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Objective and Subjective Outcome of Corneal Collagen Crosslinking in Keratoconic Patients According to Keratoconus Grading

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Abstract

Background: Keratoconus is a progressive bilateral disease characterized by corneal thinning. Cross linking is one of the most effective treatments of keratoconus and here we studied its objective and subjective effects.

Aim of Study: This study aims to investigate differences in objective and subjective outcome of collagen corneal crosslinking of different keratoconus grades.

Patient and Method: Twenty-four eyes of twenty-four patients with keratoconus were enrolled in this prospective study arranged into 2 groups according to k reading (Group I: Less than 48, Group II: 48-52); 12 eyes of patients in each group all the eyes underwent full ophthalmological clinical evaluation (Best Spectacle Corrected Visual Acuity (BSCVA) by log MAR and wave light Pentacam assessment to investigate Keratometry readings, Central Corneal Thickness (CCT), and Aberrations scan by Zernike analysis. Evaluations were done at baseline and 3 months' post CXL.

Results: The BCVA insignificantly deteriorated in group I & II after 3 months follow-up by (0.016 ±0.04) p=0.166 and (0.016±0.08) p=0.503 respectively. The mean average K insignificantly decreased in group I & II by (0.216 ±0.63) p=0.261 and (0.250± 1.66) p=0.619 respectively. The mean central corneal thickness increased in group I by (11.00 ±31.97) p=0.258 while decreased in group II by (5.750± 16.75) p=0.259. The mean of total aberration of group I decreased by (0.033 ± 0.09) p=0.219, while in group II increased by (0.666 ±0.49) p=0.503.

Conclusion: We found insignificant decrease in (BCVA, Average K,) in the two groups the mean CCT increased in group I and decreased in group II. The mean of total aberration decreased in group I while increased in group II.

Key Words: *Cornea – Crosslinking – Keratoconus.*

Introduction

KERATOCONUS is a bilateral corneal ectasia characterized by progressive corneal thinning leading to progressive myopia, irregular astigmatism and corneal scanning.

Keratoconus often starts when people are in their late teens to early 20s. The vision symptoms slowly get worse over a period of about 10 to 20 years **[1]**. Early stages of keratoconus can include: - Mild blurring of vision. - Slightly distorted vision, where straight lines look bent or away. - Increased sensitivity to light and glare. - Eye redness and swelling in later stages: - Increased nearsightedness or astigmatism. - Not being able to wear contact lenses. Visual correction of early keratoconus may be achieved with spectacles and a large proportion of cases with advanced keratoconus may be correctable with rigid contact lenses. Surgical intervention is necessary when conservative Management fails to achieve adequate visual rehabilitation **[2,3]**.

Corneal Collagen Crosslinking (CXL) is a procedure that uses ultraviolet irradiation (UVA) and riboflavin to induce crosslinks within the corneal stroma with an aim to increase the tensile strength of the cornea. It has been shown to slow down the progression of keratoconus with favorable clinical and topographic results **[4-7]**.

All eyes underwent epithelium-off procedures performed by the same surgeon (JJM). Accelerated CXL was done using the Innocross system; 30min riboflavin (Innocross R, IROC Innocross AG, Zug, Switzerland) presoak and 10min of 370nm, 9mW/cm^2 UVA light exposure.

Aim of study:

This study aims to investigate differences in objective and subjective outcome of collagen corneal crosslinking of different grades.

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Patients and Methods

A prospective study was carried on 24 eyes of 24 patients underwent collagen corneal cross linking arranged into 2 groups according to k reading (Group 1: Less than 48, Group 2: 48-52); 12 eyes of patients in each group. All the patients were managed at Ain Shams University Hospital. Between August, 2018 till March, 2019.

Inclusion criteria:

Age from12-40 years old, no previous intervention, K reading: Up to 52D, corneal thickness more than 400 Microns and Clear media.

Exclusion criteria:

Age less than 12 years old & more than 40 years old, previous intervention, corneal thickness less than 400 Microns, media opacity and any other ocular or systemic diseases.

All patients signed a comprehensive informed consent prior to participation in the study.

All 24 patients underwent full ophthalmological clinical evaluation:

Full history taking, full ocular examination (visual acuity unaided & best corrected spectacles by Log MAR, slit lamp examination (cornea, iris and lens), Tear film examination, Pupillary reflex, Fundus examination using 90D lens and Intraocular pressure) and pre-operative and post-operative changes in wave light oculus Pentacam (Keratometry readings (average K, Central corneal thickness (CCT) and Aberrations scan by Zernike analysis).

Results

1- Pre-operative and post-operative changes in BCVA in the different study groups:

The BCVA insignificantly deteriorated in group I & II after 3 months follow-up with difference of the mean (0.0166±0.0389) p=0.166 and (0.016± 0.083) p=0.503 respectively.

The difference between the means of BCVA difference group I and BCVA difference group II was insignificant, unpaired *t*-test >0.99 as shown in (Table 1).

2- Pre-operative and post-operative changes in average K in the different study groups:

The mean average K insignificantly decreased in group I & II with difference of the mean (0.216 ±0.633) p=0.261 and (–0.250± 1.665) p=619 respectively.

The difference between the means of average K difference group I and average K difference group II was insignificant, unpaired *t*-test=0.950 as shown in (Table 2).

3- Pre-operative and post-operative changes in central corneal thickness in the different study groups:

The mean central corneal thickness increased in group I with difference of the mean (11.00 ± 31.966) p=0.258 while decreased in group II with difference of the mean (–5.750 ± 16.745) p=0.259.

The difference between the means of CCT difference group I and CCT difference group II was insignificant, unpaired *t*-test=0.127 as shown in (Table 3).

4- Pre-operative and post-operative changes in the total aberration in the different study group:

The mean of total aberration of group I decreased with difference of the mean (–0.033 ±0.088) p=0.219 while in group II increased with difference of the mean (0.666 ±0.492) p=0.503.

The difference between the means of total aberration difference group I and total aberration difference group II was insignificant, unpaired *t*-test=0.503 as shown in (Table 4).

Table (1): Pre-operative and post-operative changes in BCVA in the different study groups.

BCVA	Groups		Unpaired Test
	Group I	Group II	
Pre:			
Range	0-0.3	0.1-0.4	>0.99
Mean ± SD	0.091±0.090	0.241±0.116	
Post:			
Range	0-0.3	0.1-0.4	
Mean ± SD	0.108±0.079	0.258±0.116	
Differences	0.0166±0.0389	0.016±0.083	
Paired Test	0.166	0.503	

Table (2): Pre-operative and post-operative changes in average K in the different study groups.

Avg K	Groups		Unpaired Test
	Group I	Group II	
Pre:			
Range	41.700-46.300	46.300-49.700	0.950
Mean ± SD	43.900± 1.503	47.667± 1.121	
Post:			
Range	41.100-46.00	44.700-51.600	
Mean ± SD	43.683± 1.699	47.417±2.015	
Differences	–0.216±0.633	–0.250± 1.695	
Paired Test	0.261	0.259	

Table (3): Pre-operative and post-operative changes in central corneal thickness in the different study groups.

CCT	Groups		Unpaired Test
	Group I	Group II	
Pre:			
Range	419-536	422-518	0.127
Mean ± SD	479.25±39.189	474.83±36.678	
Post:			
Range	425-543	410-514	
Mean ± SD	490.25±35.927	469.08±40.973	
Differences	11.00±31.966	–5.750±16.745	
Paired Test	0.258	0.259	

Table (4): Pre-operative and post-operative changes in the total aberration in the different study groups.

Total abberation	Groups		Unpaired Test
	Group I	Group II	
Pre:			
Range	1.200-2.600	1.300-4.600	0.503
Mean ± SD	1.650±0.500	2.717±1.016	
Post:			
Range	1.200-2.500	1.400-5.600	
Mean ± SD	1.617±0.442	2.783±1.147	
Differences	–0.033±0.088	0.666±0.492	
Paired Test	0.219	0.648	

Discussion

Keratoconus is a progressive, ectatic corneal disease that leads to irregular astigmatism due to weakening of the stromal collagen layers and subsequent stromal thinning. These changes are due to reduction of the number of intralamellar and interlamellar cross-links in KC patients compared with normal controls. Keratoconus doesn't affect corneas with an increased number of natural cross-links, such as in the elderly, smokers, and patients with diabetes **[8,9]**.

CXL has been approved to stop the progression of KC due to increase of the biomechanical feature of the corneal stroma. Our study aimed at evaluating the posterior corneal surface changes that occurred in Keratoconic corneas of different grades after 3 months of corneal cross linking.

In group I (K2 lessthan 48D) and group II (K2 48-52) BCVA insignificantly deteriorated after 3 months' post-operative by (0.0166 ±0.0389 and 0.016±0.083). This finding was in contrast with the results of CosimoMazzotta et al's study **[10]** and Hassan Hashemi et al's study **[5]** who found improvement in BCVA by (0.11 log MAR) and (0.06 log MAR) respectively p=(0.065) and (0.048) respectively. Both investigated groups of patients equivalent to grade I & II in our study only.

The mean average K decreased in group I & II by (0.216±0.633 and 0.250± 1.665) respectively p=0.261 and 0.619 respectively.

These findings were in parallel to those of Ahmet Kırgız et al's study **[11]** and Paolo Vinciguerra et al's study **[12]** who showed decrease in the mean average K by (0.13D), (2.74D) respectively p=(0.240) and (<0.05) respectively.

In our study we found that the mean central corneal thickness in group II decreased by (5.750± 16.745) p=0.259. This finding was in parallel to Hassan Hashemi et al's study **[5]** and Christine witting silva et al's study **[13]** who denoted decrease in the CCT by (20.87 µm), (93.00±7.98 µm) respectively p (<0.001) and (0.181) respectively. Although these results were in contrast to our results of group I as we found insignificant increase by (11.00 ± 31.966) p=0.258. This contradiction could be due to the presence of corneal edema, causing artifacts in CCT measurements.

The mean of total aberration of group I decreased with difference of the mean (0.033 ±0.088), p=0.219. This result was parallel to Steven A. Greenstein et al's study **[14]** and Paolo Vinciguerra et al"s study **[12]** who denoted decrease in the total HOA by (0.46), (3.56) respectively p (<0.001) and (0.047) respectively. Both investigated groups of patients equivalent to grade I and II in our study. while in group II increased with difference of the mean (–0.666±0.492) p=0.503. This result was consistent with the result of Siamak Zarei-Ghanavati et al's study **[15]** who investigated groups of patients equivalent to grade I and II in our study and denoted increase in the total HOA by (0.04) p=(0.001).

Conclusion:

Our study confirms the efficacy of the collagen cross-linking as a treatment modality to different grades of keratoconus.

Although there was no significant improveme ntin group I & II there was stabilization of parameters three months post-operative.

Recommendation:

Collagen cross linking is efficient in stabilizing keratoconic corneas of grads I & II.

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النتائج الشيئية والشخصية لتثبيت القرنية فى مرضى القرنية المخروطية بناءاً على درجات القرنية المخروطية

تعتبر القرنية المخروطية بروز فى القرنية يصيب كلا العينين. يتميز بنقص تطورى فى سمك القرنية يؤدى إلى قصر نظر تطورى ولا نقطية غير منتظمة وندبة بالقرنية. دائماً يبدأ فى الظهور فى الأشخاص فى أواخر سن المراهقة وبداية العشرينات.

تثبيت القرنية هو إجراء يستخدم الأشعة فوق البنفسجية وفيتامين ب ٦ لإحداث تقوية فى روابط بطانة القرنية بهدف زيادة قوة القونية وهذا لإبطاء تطور القرنية المخروطية بنتائج مفضلة على المستوى الإكلينيكى وعلى خريطة القرنية.

تعتبر الكاميرا الخماسية وسيلة لا تلامسية سريعة ومتعددة الأهداف تستخدم لفحص الجزء الأمامى من العين تتكون من كاميرا شيمفلوج دوارة بالإضافة إلى كاميرة أخرى ثابتة لإلتقاط صور متعددة للجزء الأمامى من العين لإنتاج صورة ثلاثية الأبعاد.

تهدف هذه الدراسة إلى فحص الإختلافات فى النتائج الشيئية والشخصية لتثبيت القرنية.

لقد تم فحص ٢٤ مريض مقسمين إلى مجموعتين حسب درجة القرنية المخروطية المجموعة الأولى أقل من ٤٨ والثانية من ٤٨ إلى ٥٢ وتم أخذ تاريخ مرضى وجراحى ودوائى لجميع المرضى وتم فحص حدة الإبصار وتضاريس القرنية وتحليل التشوهات البصرية العليا قبل إجراء تثبيت القرنية وبعدها بثلاثة أشهر.