

12 Months' Outcomes of Corneal Collagen Cross-Linking for Keratoconus Patients in Saudi Arabia

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ABSTRACT

Background: keratoconus is a degenerative disorder of the eye in which structural changes within the cornea becomes thin and accompanied by changes in its shape. Corneal collagen cross linking is one of the options to treat keratoconic eye by using riboflavin drops and UV light.

Purpose: was to assess the safety and efficacy of corneal collagen cross-linking and to investigate the refractive and topographic outcomes before and after the surgery.

Methods: this is a retrospective randomized study enrolling 77 patients with keratoconic eyes, we gathered the data of refractive (Sphere and cylinder), keratometry (K1, K2), pachymetry readings before and up to 12 months after corneal collagen cross-linking procedure in Binrushd Ophthalmologic Clinic Centre.

Results: in this study, male to female ratio was 2.6:1. Age of patients ranged between 15-41 years old. Mean outcomes at 1 year postoperatively were K2 (-0.89) Dipolar, K1 was -0.53) Dipolar. The thinnest area of the cornea (Pachymetry) improved by a mean of 23 microns. In addition to that, the results showed a clinically significant improvement in K-reading, pachymetry and refractive error in both males and females patients regarding to the p value which reached 0.23.

Conclusion: corneal collagen cross-linking is a safe modality to treat keratoconic eye in delaying or preventing the progression of the disease.

Keywords: Cornea, Collagen, Cross-Linking, keratoconic eyes.

INTRODUCTION

Keratoconus is a noninflammatory, bilateral progressive degeneration of cornea. It characterized by protruding and thinning of the cornea, abnormal astigmatism and progressive myopia.

Vision loss occurs because of the corneal apex being displaced, thus creating irregular astigmatism^[1].

The most promising technology for treating Keratoconus called collagen cross linking with UVA^[2].

The interest is rapidly growing in corneal collagen cross-linking since the publication of the first report by Spoerl *et al.* in 2003^[3] which was followed in 2004^[4] with another article explaining the ncreased resistance of cross-linked cornea against enzymatic digestion .

The use of corneal collagen cross-linking helps to strength the cornea by using riboflavin (Vitamin B2) and a longer wavelength ultraviolet violet radiation.

In addition to that, corneal collagen cross-linking can delay or prevent corneal transplantation in patients with these conditions is of a great benefit.

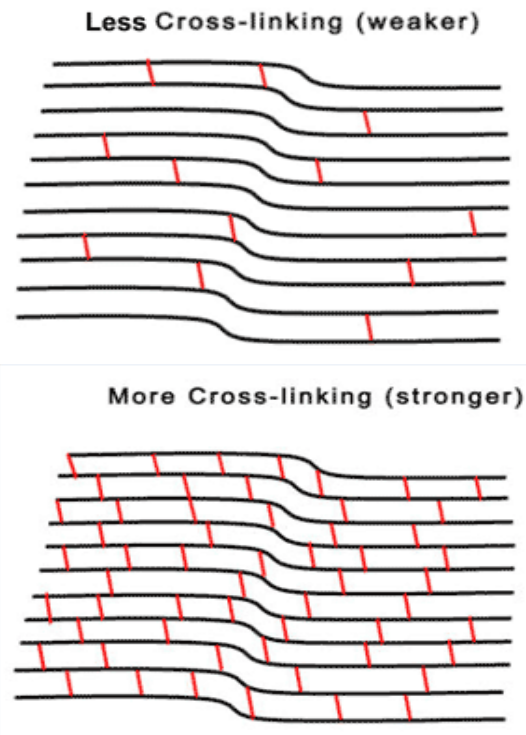


Fig.1: shows cornea layers before cross-linking.
Fig. 2: indicates increased cross-linking after treatment^[5].

METHODS

Study design

This was a retrospective, randomized study and it was carried out in BinRushd Clinic. This study aimed to assess the safety, efficacy and 12 months outcomes of corneal collagen cross linking to treat the progressive keratoconus.

The outcomes that the study focused on were age, gender, keratometry K1 and K2 (pre and post op) values of the steepest axis on corneal topography, pachymetry (which measures the thickness of the eye's cornea) before and after the surgery.

The fifth outcome was measuring the refraction of the eye (spherical, cylinder) before and after the treatment.

Participants

Patients attended at Binrushd Ophthalmologic Clinic Center confirmed diagnosis of progressive Keratoconus from 2009-2014. Corneal collagen cross-linking was performed after the diagnosis. Inclusion criteria were patients who were suffering from progressive keratoconus and performed corneal collagen cross-linking after confirming the diagnosis and who had 12 months follow up with no male or female preference.

Assessment

At baseline and postoperative visit after 12 months, the following assessments were performed:

- A manual dry refraction to measure manifest sphere and cylinde). The patient sat down behind the phoropter or wore a trial frame then was asked to look at an eye chart. Soon after , Patient's ophthamologist or eye-care professional would change the patient's lenses and other settings, while asking the patient for feedback on which set of lenses give you the best vision.

Additionally, topography measurement were performed as well (Wavelight- Allergo Oculyzer) to assess K1(flat axis), K2 (steep axis) and the thinnest area of the cornea (Pachymetry).

Procedure

Treatment where performed after confirming the diagnosis for patients. The primary goal of the first stage of therapy was to allow riboflavin (vitamin B2) to diffuse into the cornea (photo-sensitizer). While, there were several variations on the techniques used to accomplish the procedure, all entail either removing or weakening the epithelial

barrier of the

cornea. Firstly, the patient was given anesthetic drops. Some ophthalmologists gave preoperative antibiotics. A lid speculum was placed. After disrupting the epithelium, drops of riboflavin 0.1% (vitamin B2) were given at intervals of 2 minutes for 15 - 30 minutes depend on nomogram which delivered by the company, or until riboflavin can been seen in the anterior chamber of the eye by using the blue filter on slit lamp examination.

Riboflavin acts both to enhance the crosslinking effect and to protect the rest of the eye from the UV exposure.

After adequate riboflavin absorption, the patient was positioned with the UV light (typically 365-370um) at a small distance from the corneal apex for 5-7 minutes depends on the total energy delivered and the machine.

After that, soft contact lens bandage was applied. The contact lens was left in place to improve healing for approximately 5 days and was then removed. Prednisone acetate 1%, 4th generation antibiotic and non steroidal anti-inflammatory drops were used for two weeks afterwards regarding to the clinic policy.

RESULTS

A total of 160 medical records were reviewed and analyzed in this study.

More than 80 patients did not come for 12 months follow up and they were excluded from this study.

Finally, 77 patients were enrolled in our study, male to female ratio was 2.6:1. Age ranged between 15-41 years old. Mean age of patients was 25.12 years old. This article reported the result of 64 treated eyes and 13 stabilized eyes. **Table 1**

Table 1: baseline characteristics of the patients enrolled in the study

Gender	Number	%
Male	56	73
Female	21	27
Total	77	
	Mean	SDV
Age (year)	25.1	6.1

TOPOGRAPHIC RESULTS

On average, there was a notable improvement in

all patients with flattening of K (max) (steep axis) by -0.89 diopters. 65 eyes improved at least -2.00 diopters in 12 months with a maximum improvement of -7 diopters observed in one eye. Conversely, 9 eyes showed an increase in K (max) after the surgery. In addition to that, there was an average improvement of the flat axis (K1) by -0.53 diopters.

Table 1: Average preoperative and postoperative K1 and K2 readings for all participants

Patients' #	Age	Pre-operative		Post-operative		Delta		
		K1	K2	K1	K2	K1	K2	
77	Average	5.1	44.3	48.1	43.7	47.2	0.53	-0.89

CORNEAL THICKNESS MEASUREMENT

There was a wide variation in corneal thickness changes in cases of Keratoconic eyes in this study.

86.9% of eyes were improved in corneal thickness after corneal cross-linking. However, 1.2% did not change after the procedure and 12.9% decreased in the corneal thickness measurement. Corneal thickness measured by using WAVELIGHT-ALLERGO OCULYZER. According to this study, the corneal thickness measurement showed a significant improvement after collagen cross linkage procedure (p-value < 0.05). Corneal thickness improved after corneal collagen cross linkage treatment by 23 microns.

However, one of the 7 eyes which had an increase in K-reading and there was a decrease in the corneal thickness measurement. In mild and moderate myopia the change in corneal thickness was significantly different than those with high myopia.

Furthermore, the thinnest area of the cornea (Pachymetry) improved by a mean of 23 microns.

Table 3

Table 3: Corneal thickness results and significance

Difference of corneal thickness	Median	25 Quartile	Low	High	n	K-W P- value
Total	19	0	-45	202	77	0.23
Male	21	1	-45	202	56	0.05
Female	19	-23	-43	48	21	
<25 years	29	0	-45	202	44	0.34
>25 years	10	-1	-39	139	33	
Pre re >-2D	5	-10	-31	202	23	
Pre re -2 to -5.9D	14.5	-20	-45	110	32	
Pre-re 6D and more	42.5	6	-8	139	18	0.07

N= Number

MANUAL DRY REFRACTION

We performed a manual dry refraction on keratoconus patients who were included in this study to assess the sphere and cylinder and to monitor any changes after the procedure. On an average, the sphere improved by 1.73 and the cylinder by 0.66 (Table 4)

Table 4: preoperative and postoperative Sphere and Cylinder outcome individual readings for all participants

	AGE	Preoperative		Postoperative		Delta for improvement	
		Sphere	Cylinder	Sphere	Cylinder	Sphere	Cylinder
Average	25.1	-3.6	-3.1	-1.8	-2.4	1.73	0.66

We excluded the axis from the study because of some difficulties in collecting data. Pre-operative refractive error is -5. However, the postoperative refractive error is -5.6. Table 5

Table 5: K readings, Refractive error and corneal thickness outcome of all patients

Pre-intervention corneal measurements	Mean	SDV
Vertical K	44.4	4.3
Horizontal K	48.1	5.5
	Median	25% quartile
Preoperative refractive error	-5	-5.8
Postoperative refractive error	-5.6	-4.7
Corneal thickness	Median	25% quartile
Preoperative	432	66
Postoperative	456	52

DISCUSSION

Gender and age are important co variable factors in patients with keratoconus. Although that keratoconus could affect both genders, it is still unclear whether a significant difference exists between males and females. In Study performed by Owens and Gamble^[6] they reported that some studies have suggested that there was no significant difference in the prevalence between genders. In contrast to a few other studies which found a higher prevalence in men, while one only study suggested that the prevalence is higher in women^[6].

Our retrospective analysis suggested that there was no difference between both genders, but male's patients who were treated with collagen cross-linking were higher than females.

According to this study, the incidence was high with an early onset and more rapid progress to the severe disease around the age of puberty.

It is much less common in middle aged and elderly individuals.

The prevalence of keratoconus patients in Saudi Arabia was 0.81 per 100,000 citizens^[7].

This article reported 12 months topographic and refractive outcomes of corneal collagen cross linking for progressive keratoconus patients in Saudi Arabia.

The result showed a significant improvement of post-operative K(max) by a mean (-1.01) Diopters. In comparison with O'Brart *et al.*^[8] who reported a decrease in K(max) by -1.16 diopters between 4-6 years^[5].

On an average, we observed that a baseline of K (max) of more than 48.18 diopters would be associated with irregular astigmatism.

In addition to that, there was an improvement in corneal thickness measurements in nearly all the patients. Corneal collagen cross-linking treatment would prevent the progression of keratoconus in most of the patients and would delay the progression in others.

We observed that K(max) above 55 diopters would need a lens transplantation after corneal collagen cross-linking and benefit less from corneal collagen cross-linking.

Corneal collagen cross-linking would help the eye to delay the progression of the disease for a short period of time. For an eye with a high k-reading (max) above 55 diopters, however, results after the procedure wasn't promising since there was a chance of progressing keratoconus. There was unlikely need of corneal collagen cross-linking after age of 40 because of natural cross-linking. In addition to that, Vinciguerra *et al.*^[9] reported the most promising results in patients between 18 to 39 years of age.

CONCLUSION

Corneal collagen cross-linking is a new, safe and effective modality to treat keratoconic eyes. Additionally, corneal collagen cross-linking halt the progression of keratoconus and ectasia by improving the biomechanical stability of the cornea, resulting in corneal flattening, improvement in topographic outcomes and vision.

Also, in the near future it can be custom designed and topography guided modality of

treatment for optimal outcomes. Additionally, it may be combined with excimer laser vision correction (Athens protocol).

In our opinion, study with larger subsample is recommended to review the effect of keratoconus on improvement of corneal thickness after collagen cross linkage procedure for more than 12 months period and to assess the efficacy of corneal collagen cross linkage properly.

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