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Visual Outcome and Corneal Aberrations in Keratoconic Patients Underwent Corneal Collagen Cross Linking

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Abstract

Aim: to evaluate visual outcome and corneal aberrations in keratoconic patients underwent corneal collagen cross-linking using the Sirius Scheimpflug analyzer.
Methods: This was descriptive, cohort and retrospective hospital based study, it was conducted at Alzarga Eye Center, Khartoum, Sudan. Data was collected from the records of cornea's clinic. The study was included 54 keratoconic eyes of 40 patients underwent corneal collagen cross linking (CXL) 14 of them in both eyes. All patients operated by one surgeon in period from December 2016 to October 2018. The eyes were saturated with riboflavin solution and were subjected for 30 minutes to ultraviolet -A (UV-A) light with irradiance of 3mW/cm2. Effectiveness of the CXL was assessed by measuring uncorrected visual acuity, manifest refraction, corneal astigmatism, corneal curvature, central corneal thickness, and corneal aberrations by the Sirius Scheimpflug analyzer. All measurements were taken prior to the CXL and 3, 6 and 12 months after CXL. Data obtained were statistically analyzed and compared using statistical package for social science (SPSS-20) and refractive error analyzed by astigmatic decomposition methods.
Results: the mean age was 20.05±4.77years (ranged: 13 – 34 years). There was a significant increase in uncorrected visual acuity (0.15±**0**.19) preoperatively to (0.24±0.27), (0.30±0.24) and (0.45±0.35) after 3, 6, and 12 months respectively (P<0.001). Mean of spherical refractive error was -12.44±5.31 Diopter (D) preoperatively and -11.07±5.39D, -8.63±5.45D and -8.46±4.52 after 3, 6, and 12 months respectively of CXL (P<0.001). The study revealed that CXL significantly decreased ocular astigmatism (P<0.001). It was -7.92±3.73D preoperatively and -6.87±3.41, -5.07±3.76 and -6.01±3.97 after 3, 6, and 12 months respectively. The corneal curvature flattened and decreased significantly by an average of 1.35D, 1.93D and 2.02D after 3, 6 and 12 month respectively (p< 0.001). The central corneal thickness significantly decreased after CXL (p< 0.001) by an average of 16. 5 μm, 26.83 μm and 46. 83μm3, 6 and 12 month respectively. Anterior corneal aberration pre CXL was decreased from 0.25±0.20µm/mm^2 to 0.24±0.17 µm/mm^2, .22±.15 µm/mm^2 and 0.21±0.11 µm/mm^2 after 3, 6 and 12 months respectively of CXL. Posterior corneal aberration pre CXL was increased from 0.62±0.66 µm/mm^2 to 0.65±0.70 µm/mm^2, 0.70±2.81 µm/mm^2 and 0.85±1.35 µm/mm^2 after 3, 6 and 12 months respectively of CXL. Corneal astigmatism decreased from -4.54±2.96D preoperatively to -4.09±3.01D, -4.41±2.61D and -4.51±3.12D after 3, 6, and 12 months respectively.
Conclusion: Corneal collagen cross linking is effective to arrest progression of keratoconus. It increased visual acuity, flattening of corneal curvature, and decreased spherical and astigmatic errors. It also reduced corneal astigmatism, corneal aberrations and keratoconus symmetry index front.
Keywords: Collagen Cross linking, corneal aberrations, Sirius Scheimpflug Analyzer, corneal flattening. Keratoconus.

Introduction

Keratoconus is a non-inflammatory process that results in thinning and deformation of the cornea [1] The cornea progressively distorts and losses its optical properties which result in visual impairment from irregular astigmatism, an increase in corneal aberrations, or stromal scarring [2]

Corneal collagen cross-linking (CXL) is a relatively new non-invasive treatment that can stop keratoconus getting worse. It is only suitable for patients where the corneal shape is continuing to deteriorate and where there is adequate corneal thickness.[3] The procedure involves the application of a photosensitive solution consisting of riboflavin (Vitamin B_2) to the cornea which is activated by illumination with ultraviolet light for approximately 4 minutes.[4] The riboflavin reacts with the ultraviolet light with wavelength 370 mm to create new collagen bonds (cross-links) throughout the cornea, which recovers and preserves some of the cornea's mechanical strength. If the procedure is performed early enough it can postpone the need for corneal grafting and prevent vision from getting worse. The procedure may be an

advantage to individuals who are unable to wear contact lenses [5]

Methods

This was descriptive, cohort and retrospective hospital based study, was conducted at Alzarga Eye Center, Khartoum Sudan, from records of cornea's clinics. The Study included 54 keratoconic eyes of 40 patients underwent corneal collagen cross linking (CXL) 14of them did CXL in both eyes and 26 in one eye in period from December 2016 to October 2018. All patients operated by one surgeon, all patients should have Keratoconus either in one or both eyes underwent CXL, their ages ranged between 15- 35 years, both gender were included. Patients with any ocular disease other than keratoconus and who have missing data at the record excluded. Data collected from records was included demographic data (age, gender), visual acuity, objective refraction and corneal topography using a rotating Scheimpflug Camera (Sirius). All data obtained from the patient's records pre and post three, Six and 12 month of CXL. Statistical analysis was carried using statistical package for social science (SPSS 20) and refractive error analyzed by astigmatic decomposition methods.

Results

The study included 40 keratoconic patients (54 eyes) 57.5% (23) males and 42.5 %(17) females, their age range between13 – 34years (table 1). Assessment of visual acuity revealed the mean of UCVA pre CXL was (0.15±0.19), after three months was (0.24±0.27), after six months was (0.30±0.24) and after twelve months was (0.45±0.35) (table 2). Assessment of manifest refraction, corneal astigmatism, corneal curvature, central corneal thickness, and corneal aberrations hows in tables from (3 to 12).

Table (1): shows the distribution of subjects according to age. Subjects less than 15 years are young children and above are young adult.

Age	Frequency	Percent
10 – 15	6	10%
15 – 20	16	30%
20 – 25	25	45%
25 – 30	2	2.5%
30 – 35	5	12.5%
Total	54	100%
Mean ± SD	20.05±4.77	
Range	13 - 34	

Table (2) shows the distribution of visual acuities in eyes pre and post CXL surgery

	Pre surgery		After 3 month		After 6 month		After 12 month	
	Frequency	Percent	Frequency	Percent	Frequency	Percent	Frequency	Percent
0.017 - 0.083	35	64.8%	27	50%	13	24.1%	3	5.6%
0.1 - 0.25	7	13%	10	18.5%	23	42.6%	21	38.9%
0.33 -0 .5	8	14.8%	7	13%	7	13%	10	18.5%
0.67 – 1	4	7.4%	10	18.5%	11	12.3%	20	37%
Total	54	100%	54	100%	54	100%	54	100%
Mean ± SD	0.15±0.19		0.24±0.27		0.30±0.24		0.45±0.35	

Subjects of (0.67 – 1) had normal visual acuity, (0.33 - 0.5) had mild vision defect, (0.1 - 0.25) had moderate visual defect and (0.017 - 0.083) had severe visual defect. Paired sample T. test revealed significant difference (P value < 0.001) between visual acuity pre and post 3, 6 and 12months of CXL.

Table (3): shows the distribution of spherical refractive error in eyes pre and post CXL surgery.

	Pre-surgery		**After 3 month**		**After 6 month**		**After 12 month**	
Sphere	Frequency	Percent	Frequency	Percent	Frequency	Percent	Frequency	Percent
0-5	2	3.7%	7	13%	16	29.6%	12	22.2%
5-10	18	33.3%	18	33.3%	24	44.4%	25	46.3%
10-15	17	31.5%	16	29.6%	5	9.3%	12	22.2%
15-20	11	20.4%	9	16.7%	5	9.3%	2	3.7%
20-25	6	11.1%	4	7.4%	4	7.4%	3	5.6%
Total	54	100%	54	100%	54	100%	54	100%
Mean± SD	-12.44±5.31		-11.07±5.39		-8.63±5.45		-8.46±4.52	

Paired sample T. test revealed significant difference (P value < 0.001) between spherical error pre and post 3, 6 and 12months of CXL.

Table (4) shows the distribution of ocular astigmatism in eyes pre and post CXL surgery.

	Pre surgery		**After 3 month**		**After 6 month**		**After 12 month**	
Cyl	**Frequency**	**Percent**	**Frequency**	**Percent**	**Frequency**	**Percent**	**Frequency**	**Percent**
0 – 5	10	18.5%	17	31.5%	32	59.2%	19	35.2%
5 – 10	27	50%	24	44.4%	19	35.2%	28	51.9%
10 – 15	12	22.2%	11	20.4%	1	1.9%	4	7.4%
15 – 20	5	9.3%	2	3.7%	2	3.7%	3	5.5%
Total	54	100%	54	100%	54	100%	54	100%
Means	7.92±3.73		6.87±3.41		5.07±3.76		6.01±3.97	

Paired sample T. test revealed significant difference (P value < 0.001) between cylindrical error pre and post 3, 6 and 12months of CXL.

Table (5): shows the distribution of corneal astigmatism in eyes pre and post CXL surgery.

	Pre surgery		**After 3 month**		**After 6 month**		**After 12 month**	
Cyl	**Frequency**	**Percent**	**Frequency**	**Percent**	**Frequency**	**Percent**	**Frequency**	**Percent**
0 – 5	37	68.5%	34	73.9%	31	67.4%	36	67.9%
5 – 10	14	25.9%	8	17.4%	13	28.3%	14	26.4%
10 – 15	3	5.6%	4	8.7%	2	4.3%	3	5.7%
Total	54	100%	46	100%	46	100%	53	100%
Mean±SD	-4.54±2.96D		-4.09±3.01D		-4.41±2.61D		-4.51±3.12D	

Paired sample T. test revealed significant difference (P value < 0.001) between spherical error pre and post 3, 6 and 12months of CXL.

Table (6): shows the means of Ocular astigmatism decomposition in eyes pre and post CXL surgery.

	Pre CXL	**Post 3 months of CXL**	**Post 6 months of CXL**	**Post 12 months of CXL**
MRE	-8.48	-7.67	-6.10	-5.46
CYL	-7.92	-6.87	-5.07	-6.00
C0	0.76	0.69	0.64	0.47
C45	-1.54	-1.28	-2.13	-1.10
Sph	-12.44	-11.07	-8.63	-8.46
Ax	180	179	179	178

Table (7): shows the distribution of corneal curvature in eyes pre and post CXL surgery.

	Pre surgery		**After 3 month**		**After 6 month**		**After 12 month**	
	Frequency	**Percent**	**Frequency**	**Percent**	**Frequency**	**Percent**	**Frequency**	**Percent**
42 – 44	8	14.8%	13	28.3%	14	30.4%	15	28.3%
45 – 50	25	46.3%	22	47.8%	23	50%	29	54.7%
More than 50	21	38.9%	11	23.9%	9	19.6%	9	17%
Total	54	100%	46	100%	46	100%	53	100%
Mean±SD	49.54± 4.59		48.19±4.59		47.61±3.45		47.52±3.64	

Less than 42 (flat), 42– 44 (normal**)**, 45–50 (mild steeping**)** and more than 50 (severe steeping)

Table (8): shows the distribution of anterior corneal curvature in eyes pre and post CXL surgery

	Pre surgery		**After 3 month**		**After 6 month**		**After 12 month**	
	Frequency	**Percent**	**Frequency**	**Percent**	**Frequency**	**Percent**	**Frequency**	**Percent**
42 – 44	5	9.3%	8	18.6%	7	15.2%	8	15.1%
45 – 50	19	35.2%	17	39.5%	21	45.7%	26	49.1%
More than 50	30	55.5%	18	41.9%	18	39.1%	19	35.8%
Total	54	100%	43	100%	46	100%	53	100%
Mean±SD	52.44± 4.59		50.51±5.80		49.65±4.58		49.25±4.74	

Table (9): shows the distribution of posterior corneal curvature in eyes pre and post CXL surgery.

	Pre surgery		**After 3 month**		**After 6 month**		**After 12 month**	
	Frequency	**Percent**	**Frequency**	**Percent**	**Frequency**	**Percent**	**Frequency**	**Percent**
4 – 8	30	55.6%	23	53.5%	24	52.2%	26	49.1%
8 – 12	24	44.4%	20	46.5%	22	47.8%	27	50.9%
Total	54	100%	43	100%	46	100%	53	100%
Mean±SD	-7.87± 1.10		-7.81±1.16		-7.91±1.11		-8.04±1.14	

Table (10): shows the distribution of central corneal thickness in eyes pre and post CXL surgery.

	Pre surgery		**After 3 month**		**After 6 month**		**After 12 month**	
	Frequency	**Percent**	**Frequency**	**Percent**	**Frequency**	**Percent**	**Frequency**	**Percent**
Less than 480	48	88.9%	39	90.7%	43	93.5%	49	92.5%
480 – 550	6	11.1%	4	9.3%	3	6.5%	4	7.5%
More than 550	0	0.00%	0	0.00%	0	0.00%	0	0.00%
Total	54	100%	43	100%	46	100%	53	100%
Mean±SD	439.52±36.13		423.02±58.59		412.69±62.26		392.69±71.02	

Less than 480 thin cornea, 480 – 550 normal thickness and more than 550 thick cornea.

Table (11): shows the distribution of anterior corneal aberrations in eyes pre and post CXL surgery.

	Pre surgery		**After 3 month**		**After 6 month**		**After 12 month**	
	Frequency	**Percent**	**Frequency**	**Percent**	**Frequency**	**Percent**	**Frequency**	**Percent**
Less than 0.3	36	66.7%	31	72.1%	37	80.4%	43	81.1%
More than 0.3	18	33.3%	12	27.9%	9	19.6%	10	18.9%
Total	54	100%	43	100%	46	100%	53	100%
Mean±SD	.25±.20		.24±.17		.22±.15		.21±.11	

Less than 0.3 (normal corneal aberration) and more than 0.3(abnormal higher corneal aberration)

Table (12) shows the distribution of posterior corneal aberrations in eyes pre and post CXL surgery.

	Pre surgery		**After 3 month**		**After 6 month**		**After 12 month**	
	Frequency	Percent	Frequency	Percent	Frequency	Percent	Frequency	Percent
Less than 0.3	13	24.1%	7	16.3%	8	17.4%	4	7.5%
More than 0.3	41	75.9%	36	83.7%	38	82.6%	49	92.5%
Total	54	100%	43	100%	46	100%	53	100%
Mean±SD	.62.± .66		.65±.70		.70±2.81		.85±1.35	

Discussion

The study showed that most of the patients were young adults 48(88.9%) their ages less than 15years, only 11.1% are young children underwent to CXL, this indicated that CXL can be performed earlier (table1). The distribution of male is greater than female, 57.5% (23) males and 42.5 %(17) females, this indicated that the attendance of males more than females at that period.

Regarding the visual acuity before CXL, more than half 64.8% of eyes had severe vision defect, only 7.41% had normal visual acuity. After three months of CXL approximately half of study population 50% had still severe vision defect but the percentage of eyes reached to normal vision increase to 18.5%. After six month of CXL the percentage of eyes with normal visual acuity increased to 20.4% After 12 months of CXL about

37.04% had normal visual acuity and only 5.6% had severe defect of vision (table2).The VA improved significantly from 0.15 pre CXL to 0.24, 0.30 and 0.44 post 3, 6 and 12 month of CXL respectively with ($p<0.001$), these results indicated that the CXL was more effective after one year as reported by Victor Penner and others. The manifest spherical refraction became less myopic by an average of (- 1.37D, -3.81D, and -3.98D) after 3, 6 and 12 month respectively, with significant difference between them $p< 0.001$(table 3).this may be due to changes of collagen bonds of stroma after CXL. Considering astigmatic error the study revealed that the CXL significantly decreased ocular astigmatism (sig = 0.00) by an average of (-1.05D, -2.85D, and -1.91D) after 3, 6 and 12 month respectively (table 4). This result agrees with Victor Penner and others they reported that the average spherical component decreased from −1.87 to −1.40 D (0.47 ± 2.12, p = 0.4). While cylinder decreased from 2.18 to 0.87 D (1.31 ± 1.14 D, $p < 0.001$). Pre CXL about 38.9% of eyes had severe corneal steepening of more than 50 diopters, only 14.8% had normal corneal curvature indicated that they were suspected of keratoconus. After three month the percentage of eyes had normal corneal curvature increased to 28.3% and after six month increased to 30.4% this because the surface of the cornea is still not stable but after one year the percentage increased to 28.3% and only 17% of eyes had severe corneal steepening (table 5). The corneal curvature flattened by an average of (1.35D, 1.93D and 2.02D) after 3, 6 and 12 month respectively of CXL and decreased significantly with $p < 0.00$. Pre CXL most of eyes 88.9% had thin cornea due to keratoconus. Only 11.1% had normal central corneal thickness, this percentage approximately equal to that found in eyes with normal corneal curvature that are suspected for keratoconus. After three month the percentage of corneal thinning increased to 90.7% and 93.5% after six months and increased to 95% after one a year. The central corneal thickness significantly decreased after CXL (sig < 0.001) by an average of 16.5 µm, 26.83 µm and 46.83µm 3, 6 and 12 month respectively after CXL (table 6). This indicated that the CXL increase the bonds between collagen fibers and lead to decrease its size. This result disagrees with Mohammad Mehdi Sadoughi and et al that reported during the follow up period, no significant difference was observed in pachymetric and elevation data postoperatively. More than half of study populations had normal anterior corneal aberration pre and post CXL. pre CXL 33.3% of eyes had abnormal higher corneal aberration and this percentage decreased to 27.9% , 19.6% and 18.9% after 3, 6 and 12 months respectively of CXL. CXL slightly increased in average of anterior corneal aberration (table11).There is a significant increase in aberration post CXL sig < 0.001).this result agrees with Victor Penner and others they reported that the aberration decreased from 0.33 to 0.29 (0.04 ± 0.17, p = 0.7). More than half of study populations had abnormal higher posterior corneal aberration pre and post CXL. pre CXL 75.9% of eyes had abnormal higher aberration and this percentage increased to 83.7% , 82.6% and 92.5% after 3, 6 and 12 months respectively of CXL.

Conclusion

CXL can be done for children. It improved visual acuity and decreased myopia by increasing flattening of the cornea. It decreased ocular astigmatism, central corneal thickness and corneal astigmatism after one year. In addition, it decreased anterior corneal aberration and increase posterior corneal aberration. CXL decreased keratoconus symmetry index in front surface and increased keratoconus symmetry index in back surface.CXL was indicated for all stages of keratoconus. CXL was prophylactic treatment of patients suspected for keratoconus.

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