Corneal Endothelium Specular Microscopic Changes in Different Protocols of Collagen Cross Linking in Keratoconus

Original Article

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ABSTRACT

Background: Corneal cross-linking is the most used strategy to treat keratoconus, aims to slow down even arresting the progression of the disease. Although collagen CXL is considered safe and effective procedure, CXL can cause endothelial failure, with significant corneal edema, and patients may require penetrating keratoplasty based on the extent of endothelial damage.

Objectives: To evaluate the corneal endothelial cell changes by Specular microscopy, after Cross-linking of the cornea in keratoconus cases, as a comparison of the Accelerated Protocol and the Standard Dresden Protocol.

Patients and Methods: This study is a prospective study, performed on twenty-two keratoconus-afflicted eyes of both sexes at ophthalmology Department, Faculty of Medicine, Menoufia University, in partnership with cornea and refractive units, Giza Research Institute of Ophthalmology, during the period from February 2023 to April 2024. Patients were divided into two groups as follows: Group (I) underwent accelerated protocol, and Group (II) underwent Standard Dresden protocol.

Results: The groups under study did not differ significantly regarding density of corneal endothelial cells, average area, coefficient of variation, hexagonal cells, and thickness of cornea (P>0.05).

Conclusion: Corneal CXL with Riboflavin and UV-A irradiation stops progression of KC in all eyes. The use of accelerated CXL had the same impact on corneal endothelium as conventional CXL.

Key Words: Accelerated, Corneal cross-linking (CXL), Dresden, Keratoconus.

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INTRODUCTION

Keratoconus is a degenerative, non-inflammatory ectatic corneal condition that is typified by stromal collagen's biomechanical instability, reducing corneal thickness (progressive thinning), variation in the cornea's anterior and posterior curvatures (irregular and too steep), and distorts vision due to irregular astigmatism[1].

The endothelium of cornea is composed of a one layer of flat, polygonal cells which line the posterior surface of the cornea, maintain the relatively dehydrated status of the stroma through ionic pumps in basolateral plasma membranes[2].

The endothelium may be normal in keratoconus or may demonstrate intracellular dark structures, pleomorphism, or elongation of cells[3].

Corneal cross-linking is nowadays the most used strategy for the treatment of keratoconus, aims to slow down even arresting the progressive course of the disease, and treats the underlying pathophysiology thus stabilizing the cornea keeping the disease one step away from keratoplasty, and recently CXL has been exploited for many corneal pathologies; from ectatic disorders to keratitis[4].

Although CXL is considered a very safe and effective procedure, collagen CXL can cause severe keratouveitis and endothelial failure, having corneal edema of optical significance[5].

In this study the corneal endothelial cell changes evaluated, following standard Dresden (3 mW/cm² UV for thirty minutes) versus accelerated (9 mW/cm² UV for

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ten minutes) CXL in mild to moderate KC, by Specular microscopy.

PATIENTS AND METHODS

Subjects

This research is a comparative, analytical, simple randomized, prospective, interventional, case series study conducted on twenty-two eyes of both genders, with a simple randomized method for all patients meeting inclusion and exclusion criteria from the Cornea and Refractive Unit, until the required sample size incorporated into this study was reached, where CXL was done and then followed up for six months at the Ophthalmology Department, Faculty of Medicine, Menoufia University, in partnership with Research Institute of Ophthalmology, during the period from February 2023 to April 2024.

All patients, before collagen cross linking with standard epithelium-off (epi-off CXL), were divided into two groups as follow: Group I (Accelerated protocol (A-CXL)): included eleven eyes of eight patients underwent 9 mW/cm² UV-illumination for ten minutes. And Group II (Standard Dresden protocol (C-CXL)): included eleven eyes of six patients underwent 3 mW/cm² UV-illumination for thirty minutes. A follow up specular microscopic examination was performed after six months of intervention, to detect variations between the two groups regarding corneal endothelial cells changes (count, size, and shape).

ETHICAL CONSIDERATION

Prior to the start of the study, each participant signed a written informed consent form outlining its purpose. Approval of the research ethical committee in Menoufia Faculty of Medicine, and Research Institute of Ophthalmology was obtained.

Inclusion criteria

keratoconus patients of both sexes, 18-40 years old, average keratometry between 49–52 D, with a corneal thickness more than 450 µm.

Exclusion criteria

patients with corneal edema with a different etiology (Fuchs' endothelial corneal dystrophy or glaucoma), corneal opacities/scars with a different etiology (pterygium, infections, or injuries), evidence of active eye inflammation, IOP > 20 mmHg, history of systemic collagen vascular disease, history of long standing (more than 1 month) use of systemic steroids or anti metabolites due to wound healing affection, previous intraocular surgical intervention, previous corneal surgery (refractive surgery), pregnancy and lactation.

Preoperative evaluation

All included patients were subject to demographic data collection, such as sex, age, occupation, residence, weight, marital state, ocular surgeries, systemic diseases and medications, comprehensive ophthalmological examination including dilated fundoscopy, slit-lamp examination, intraocular pressure (IOP) measurement, and best-corrected visual acuity measurement, specular microscopy, visual acuity measured in decimal by "Tumbling E" Chart with Auto Chart Projector (Topcon ACP-8) as trial after automated kerato-refractometer (Topcon KR-800) examination, Analyzing the anterior segment using slit-lamp biomicroscopy (Righton NS-2D), measuring intraocular pressure using an applanation tonometer, and evaluating the dilated fundus using a 90D lens or indirect ophthalmoscopy, Pentacam Corneal Tomography using Oculus Pentacam HR, corneal specular microscopy using NIDEK CEM-530. Collagen cross linking.

Procedure

The patient is prepared with full lab investigations before intervention. Topical anesthesia (Benoxinate Hydrochloride 0.4%) is applied. A 1:10 diluted betadine is used to sterilize the eye, followed by placing a lid speculum, applying a micro sponge dipped in 20% diluted alcohol to brush the cornea and release the epithelium, removal of 8 to 9 mm diameter of corneal epithelium by scraping using a hockey-blade gently, then corneal soaking with riboflavin, One drop of an isotonic 0.1% riboflavin prepared solution (10 mg of riboflavin in 10 ml 20% dextran), was applied to the cornea every two minutes for thirty minutes in total. Then, the patient is placed beneath a UV-illuminating apparatus (avedro), the beam diameter to corneal diameter is adjusted, and the corneal cross-linking system is activated and focused, the distance between the patient's eye and the beam aperture was five centimeters. Group I patients (Accelerated protocol) were subjected to 9 mW/cm² UV-illumination for ten minutes. Group II patients (Standard Dresden protocol) were subjected to 3 mW/cm² UV-illumination for thirty minutes, with additional administration of riboflavin solution every

two minutes. Following UV exposure, the corneal cross-linking machine is automatically turned off. The cornea is then treated with antibiotic eye drops and covered with a bandage contact lens.

Postoperative measures

Patients received topical antibiotic (Gatifloxacin eye drops) five times daily for one week and Diclofenac 0.1% eye drops three times daily for 1 month. Fluorometholone eye drops were used three times daily in cases of exaggerated stromal haze.

Post operatives follow up: Follow-up first done after one day to exclude infection then after 5 days for contact lens removal and evaluation of corneal re-epithelialization, then after 6 months, where VA (UCVA – BCVA) was recorded and Specular microscopy was done for all groups participants.

Statistical Analysis: A standard computer application, specifically Excel for Microsoft 365 and SPSS V.26 for Microsoft Windows 10, was used to tabulate and statistically evaluate the results. There were two kinds of statistics performed: The descriptive statistics that describe the data were expressed as frequency and proportion for qualitative data and mean (±) SD for quantitative data. Analytical statistics: that includes Independent- T Test, and Independent- Mann-Whitney U Test to collectively show whether a normally distributed quantitative variable has any significant differences between many groups. *P value* <0.05 was considered statistically significant, *P value* <0.01 was considered statistically highly significant.

RESULTS

The study population: Of the 85 patients who attended cornea unit at Research Institute of Ophthalmology, 14 patients were willing to participate in the study and gave their agreement, whereas 56 patients did not match the inclusion criteria, and 15 patients declined consent, resulting in the exclusion of 63 patients from the study.

The twenty-two eyes distributed in fourteen patients were divided into two groups; Group (I) eight patients (50%male, 50%female) with 11 eyes underwent accelerated protocol CXL (9 mW/cm² UV for ten minutes) and Group (II) six patients (50%male, 50%female) with 11 eyes underwent Standard Dresden (conventional) protocol CXL (3 mW/cm² UV for thirty minutes). The mean patient age was 25.10± 5.23 years, Range (18–40). All completed 6 months follow-up after treatment.

Regarding demographic data and eye side, no statistically significant differences were found between studied groups, where age→ *P-value* is (0.065), sex→ *P-value* is (1.00), residence→ *P-value* is (0.52), and occupation→ *P-value* is (1.00).

Additionally, comparison between studied groups regarding pre-operative UCVA, BCVA, IOP, K1, K2, K max, astigmatism, and thinnest location showed no statistically significant differences, where, UCVA→ *P-value* is (0.1), BCVA → *P-value* is (0.26), IOP → *P-value* is (0.93), K1 → *P-value* is (0.38), K2 → *P-value* is (0.25), K max → *P-value* is (0.53), astigmatism → *P-value* is (0.92), and thinnest location → *P-value* is (0.28) (Figure 1).

Moreover, comparison between studied groups regarding preoperative cell count, cell density, coefficient variation, hexagonal cell, corneal thickness, showed no statistically significant differences, where, cell count→ *P-value* is (0.12), cell density→ *P-value* is (0.2), coefficient variation→ *P-value* is (0.84), hexagonal cell→ *P-value* is (0.09), corneal thickness→ *P-value* is (0.47) (Figure 2).

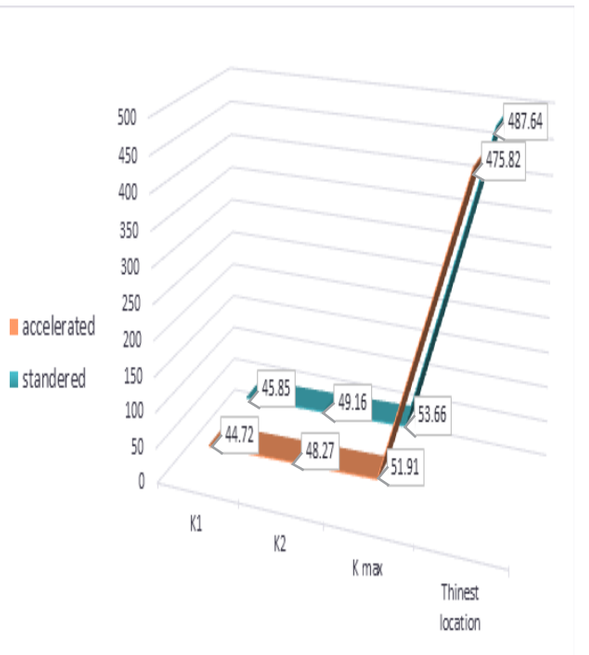

Fig. 1: Preoperative mean of K1, K2, K max, and TL between accelerated & standard CXL.

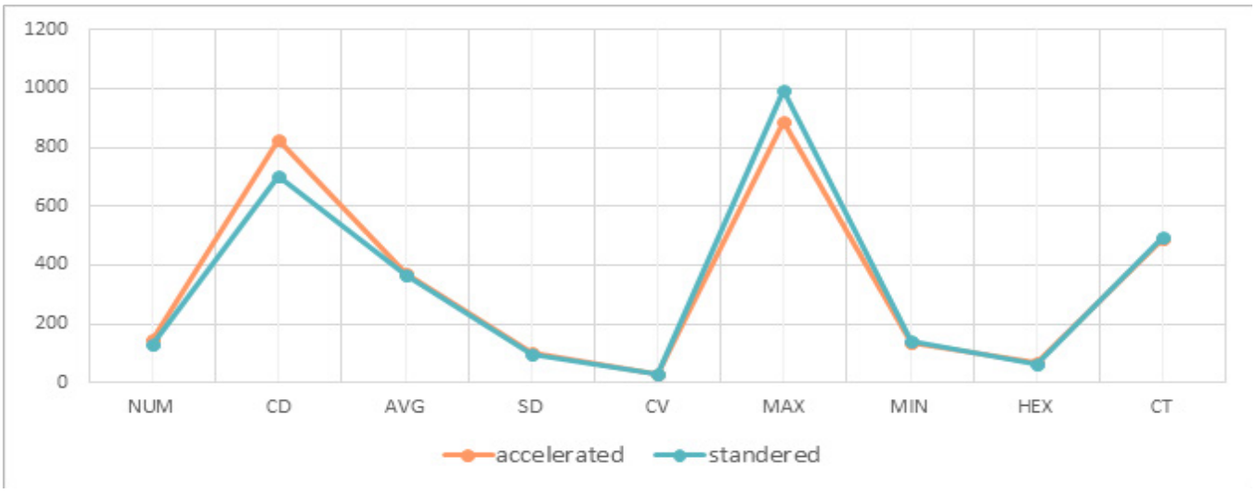

Fig. 2: Preoperative mean of specular microscopic indices between accelerated & standard CXL.

Six months after CXL.

1. comparison between Pre-Operative and Post-Operative data for every protocol shows:

    - In the accelerated protocol, there is a statistically significant difference in the number of cells between per operative "Mean ± SD"(147.36 ±27.02) and postoperative "Mean ± SD"(115.91 ±22.07) where *P-value* is 0.0072, and a statistically significant difference in min Area between per operative "Mean ± SD"(134.27 ±18.58) and post operative "Mean ± SD"(155.18 ±17.78) where *P-value* is 0.014, statistically significant differences in corneal thickness between preoperative "Mean ± SD"(488.36 ±20.32) and postoperative "Mean ± SD"(468.36 ±21.68) were *P-value* 0.0372, and finally there is statistically no significant difference between preoperative and postoperative in other indices. (Table 1)

    - In the Dresden protocol, there is a statistically significant difference in the number of cells between preoperative "Mean ± SD"(128.82 ±26.94) and postoperative "Mean ± SD"(104.82 ±25.41) where *P-value* is 0.044; a statistically significant difference in corneal thickness between preoperative "Mean ± SD"(497.09 ±33.80) and postoperative "Mean ± SD"(463.73 ±35.42) where *P-value* is 0.0351, and finally there is statistically no significant difference between preoperative and postoperative in other indices. (Table 2)

Table 1: Comparison between Pre-Operative and Post-Operative specular microscopic data in group underwent for accelerated protocol.

		Pre-Operative	Post-Operative	*P-value**
Number of Cells (NUM)	Mean ± SD	147.36 ±27.02	115.91 ±22.07	0.0072
Cell Density (CD)	Mean ± SD	2825.45 ±190.31	2752.27 ±194.82	0.3834
Average Area (AVG)	Mean ± SD	364 ±27.10	353 ±26.15	0.3442
Standard Deviation (SD)	Mean ± SD	95.36 ±14.26	104.18 ±15.57	0.1812
Coefficient of Variation (CV)	Mean ± SD	28.73 ±5.06	32.64 ±6.39	0.1273
Max Area (MAX)	Mean ± SD	889.82 ±225.04	938.45 ±245.33	0.6333
Min Area (MIN)	Mean ± SD	134.27 ±18.58	155.18 ±17.78	0.014
Hexagonal Cells (HEX)	Mean ± SD	68.64 ±5.30	67.09 ±5.52	0.5094
Corneal Thickness (CT)	Mean ± SD	488.36 ±20.32	468.36 ±21.68	0.0372

^: Mann-Whitney U Test, *: Independent- T Test

Table 2: Comparison between Pre-Operative and Post-Operative Regarding specular microscopic data in group underwent for Standard Dresden protocol.

		Pre-Operative	Post-Operative	*P-value**
Number of Cells (NUM)	Mean ± SD	128.82 ±26.94	104.82 ±25.41	0.044
Cell Density (CD)	Mean ± SD	2703.18 ±236.30	2803.09 ±437.54	0.513
Average Area (AVG)	Mean ± SD	370.36 ±36.27	360.55 ±34.72	0.524
Standard Deviation (SD)	Mean ± SD	101.55 ±22.53	109.36 ±25.03	0.451
Coefficient of Variation (CV)	Mean ± SD	28.27 ±5.14	29.73 ±4.96	0.506
Max Area (MAX)	Mean ± SD	994.18 ±287.13	1058 ±334.28	0.636
Min Area (MIN)	Mean ± SD	143.36 ±18.08	153 ±21.67	0.271
Hexagonal Cells (HEX)	Mean ± SD	62.91 ±9.06	63.36 ±11.53	0.9199
Corneal Thickness (CT)	Mean ± SD	497.09 ±33.80	463.73 ±35.42	0.0351

^: Mann-Whitney U Test, *: Independent- T Test

2. Comparison between two groups (protocols) regarding Post-Operative data shows that there were no statistically significant differences found between two groups regarding pre-operative UCVA and BCVA. Furthermore, comparison between studied groups regarding post-operative cell count, cell density, coefficient variation, hexagonal cell, corneal thickness showed that there were no statistically significant differences found between two groups regarding all specular microscopic indices. (Table 3) (Figure 3).

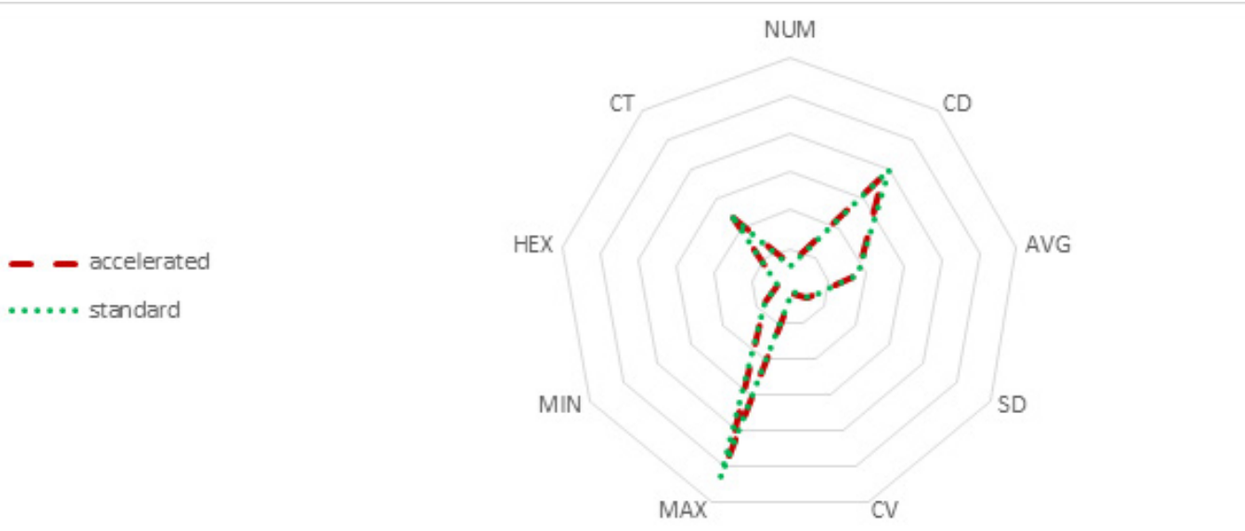

Fig. 3: Comparison between studied groups regarding Post - operative specular microscopic indices.

Table 3: Comparison between studied groups regarding Pre & Post – operative specular microscopic indices.

			Accelerated	standard Dresden	*P-value**
UCVA	Pre - Operative	Mean ± SD	0.46 ±0.19	0.35 ±0.09	0.1
	Post - Operative	Mean ± SD	0.51 ±0.19	0.41 ±0.12	0.16
BCVA	Pre - Operative	Mean ± SD	0.82 ±0.16	0.75 ±0.12	0.26
	Post - Operative	Mean ± SD	0.9 ±0.13	0.83 ±0.11	0.18^
Number of Cells (NUM)	Pre - Operative	Mean ± SD	147.36 ±27.02	128.82 ±26.94	0.12
	Post - Operative	Mean ± SD	115.91 ±22.07	104.82 ±25.41	0.29
Cell Density (CD)	Pre - Operative	Mean ± SD	2825.45 ±190.31	2703.18 ±236.30	0.2
	Post - Operative	Mean ± SD	2752.27 ±194.82	2803.09 ±437.54	0.73
Average Area (AVG)	Pre - Operative	Mean ± SD	364 ±27.10	370.36 ±36.27	0.65
	Post - Operative	Mean ± SD	353 ±26.15	360.55 ±34.72	0.57
Standard Deviation (SD)	Pre - Operative	Mean ± SD	95.36 ±14.26	101.55 ±22.53	0.45^
	Post - Operative	Mean ± SD	104.18 ±15.57	109.36 ±25.03	0.57
Coefficient of Variation (CV)	Pre - Operative	Mean ± SD	28.73 ±5.06	28.27 ±5.14	0.84
	Post - Operative	Mean ± SD	32.64 ±6.39	29.73 ±4.96	0.25
Max Area (MAX)	Pre - Operative	Mean ± SD	889.82 ±225.04	994.18 ±287.13	0.35
	Post - Operative	Mean ± SD	938.45 ±245.33	1058 ±334.28	0.35
Min Area (MIN)	Pre - Operative	Mean ± SD	134.27 ±18.58	143.36 ±18.08	0.26
	Post - Operative	Mean ± SD	155.18 ±17.78	153 ±21.67	0.8
Hexagonal Cells (HEX)	Pre - Operative	Mean ± SD	68.64 ±5.30	62.91 ±9.06	0.09^
	Post - Operative	Mean ± SD	67.09 ±5.52	63.36 ±11.53	0.34
Corneal Thickness (CT)	Pre - Operative	Mean ± SD	488.36 ±20.32	497.09 ±33.80	0.47
	Post - Operative	Mean ± SD	468.36 ±21.68	463.73 ±35.42	0.7154

DISCUSSION

Corneal cross-linking (CXL) has shown promise as a treatment to slow the advancement of keratoconus in recent years[6]. A variety of procedures, including standard and accelerated methods (with varying irradiation intensity and periods), have been used to produce CXL[7].

The purpose of the current study was to evaluate the outcomes and impacts of both conventional and accelerated corneal CXL on corneal endothelial cells by specular microscopy.

The study included twenty-two eyes who were randomly divided into two groups each of eleven eyes; Group I eyes underwent accelerated protocol CXL (9 mW/cm² UV for ten minutes), and Group (II)eyes underwent standard Dresden (conventional) protocol CXL (3 mW/cm² UV for thirty minutes).

There was a non-statistically significant difference between the two groups in the current study regarding demographic data (age, sex, residence, and occupation).

After six-months, by specular microscopic examination we discovered that:

Between the two groups, there were no statistically significant differences regarding number of cells→ (*P-value* =0.29), but statistically significant differences were found between preoperative and postoperative number of cells in the cases that underwent accelerated protocol (*P-value* =0.0072) and, in the cases that underwent Dresden protocol (*P-value* =0.044).

This came in accordance with study of ***Shiwy, et al.***[8], which reported that, there was significant reduction in two groups regarding number of cells (NUM) postoperatively, but corneal endothelial count was brought back to the baseline values at six months with no significant difference between the two groups.

On the contrary, the research conducted by ***Vinciguerra, et al.***[9], reported that, the mean baseline endothelial cell counts decreased post-operatively. However, this decrease did not reach statistical significance.

In our study, regarding cell density, there were no statistically significant differences between the two groups preoperatively (*P-value* =0.73). However, there were slight differences between preoperative and postoperative regarding cell density in the cases that underwent accelerated protocol (*P-value* =0.38) as well as those that underwent Dresden protocol (*P-value* =0.51), but the mean of this reduction was negligible.

This came in accordance with study of ***Ostadian, et al.***[10] Results revealed that the reduction in corneal endothelial cell density in the two groups was similar, and there were no appreciable variations between them (*P* = 0.64).

On the contrary, the study of ***Woo, et al.***[11] reported no statistically significant reduction in endothelial cell density for both groups at all intervals during the follow-up but statistically differences were found between preoperative and postoperative values. In the conventional group, the baseline ECD was 2860 cells/mm² while that at twelve months was 3002 cells/mm² (*P*=0.05). Similarly, in the accelerated group, the preoperative ECD was 3146 cells/mm² while that at twelve months was 2912 cells/mm² (*P*=0.06).

In our study there were no statistically significant differences between the two groups regarding coefficient of variation (*P-value* =0.25). Minimal differences were found between preoperative and postoperative values regarding coefficient of variation in the cases that underwent accelerated protocol (*P-value* =0.12) and, in the cases that underwent Dresden protocol (*P-value* =0.50), but the mean of this reduction was negligible. The post-operative mean ± SD in group 1 and group 2 eyes was (32.64 ±6.39) and (29.73 ±4.96) respectively (less than 33 is considered normal). An elevated coefficient of variation is often considered an early sign of endothelial disease, as this is a marker of endothelial cell remodeling).

This came in accordance with the study of Shajari and his colleagues[12], which reported that the coefficient of variation of endothelial cells was not significantly different in statistics in both groups (*P-value* =0.4).

But contrasts with the study of ***Cingü, et al.***[13], which reported that, statistically significant changes in endothelium morphology (CV) after the accelerated treatment was observed at one week and one month following the procedure, but returned to the baseline values after three months with no statistically significant differences among the two groups.

In our study there were no statistically significant differences between the two groups regarding hexagonality of cells → (*P-value* =0.35). Also, no statistically significant differences were found between preoperative and postoperative hexagonality of cells in group 1 cases (*P-value* = 0.509) and, in group 2 cases (*P-value* = 0.91).

This came in accordance with study of ***Shajari, et al.***[12], which reported that the percentage of hexagonal endothelial cells was not significantly different in statistics in both groups (*P-value* = 0.6).

But contrasts with the study of ***Ostadian, et al.***[10], which reported that there were no statistically significant differences between postoperative and baseline values in cases that underwent C-CXL (*P*= 0.588), but there were statistically significant differences between postoperative and baseline values in cases underwent A-CXL (*P*= 0.048), and there were statistically significantly among two groups regarding hexagonal cells (HEX) (*P*= 0.015).

In our study there were no statistically significant differences between the two groups regarding corneal thickness → (*P-value* =0.71). But statistically significant differences were found between preoperative and postoperative corneal thickness in Group I cases (*P-value* =0.037) and, in Group (II)cases (*P-value* =0.035),

This came in accordance with study of ***Sadoughi, et al.***[14], which stated that after six months, there was a significant reduction in the central corneal thickness in both groups, although the change was not significant between the two groups.

In contrast, the study of ***Shiwy, et al.***[8], found that conventional CXL lead to a greater reduction in thickness

than the accelerated treatment. There was a significant reduction in pachymetry in conventional group at six months than the preoperative values ($P < 0.001$). It was reduced from 460.42 ±39.59 µm pre-operatively to 441.45 ±47.49 µm at six months. Compared to the accelerated protocol group, pachymetry value at thinnest location preoperatively was 443.16±40.78 µm and at six months it was 438.28±38.44 µm with *p-value* at (0.113).

CONCLUSION

Corneal CXL with Riboflavin and UV-A irradiation stops progression of KC in all eyes. This minimally invasive procedure delays the need for lamellar keratoplasty, or PK, by altering the stromal architecture of the cornea and enhancing corneal stability. The use of CXL shows an insignificant improvement in UCVA and BCVA from the preoperative.

The use of accelerated CXL (9 mW/cm² for ten minutes) had the same impact on corneal endothelium as conventional CXL.

DECLARATIONS

Redundant or duplicate publication:

The authors attest that this work has not been accepted for publication anywhere else and has not been published in its present or substantially similar form elsewhere, including on a website.

Ethics approval and consent to participate:

This study was carried out in compliance with the ethical guidelines established in the 1964 Declaration of Helsinki and its subsequent revisions after receiving approval from the Institutional Review Board of the Menoufia University Faculty of Medicine Research Ethics Committee (IRB 3/2022 OPHT3). Before being included, each participant gave their informed consent.

Availability of data and materials:

Upon reasonable request, the corresponding author will provide the datasets used and/or analyzed in the current study.

CONFLICT OF INTERESTS

The authors affirm that they have no competing interests.

ABBREVIATIONS

CXL: Corneal Cross-linking

C-CXL: Conventional - Corneal Cross-linking

A-CXL: Accelerated -Corneal Cross-linking

UCVA: Uncorrected Visual Acuity

BCVA: Best Corrected Visual Acuity

KC: Keratoconus

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دراسة مجهرية منظاريه للتغيرات التي تحدث بالخلايا البطانية للقرنية في البروتوكولات المختلفة لعملية تثبيت انسجة الكولاجين في القرنية المخروطية

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تم استخدام ربط القرنية بالكولاجين (CXL) كخيار علاجي في المرضى الذين يعانون من القرنية المخروطية.

الغرض من ربط القرنية هو تثبيت القرنية وتأخير او منع تطور القرنية المخروطية. وقد أظهرت الدراسات على البشر المصابين بالقرنية المخروطية نتائج مرضية قصيرة وطويلة الأمد مع تحسن كبير في الطبوغرافيا والانكسار بعد العلاج.

في دراستنا، هدفنا إلى تقييم الاختلافات (السلامة والفعالية) بين بروتوكولات الربط المتسارع والتقليدي (CXL) على بطانة القرنية في القرنية المخروطية.

شملت دراستنا اثنين وعشرين عينًا خضع نصفها لربط القرنية المخروطية التقليدي C-CXL، وخضع النصف الآخر لربط القرنية المخروطية المتسارع A-CXL. تم تقييم جميع المرضى قبل الجراحة من حيث قراءات UCVA وBCVA وK ودرجة اللابؤرية القرنية وقياس سمك القرنية (باستخدام Pentacam) والمجهر المراوي.

في كلتا المجموعتين. انخفضت سمك القرنية بعد ستة أشهر من الجراحة دون اختلافات كبيرة بين المجموعتين. انخفض عدد الخلايا البطانية وكثافتها بعد ستة أشهر من الجراحة في كلتا المجموعتين دون اختلافات كبيرة بين المجموعتين.

لم يظهر جميع المرضى بعد ٦ أشهر اختلافًا كبيرًا بين البروتوكولين في نتائج UCVA وBCVA وسمك القرنية وعدد الخلايا البطانية في القرنية وشكلها.

لم نواجه أي مضاعفات خطيرة في جميع المرضى المشمولين في دراستنا.

يوصى بـ CXL كإجراء ناجح وآمن وغير مكلف للمرضى الذين يعانون من توسع القرنية مما يساعد على تأخير الحاجة إلى زراعة القرنية لاحقًا إن لم يكن منعها وتحقيق جودة بصرية جيدة لهؤلاء المرضى.