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Med Arh. 2015 Apr; 69(2): 91-94
 Received: March 15th 2015 | Accepted: April 05th 2015

Published online: 06/04/2015 Published print: 04/2015

Assessment of the Tomographic Values in Keratoconic Eyes After Collagen Crosslinking Procedure

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ABSTRACT

Goal: This study aimed to investigate the differences in values of K1 and K2 readings, the central corneal thickness (PAH) before the collagen crosslinking procedure (CXL) and 3, 6, 12 months later. **Methods:** 64 eyes were evaluated in retrospective cross sectional study. The corneal biomechanical parameters were taken with WaveLight Allegro Oculyzer produced by Alcon before the CXL, 3, 6, 12 months after the procedure. The curvature of K1 reading and K2 reading were taken and the central corneal thickness were considered due to the time after CXL. **Results:** The value of K1 reading before the treatment was 48.8 diopters (D) (46.65-50.50) and was statistically significant lower comparing to the value of K1 3 months after the collagen CXL procedure 46.30 D (43.57-49.45) ($p=0.0006$), K1 reading one year post collagen CXL procedure was 47.20 D (44.35-50.07) ($p=0.002$). The value of K2 reading before the collagen CXL procedure was 52.65 D (47.55-54.72), 3 months after the procedure was 51.4 (45.05-54.0), 6 months later 48.55 D (47.20-50.62), 12 months later 51.30 D (47.22-54.77). There is statistically significant lower value of K2 reading 6 months after the treatment comparing to the values 3 months postoperatively ($p=0.014$). However there is significantly lower values of K2 reading 12 months postoperatively comparing to preoperative period ($p=0.006$). The value of central corneal thickness preoperative was 431.0 microns (398.0-446.25), 3 months after collagen CXL procedure was 373.50 microns (363.25-430.75), 6 months later 435.0 microns (360.0-464.75), 12 months after the CXL procedure was 429.50 microns (357.75-496.25). There is statistically significant lower values of central corneal thickness 3 months after collagen CXL treatment comparing to the central corneal thickness preoperative ($p<0.005$). There is statistically significant lower values of pachymetry 12 months after the CXL procedure comparing to the values 6 months later ($p=0.036$) and those preoperatively ($p=0.032$). There is no statistically significant difference in the values of central corneal thickness in the period from 3 and 6 months postoperatively. **Conclusion:** After riboflavin-UVA CXL in eyes with keratokonus there was significant decrease in central corneal thickness 3 and 6 months after the procedure and the thickness is almost the same 12 months. However, K2 (Kmax) reading is significantly changed 3 and 6 months later and is followed by changing of K1 reading.

Key words: keratokonus, collagen crosslinking, riboflavin, ultraviolet irradiation, central corneal thickness, K1, K2 readings

1. INTRODUCTION

Keratoconus (KC) is a progressive, non-inflammatory always bilateral (very often hidden or asymmetric) corneal condition of ectasia with final result in substantial alterations in the shape, thickness and biomechanical properties of the cornea (1,2). The prevalence of KC is stored to

be 1 in 2000 persons worldwide, numbers vary depending on size of the study and region (3,4,5). KC is known to typically initiate at puberty and progress until the third or fourth decade then it usually arrests (6,7,8). The rate of progression varies between individuals and not everyone will experience the final very severe stage of disease. It is

estimated that 10% to 15% of diagnosed KC eyes will lead to final stage and require corneal transplantation in order to save visual ability (1,2,3,4,9,10,11,12). Corneal collagen cross-linking with riboflavin (CXL) involves the application of riboflavin solution to the eye activated by illumination with ultraviolet A (UVA) light (13). Since 1998 this CXL strategy was proposed as a therapeutic corneal treatment with aim to make the new bonds across adjacent corneal stroma collagen stands and ground substance leading to strengthening of corneal stroma mechanics (13,14,15).

2. AIM OD THE STUDY

The aim of current study was to analyze biomechanical changes of the ectatic cornea before and after CXL procedure by applying in vivo WaveLight Allegro Oculyzer tomography. Try to emphasize which one of biomechanical properties of the cornea was the most important for monitoring postoperative keratokonus depending on time after the CXL.

3. METHODS

This retrospective study was performed with 64 ectatic diagnosed eyes before and after crosslinking procedure for progressive keratoconus during one year after CXL at PZU Očna poliklinika "Dr. Sefić". The patients were examined with slit lamp, funduscopy, measurements of uncorrected visual acuity, best spectacle visual acuity, pachymetry, tomography. We used Snellen chart for determination of visual acuity and WaveLight Allegro Oculyzer tomography to determine the changes of K1,K2 readings and central cornea thickness. Inclusion criteria for CXL were:

- Diagnosis of KC by tomography documented progression of maximum K values >0.5 D within 6 months. The diagnosis of KC was confirmed by asymmetry of the corneal surface (KISA) of >100 (16). All the patients were classified as stage 1 or 2 according to the Amsleer-Krumeich classification (17).
- Best corrected visual accuracy of at least 0,3 (Snellen chart)
- Absence of corneal scars and striae

Exclusion criteria for the study were:

- Central corneal thickness <380 microns (intraoperative corneal swelling with hypotonic solution)
- Pregnancy
- Severe dry syndrome
- Any inflammatory process on the ocular surface before CXL procedure.

Statistical analyses: Results were analyzed using standard statistical methods using SPSS computer program for statistical analysis (SPSS Statistical Package for Social Sciences) version 13.0. Results are presented as median and interquartile range (25-75 percentile), as mean ± SEM, and as percentage value (%). To test the significance of the difference in deviation from the normal distribution, Kolmogorov–Smirnov test was used. The results are analyzed by appropriate non-parametric tests (Wilcoxon and Friedman Tests). Values of $p < 0.05$ are considered as statistically significant.

4. RESULTS

From total number of 64 eyes, 8 eyes were female patients (12.5%), while the other 56 eyes (87.5%) were male patients. The average age of the patients was 25.0 ± 1.13 years. The average age of female patients was 21.12 ± 2.68 years, and the average age of male patients was 26.40 ± 1.40 years.

Test Statistics(c)				
	K13-K1	K16-K13	K112-K16	K112-K1
Z	-3.392	-1.790	-1.220	-3.081
p	0.00069	0.073	0.222	0.0020

Table 1. K1 reading. K1-pre-collagen CXL procedure. K13-3 months after collagen cxl procedure. K16 - 6 months later. K112 - 12 months later

The value of K1 reading before the treatment was 48,8 diopters (D) (46.65-50.50) and was statistically significant lower comparing to the value of K1 3 months after the collagen CXL procedure 46.30 D (43.57-49.45) ($p=0.0006$), K1 reading one year post collagen CXL procedure was 47.20 d (44.35-50.07) ($p=0.002$). The value of K1 reading 6 months later after the CXL treatment was 46.9 D (44.67-47.52). There is no statistically significant difference between the value of K1 reading 3 months and 6 months after the operation. There is no statistically significant difference in the values of K1 readings 6 and 12 months after the collagen crosslinking procedure.

Test Statistics(c)				
	K23-K2	K26-K23	K212-K26	K212-K2
Z	-1.690	-2.440	-0.762	-2.715
p	0.090	0.014	0.445	0.0066

Table 2. K2 reading. K2-pre-collagen CXL procedure. K23-3 months after collagen CXL procedure. K26 - 6 months later. K212 - 12 months later

The value of K2 reading before the collagen CXL procedure was 52.65 D (47.55-54.72), 3 months after the procedure was 51.4 D (45.05-54.0), 6 months later 48.55 D (47.20-50.62), 12 months later 51.30 D (47.22-54.77). There is statistically significant lower value of K2 reading 6 months after the treatment comparing to the values 3 months postoperatively ($p=0.014$). However there is significantly lower values of K2 reading 12 months postoperatively comparing to preoperative period ($p=0.006$). There is no statistically significant difference between the values of K2 reading 3 months after the CXL procedure and the value of K2 preoperative. There is no statistically difference between the values of K2 readings 6 and 12 months after the collagen CXL procedure.

Test Statistics(c)				
	PAH3-PAH	PAH6-PAH3	PAH12-PAH6	PAH12-PAH
Z	-3.98858	-1.6221	-2.0959247	-2.138456
p	<0.005	0.104	0.0360	0.032

Table 3. Central corneal thickness - pachymetry. PAH-pre-collagen crosslinking procedure. PAH3-3 months after collagen cxl procedure. PAH 6 - 6 months later. PAH 12 - 12 months later

The value of central corneal thickness preopratively was 431.0 microns (398.0-446.25), 3 months after colla-

gen CXL procedure was 373.50 microns (363.25-430.75), 6 months later 435,0 microns (360.0-464.75), 12 months after the CXL procedure was 429.50 microns (357.75-496.25). There is statistically significant lower values of central corneal thickness 3 months after collagen CXL treatment comparing to the central corneal thickness preoperative ($p < 0.005$). There is statistically significant lower values of pachymetry 12 months after the CXL procedure comparing to the values 6 months later ($p = 0.036$) and those preoperatively ($p = 0.032$). There is no statistically significant difference in the values of central corneal thickness in the period from 3 and 6 months postoperatively.

5. DISCUSSION

K2 and central corneal thickness as the spots to be assessed before and after the treatment. Our study identified statistically significant differences between three parameters obtained before, 3, 6 and 12 months after CXL procedure. The changes of K1, K2 and PAH is according to study Tomita et al (18). They used "Corneal Visualization Scheimpflug Technology". Oculus introduced a new device for in vivo analyses of cornea known as CST. It used a precise collimated air pulse to cause the cornea to move inwards using high speed Scheimpflug technology to follow up that movements. In this way a range of parameters are generated which enable complex analyses of viscoelastic properties of cornea. Till now, only a several studies comparing biomechanical properties of KC and normal eyes have been published. They found changes in three parameters: the deformation amplitude (DA; -0.02 mm), the distance between corneal bending points (peak distance $+0.42$ mm) and the radius of curvature at the time of highest concavity of the cornea ($+0.1$ mm). Although these changes indicate a higher stiffness of the cornea and the changes are not statistically significant at 1 year after standard procedure of CXL.

Stainbegr et al (19) demonstrated that the peak distance and the radius at the time of highest concavity changed with the same direction as did Ali et al (20). All of them did not reach a statistically significant level (peak distance -0.49 mm, $p = 0.165$; radius $+0.17$ mm; $p = 0.488$).

Huseynova et al (21) strongly showed that the structural characteristics of cornea measured with CST are hardly influenced by pachymetry. An increase of pachymetry and central corneal thickness leads to increase in the measured IOP values. Our study confirm the relation between the central corneal thickness, pachymetry and K1 and K2. All of them have direct influence to the corneal stiffness.

Kohlhaas and colleagues (22) in animal study showed a significant increase in corneal rigidity of porcine and rabbit corneas after CXL procedure. Studies on humans suffering with KC have demonstrated statistically significant short term and long term findings with topographic and structural changes of K1 and K2 readings after cxl treatment (23, 24). Vinciguerra and colleagues (23) emphasize the refractive, topographic, tomographic and aberrometric analysis of keratoconic eyes undergoing corneal cross-linking procedure.

The central corneal thickness and the values of pachymetry are statistically better 12 months later the CXL protocol according to Greenstein and colleagues (24).

The study of Razmjoo and colleagues (13) shows that CXL protocol with riboflavin is effective in healing and decreasing in progression of KC. Their result are almost the same to the research of Saffarian and colleagues (25). It showed a statistically significant decrease in cylindrical power ($p < 0.001$) and decline of 0.18 ± 0.79 D in spherical power ($p < 0.05$). Raikup –Wolf et al (26) described their prospective study included 241 eyes with KC that best corrected visual acuity and maximum simulated kerotomy values Kmax at 12 months. Flattening was observed in 54% of treated eyes with a mean change of K2 or K max of 1.91 D ($p < 0.01$). The same results published from other different centers Caporossi and colleagues (22) They illustrated that the mean spherical equivalent declined 2.5 D postoperatively. These results were topographically confirmed by reduction in mean kerotometry.

Koller et al. (27) found a significant improvement in four of seven Pentacam topography indices (central keratoconus index, keratoconus index, index of height asymmetry and minimum radius curvature) 12 months after CXL procedure. They emphasize the improvements of corneal pachymetry including the mean corneal thickness. The authors reported that CXL leads to a dose-controlled and depending keratocyte damage which must be expected in human corneas down do depth of 300 microns using the surface UVA dose of 5.4 J/cm². They reported that standard surface UVA dose of 3 mW/cm has a toxic effect on the endothelial cells of corneas thinner than 400 microns. Our study exclude all the corneas thinner than 380 microns.

There are many of benefits of CXL procedure. The satisfactory results are obvious, there is no cutting of cornea and risks like infection, cataract, secondary glaucoma and postoperative astigmatism. The positive and expected effects are long lasting, the visual acuity is improving by years and the procedure could be repeated if needed in years even decades.

6. CONCLUSION

Our study showed a significant improvement in topographic corneal changes and refractive results in patients with KC. We identified three parameters (K1, K2 and central corneal thickness) that indicate the changing and improvements of biomechanical properties after corneal CXL for progressive KC.

K1 parameter is decreasing later, after K2 which showed prompted drop out even 3 months after CXL procedure. The central corneal thickness in decreasing immediately after the procedure, which means thinning later, but after 6 months it is recovering in thickness and getting the start positions 12 months later. It means thinner (5 to 10 % then preoperative) but stronger.

In KC being able to restore vision is vital for quality of life. The arrival of CXL has definitely changed the KC standards. The number of people that will require corneal transplantation is getting down with help of CXL benefits.

CONFLICT OF INTEREST: NONE DECLARED.

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