The Egyptian Journal of Hospital Medicine (July 2018) Vol. 72 (3), Page 4100-4103

Assessment of Corneal Higher Order Aberrations Before and After Corneal Collagen Cross-Linking in Patients with Keratoconus

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ABSTRACT

Purpose: This study aimed at assessing the shortterm effect of corneal collagen crosslinking on higher order aberrations of cornea in patients with keratoconus using corneal topography.

Patients and Methods: The study was a prospective cohort study that was conducted in a private specialized eye hospital on 40 eyes of 28 keratoconus patients. Each patient was fully assessed preoperatively including doing corneal topography using Pentacam® HR. Transepithelial accelerated CXL was done to all patients. Postoperative corneal topography was done at six months and data was retrieved and analyzed.

Results: RMS HOA recorded a higher mean value preoperatively, with a high statistically significant difference (p=0.00). All elements of HOAs showed lower postoperative values except for trefoil 30º. The difference was statistically significant in comma 0º, comma 90º, spherical aberrations and fifth order comma 90° (p=0.026, p= 0.003, p=0.005, and p=0.001 respectively).

Conclusion: Transepithelial corneal collagen cross-linking improves corneal higher order aberrations. The maximum effect of the procedure is on comma 0º, comma 90º, spherical aberrations and fifth order comma 90° elements.

Key words: Keratoconus, Corneal collagen cross-linking, Higher order aberrations.

INTRODUCTION

The cornea represents a transparent avascular connective tissue that has a primary infection and structural barrier function. With the overlying tear film, it forms the anterior refractive surface of the eye optical system [(1)].

The cornea exhibits elastic and viscous properties, which give it the quality of hysteresis. Elasticity refers to the ability of a substance to deform reversibly under stress. Viscous materials, on the other hand, flow when an external shear force is applied and do not regain their original shape when the force is removed. Viscoelastic materials exhibit characteristics of both viscosity and elasticity, resulting in energy dissipation when stress is applied. The energy lost in this dissipation process is called hysteresis [(2)].

Any disruption of the corneal fiber network can result in decreased structural integrity of the cornea, leading to decreased vision. One of the diseases that exhibit these pathological changes is keratoconus.

Keratoconus is a progressive ectatic disorder. It is usually a bilateral, asymmetric, non-inflammatory degeneration which results in central and paracentral thinning. The degeneration occurs at the level of the chemical composition of the material of corneal stroma, leading to increased strain, and redistribution of stress [(3)].

One of the important modalities in keratoconus treatment that is gaining more and more importance is corneal collagen cross-linking (CXL). It is proposed that it slows, stops or even to a limited extent reverses the pathology underlying keratoconus [(4)].

METHODOLOGY

The study was conducted on 40 eyes of 28 patients. The study was done in accordance with the ethical standards of the institutional review board of the faculty of Medicine, Ain Shams University.

Inclusion criteria: Axial topography consistent with keratoconus according to Rabinowitz criteria. Pachymetry more than 400 microns. BSCVA 6/24 or better. Absence of apical corneal scarring. Absence of systemic collagen diseases.

Exclusion criteria: History of corneal surgery. Chemical injury.

Preoperative assessment: Full history was taken with stress on the points related to inclusion and exclusion criteria. This was followed by performing full ophthalmological examination including UCVA, BSCVA, slit lamp biomicroscopy and fundus examination. Preoperative (base-line) corneal topography was done using Pentacam® HR (OCULUS Optikgeräte GmbH) machine.

Corneal collagen cross linking: Epithelium on accelerated technique was used. Topical anesthesia was administered followed by draping. ParaCel™ was applied every 1.5 minutes for four times followed by Vibex Xtra™ drops every 1.5 minutes for four times. Corneal stromal absorption was verified by slit lamp examination. Exposure to UVA by the Avedro's KXL® system (Avedro Inc.) 7.2 joules pulsed (1second on,1 second off) for 5 minutes and 20 second, achieving total delivery of 120 mWatt.

Received:2/5/2018
Accepted:11/5/2018

Postoperative assessment: First day follow–up was done. Performance of full ophthalmological examination, UCVA and BSCVA were done at 2 weeks, 3 months and 6 months. Follow-up corneal topography was performed at the 6-months follow-up visit.

Data collection and analysis: Data from 4 map refractive analysis and Zernike analysis were retrieved from preoperative and 6-months follow-up corneal topographies for all patients. Statistical analysis was then performed using a commercially available software program (SPSS 18; SPSS, Chicago, IL, USA). Values were presented as mean and standard deviation (SD). Data were explored for normality using Kolmogorov-Smirnov test of normality. The results of Kolmogorov-Smirnov test indicated that most of the data were normally distributed (parametric data), so paired (dependent) t test was used to compare pre and post values.

RESULTS

The study included 40 eyes of 28 patients [19 eyes for females (47.5%), 21 eyes for males (52.5%)]. Age ranged from 12 to 38 years, with a mean age of 27.05±5.98. Fifty per cent of the treated eyes were right and the rest were left eyes. All patients completed their six months follow-up period.

RMS HOA recorded a higher mean value preoperatively, with a very high statistically significant difference (p=0.00). Table 1 and figure 1 show the values.

Table (1): RMS HOA Pre and postoperative values (paired t test).

		Mean	Std. Dev	Std. Error Mean	t	P
RMS HOA	Pre	3.89	2.49	0.39	4.185	.000*
	Post	3.45	2.33	0.37		

Significance level P<0.05, *=significant, #=insignificant.

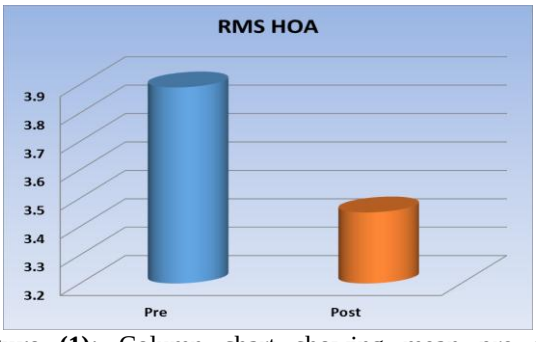

Figure (1): Column chart showing mean pre and postoperative values of RMS HOA.

Regarding trefoil 0º, comma 0º and comma 90º, higher values were recorded preoperatively. Paired t test revealed that the difference between pre- and postoperative mean values was insignificant in trefoil 0º (p=0.373), but was statistically significant in comma 0º and comma 90º (p=0.026, 0.003 respectively). However, trefoil 30º recorded a higher value postoperatively, with no significant difference between the pre- and postoperative mean values (p=0.466).

Spherical aberrations recorded a higher mean value preoperatively, with a statistically significant difference (p=0.005).

Regarding fifth order trefoil 0º, fifth order trefoil 30º, fifth order comma 0º and fifth order comma 90º, higher values were recorded preoperatively. Paired t test revealed that the difference between pre- and postoperative mean values was insignificant in fifth order trefoil 0º, fifth order trefoil 30º and fifth order comma 0º (p=0.331; p=0.055; p=0.149), but was statistically significant in fifth order comma 90º (p=0.001).

Comparison of HOA anterior pre- and postoperative values is presented numerically in table 2 and graphically in figures 2-4.

Table (2): Comparison of HOA anterior pre- and postoperative values (paired t test)

		Mean	Std. Dev.	Std. Error Mean	t	P
Trefoil 0˚	Pre	0.252	0.245	0.039	.902	.373#
	Post	0.219	0.178	0.028		
Trefoil 30˚	Pre	0.288	0.184	0.029	-.735	.466#
	Post	0.313	0.206	0.033		
Comma 0˚	Pre	0.616	0.552	0.087	2.318	.026*
	Post	0.486	0.398	0.063		
Comma 90˚	Pre	2.037	1.175	0.186	3.170	.003*
	Post	1.701	0.895	0.142		
Spherical aberrations	Pre	0.533	0.633	0.100	2.960	.005*
	Post	0.386	0.488	0.077		
Fifth order trefoil 0˚	Pre	0.044	0.051	0.008	.984	.331#
	Post	0.037	0.026	0.004		
Fifth order trefoil 30˚	Pre	0.081	0.075	0.012	1.980	.055#
	Post	0.053	0.058	0.009		
Fifth order comma 0˚	Pre	0.123	0.118	0.019	1.473	.149#
	Post	0.098	0.076	0.012		
Fifth order comma 90˚	Pre	0.375	0.302	0.048	3.517	.001*
	Post	0.296	0.201	0.032		

Significance level P<0.05, *=significant, #=insignificant

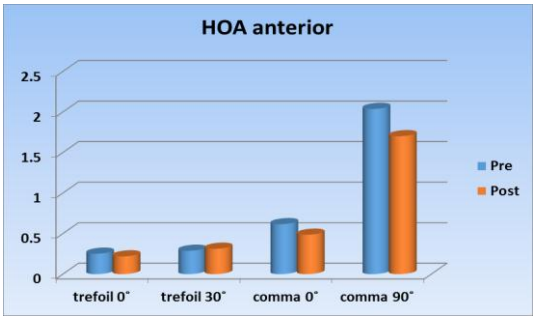

Figure (2): Column chart showing mean pre- and postoperative values of trefoil 0º, trefoil 30º, comma 0º and comma 90º.

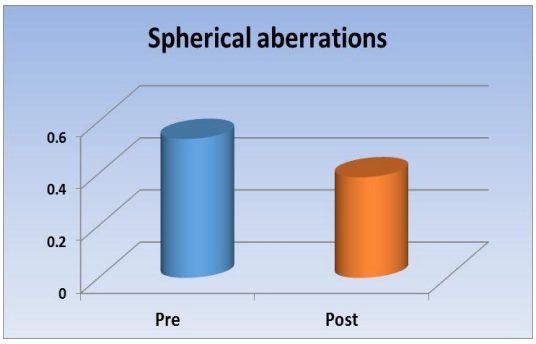

Figure (3): Column chart showing mean pre- and postoperative values of spherical aberrations.

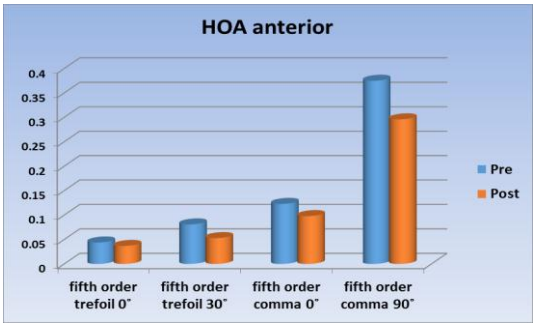

Figure (4): Column chart showing mean pre- and postoperative values of fifth order trefoil 0º, fifth order trefoil 30º, fifth order comma 0º and fifth order comma 90º.

DISCUSSION

Corneal collagen cross-linking that was originally introduced to slow down or ideally prevent further progression of keratoconus has shown to be efficient in improvement of clinical, topographical, and aberrometric indices [(5)]. One of the optical sequelae of keratoconus is increased higher order aberrations that results in vision deterioration and visual dysfunction [(6)].

Naderan et al., in their study compared 80 eyes with keratoconus and 91 normal eyes found that all aberrometric parameters were significantly higher in the keratoconus group (P< 0.001) [(7)].

In our study we aimed at assessing the effect of epithelium-on (transepithelial) accelerated CXL technique on corneal higher order aberrations. With the exception of transient hyperemia, foreign body sensation, and photophobia during the first few hours and days after treatment, there were no complications associated with the transepithelial CXL treatment over the 6-month follow-up. None of the patients showed either a complication or deterioration that required further intervention during the follow-up period.

There are many studies about the effect of epithelium off CXL technique on HOAs, but the reports on epi-on technique are very scarce.

Our study showed a highly statistical significant improvement in total corneal HOAs. This was demonstrated by the improvement occurred with RMS HOAs (P=0.00). Thirty eight out of the forty eyes included in the study showed this improvement after the 6-month follow-up period. The 2 eyes that suffered deterioration in RMS HOAs also showed evidence of deterioration regarding other topographic indices indicating failure of the CXL. These findings are consistent with the results of previous studies.

There are few reports regarding the effect of transepithelial or epithelium-on (epi-on) CXL technique on corneal HOAs. The results of most of those reports are consistent with ours.

Filippello et al., in their study which enrolled 20 patients with bilateral keratoconus, treated the worse eye with epi-on technique and left the other untreated as control. They reviewed the patients at 6, 12 and 18 months. The corneal RMS HOA improved significantly postoperatively; the reductions were greatest at 6 months and continued to improve throughout the 18-month follow-up (P<0.05). In contrast, it showed a trend towards worsening in control eyes throughout the follow-up [(8)].

In a study conducted by ***Caporossi et al.***, who performed epi-on technique on 26 eyes, there was an initial improvement in corneal HOAs over the first 3 to 6 months. At 24 months follow-up, there was an insignificant change in HOAs. This might be attributed to the fact that most of their patients showed worsening in the other corneal parameters and progression of keratoconus to the extent that 50% of the eyes needed to be re-treated using epi-off technique. This might indicate failure of the procedure or poor technique [(9)].

Our study compared the pre- and postoperative values of the following elements of

HOAs: trefoil 0°, trefoil 30°, comma 0°, comma 90°, spherical aberrations, fifth order trefoil 0°, fifth order trefoil 30°, fifth order comma 0° and fifth order comma 90°. These subtypes were chosen because it was reported that they are the most affected by keratoconus [10].

All elements showed lower post-operative values except for trefoil 30º, which had higher postoperative value but with no statistically significant difference (p=0.466). Paired t test revealed that the difference between pre- and postoperative mean values was insignificant in trefoil 0º, fifth order trefoil 0º, fifth order trefoil 30º and fifth order comma 0º (p=0.373, p=0.331, p=0.055 and p=0.149 respectively). The difference was statistically significant in comma 0º, comma 90º, spherical aberrations and fifth order comma 90° (p=0.026, p= 0.003, p=0.005, and p=0.001 respectively). Most of these findings are consistent with the other similar studies.

Filippello et al., in their study found that coma and spherical aberration values decreased significantly. The reductions were greatest at 6 months and continued to improve throughout the 18-month follow-up. In contrast, the aberrations showed a trend toward worsening in control eyes throughout the follow-up. They didn't comment on other subtypes of HOA [8].

In the study conducted by ***Caporossi et al.***, comma aberrations showed no statistically significant change. Spherical aberrations increased at 24 months [9].

Greenstein et al. found that there is a statistically significant improvement in comma 0º, comma 90º, spherical aberrations and total comma (summation of third order and fifth order comma). The trefoil improvement was statistically insignificant [11].

CONCLUSION

Transepithelial corneal collagen cross-linking improves corneal higher order aberrations. The maximum effect of the procedure is on comma 0º, comma 90º, spherical aberrations and fifth order comma 90° elements.

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