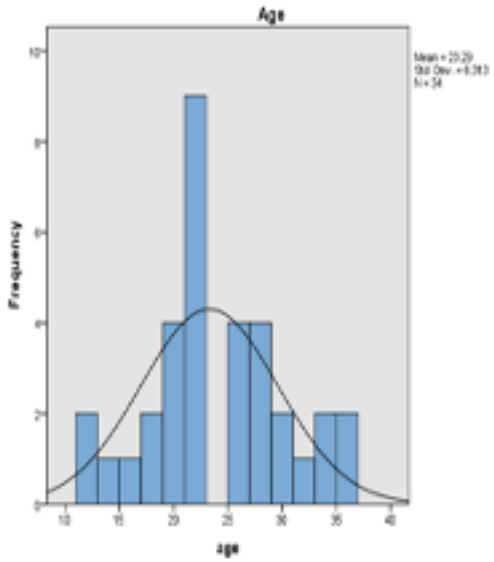
		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	preK1 - postK1	.16118	.41221	.07069	.01735	.30500	2.280	33	.029
Pair 2	prek2 - postk2	.75588	.53097	.09106	.57062	.94115	8.301	33	.000
Pair 3	Pre cct – post cct	10.14706	4.85631	.83285	8.45261	11.84151	12.184	33	.000

Table 2. Change in Keratometry and central corneal thickness.

Variables	Mean
preK1	44.5574
postK1	44.3962
prek2	47.4882
postk2	46.7324
precct	466.2647
postcct	456.1176

Table 3. The changes in keratometry.

	Sex		Paired Differences					t	df	Sig. (2-tailed)
			Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
						Lower	Upper			
Male	Pair 1	preK1 - postK1	.05867	.45346	.11708	-.19245	.30978	.501	14	.624
	Pair 2	prek2 - postk2	.67333	.64417	.16632	.31660	1.03006	4.048	14	.001
	Pair 3	precct - postcct	9.26667	4.74291	1.22462	6.64013	11.89321	7.567	14	.000
Female	Pair 1	preK1 - postK1	.24211	.36865	.08458	.06442	.41979	2.863	18	.010
	Pair 2	prek2 - postk2	.82105	.42892	.09840	.61432	1.02779	8.344	18	.000
	Pair 3	precct - postcct	10.84211	4.95831	1.13751	8.45228	13.23193	9.531	18	.000



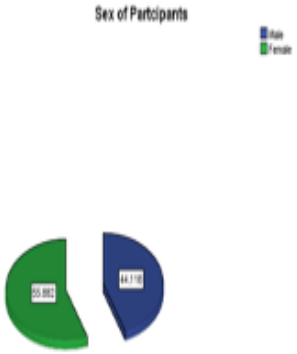


Figure 2. Age and Gender distribution of participants.

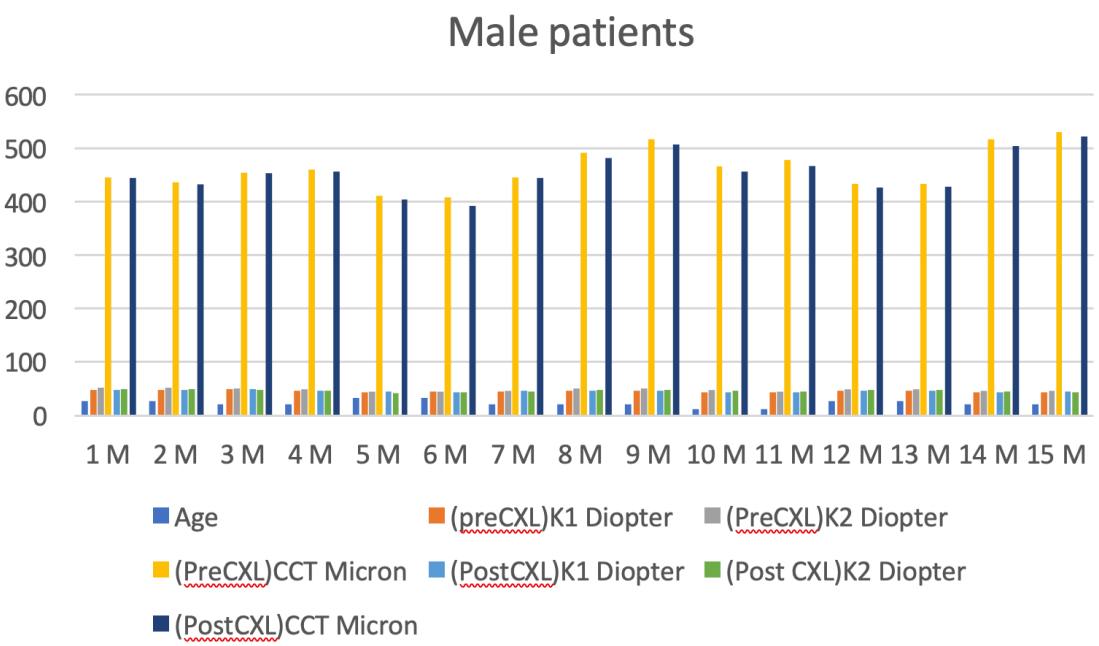
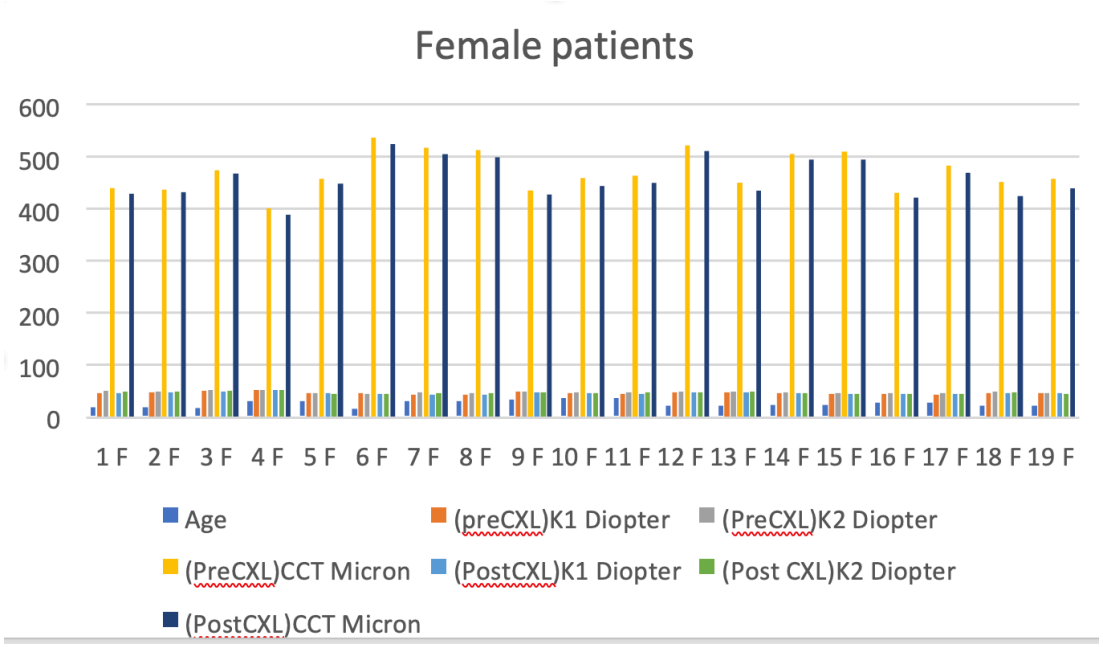


Figure 3. Details of male patients.



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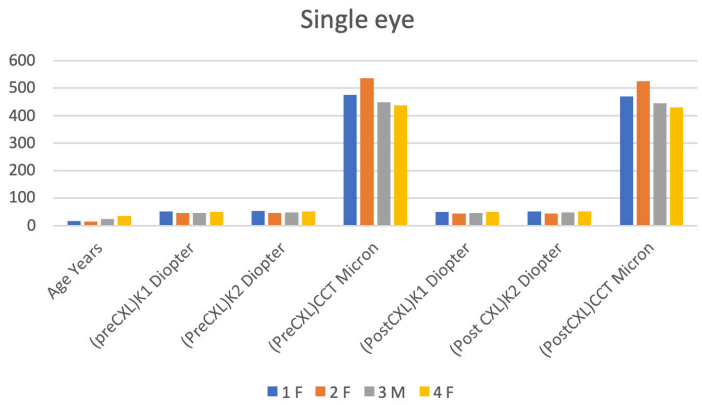

Figure 5. Details of unilateral eye.

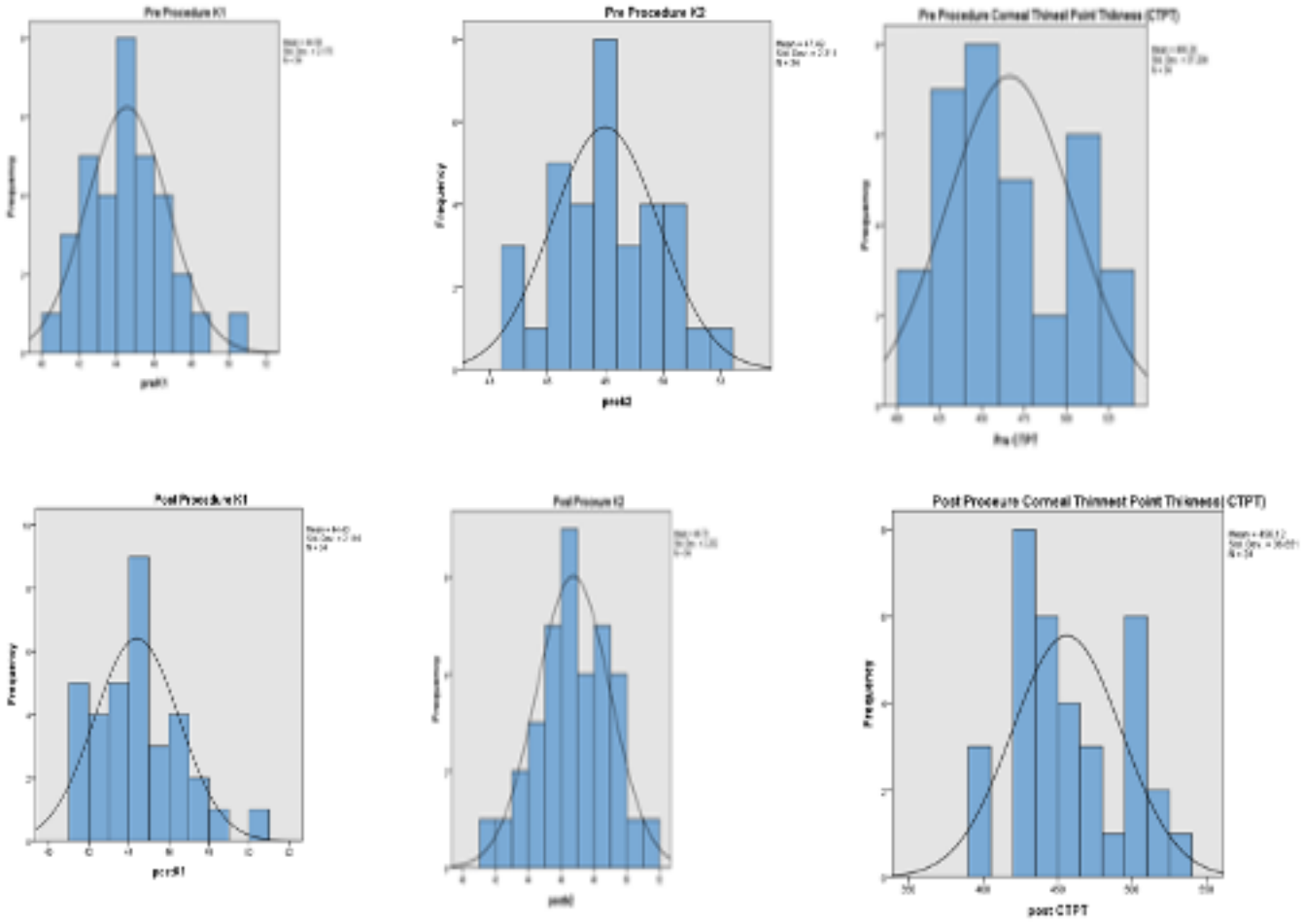

Figure 6 K1, K2, and CTPT before and after Corneal cross linking

DISCUSSION

Corneal cross-linking (CXL) is the only validated therapy to prevent or reduce Keratoconus progression [4, 8, 9], CXL is not only a less invasive but time-consuming innovative treatment which has become very common in progressive keratoconus within a few years. CXL also eliminates or even replaces the need for corneal transplants as well as other benefits in these situations.

The efficacy ranged from 40.91% in the UK11 to as high as 98% in Germany.[12]The patient was usually treated by ophthalmologist and tried to prevent the disease from worsening with successfully treated patients with advanced keratoconus[2,7.13,14]. Keratoconus in Asian descent people (mostly from northern Pakistan) in the UK have shown to be as high as 1 in 4000 per annum compared with 1 in 30 000 per annum in the local white Caucasus people. The results of these data suggest that ethnic backgrounds have a significant impact in the incidence and severity of a keratoconus since Asians are present at a significantly younger age than Caucasian subjects, and appear to also suffer from a worse form of ectatic diseases [14, 15]. However all of the cases included in this study had the same ethnic background, as a result the effect of ethnicity can't be rollout but sex of the patients had effect on keratometry reading. In addition age of the patients have not any effect on the outcome of cross-linking procedure.

This result is comparable to previous studies, in research published by UK researchers) concluded that Age ≥35 years had no effect on the changes of BCVA (−0.02 (95% CI −0.13 to 0.09); P=0.757) or K_{max} (0.58 (95%CI −0.51 to 1.68); P=0.294) as compared with younger patients. [16]

However in the current study sex has relation to the outcome of corneal cross linking, but there are studies contradicts this outcome. In a study of 96 patients who had unilateral CXL treatment for progressive keratoconus, Gender, preoperative maximum K, and baseline topographic cone location did not show significant effect on postoperative visual acuity and maximum keratometry (P>0.05). [17] In the research for other studies supporting that the sex of the patient has effect on the outcome, no literatures could be found to assess the effect of sex on cross linking outcome specifically. Studies with larger sample size or meta-analysis of the data from available literature may help to overcome inherent limitations such repeatability of the results to offer more reliable data.

In addition, the short-term follow-up to this analysis is the downside. In this report, the following risks were also not addressed, such as secondary infections, temporary corneal haze, permanent bruises, endothelial injuries, sterile infiltration and herpes reactivation. Tests with a larger populations and long term follow-up are suggested in order to confirm the efficacy and protection of CXL in the management of progressive keratoconus.

In conclusion, corneal Cross Linking was found to be effective in inducing regression or halting progression of Keratoconus after six months of follow-up, while efficacy of corneal cross-linking was been affected by patients gender but not by age.

Consent and ethics

Written informed consent was obtained from the parents/guardian of our patient for publication of this research and any accompanying images. A copy of the written consent is available for review. Sulaimani university ethical approval board gave us the ethical approval for this research

Competing interests

The author declares that she has no competing interests.

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