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Effect of corneal cross linkage (CXL) on intraocular pressure (IOP) measurements in keratoconus patients

Purpose

This study aims to determine the effect of corneal cross-linkage (CXL) on intraocular pressure (IOP) in keratoconus patients.

Methods: A quasi-experimental study was carried out at the Cornea Clinic of Al Ibrahim Eye Hospital Malir, Karachi. A total of 60 eyes of 36 subjects with progressive keratoconus with the age range of 15 to 31 years were fulfilling the criteria of the study. Subjects were selected with convenient sampling and subjects with a previous history of CXL were excluded from the study. A complete history of the patient, clinical examination with slit-lamp biomicroscopy, and visual acuity (VA) with Snellen chart were recorded. Intraocular pressure (IOP) measurements of each subject were recorded with Goldman Applanation Tonometer (GAT) before and immediately after 15 minutes of CXL and on the 2nd day of CXL, 1month, and 3 months after CXL. SPSS version 22 was used to analyze the data.

Results: The average preoperative measured intraocular pressure (IOP) was 20.22 +/- 3.97 mmHg. There was a statistically significant decrease in IOP measurements 18.96 +/- 3.73 mmHg on the same day after the corneal cross linkage procedure with (P 0.001) while there was no statistically significant change in intraocular pressure (IOP) measurements was observed on the 2nd day, 1 month and 3 months after CXL. The postoperative mean of IOP measurements was 19.61 +/- 3.47 mmHg on the 2nd day, 19.67 +/- 3.14 mmHg on 1 month, and 19.33 +/- 3.64 mmHg at 3 months respectively.

Conclusion: This study shows that reductions in intraocular pressure (IOP) measurements were observed on the immediate response of corneal cross-linkage (CXL) on the same day. This change might be due to immediate alteration in the biomechanics of the cornea during corneal cross-linkage. These changes return to the normal position later because no change was seen on different follow-ups of patients after CXL in eyes with keratoconus.

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Introduction

Keratoconus is the most common progressive, non-inflammatory, bilateral disease of the eye that affects the structure of the cornea, which is characterized by the forward protrusion of the cornea. It involves two-thirds of the cornea.[1] The estimated prevalence in the general population is 54 per 100,000.[2] but the most commonly cited prevalence is 0.054% in Minnesota, USA.[3] The growth of keratoconus increases at the time of puberty in the Asian population.[4] The disease may progress in an earlier life but decline or even stop in older age.[5] Keratoconus can be treated with different modalities including spectacles, hard contact lenses, intracorneal ring segments, and corneal transplants.[6]. In the case of progression, corneal cross linkage might be indicated to prevent the further development of keratoconus.[7] This is a newer action that has the potential to avoid the need for a corneal transplant in the future. Hence, it is to be considered that after corneal cross-linkage (CXL) and stiffening of the cornea, the intraocular pressure (IOP) measurements would be altered.

The intraocular pressure (IOP) readings with Goldman Applanation Tonometer (GAT) are highly affected by the changes in corneal parameters like corneal thickness and stiffness probably related to intraocular pressure (IOP) changes after corneal cross-linkage (CXL) and research studies suggested that intraocular pressure (IOP) has been increased after corneal cross-linkage (CXL).[8]

Methods

This quasi-experimental clinical-based study enrolled 60 eyes of 36 subjects of both genders with progressive keratoconus who underwent the corneal cross-linkage (CXL) induced by riboflavin and UVA in one or both eyes at Al Ibrahim Eye Hospital Malir Karachi with the age ranged from 15 to 35 years. Complete demographics of all patients including age, sex, citizenship, occupation, and previous history of CXL were recorded. Preoperative comprehensive ophthalmic examination of each subject was done with slit-lamp biomicroscopy, and the clinical diagnosis of keratoconus was made on the corneal topography data using a topographic device PentaCam oculus (D-35582 Wetzler, Germany). Intraocular pressure (IOP) measurements were recorded before and immediately after CXL on the same day and 2nd day, 1 month, and 3 months after CXL with Goldman Applanation Tonometer (Haag-StreitAT900, Switzerland) with sterile sodium Fluorescein strip (Optitech Eye Care). The same Tonometer was used throughout the study period. The central cornea was used to obtain measurements after administration of topical anesthetic drops (Proparacaine hydrochloride 0.5%).

Surgical procedure

Corneal Cross Linkage (CXL) was performed on all participants by a single qualified ophthalmologist with the same technique (Transepithelial Epi-ON) under sterile conditions throughout the study period. Preoperative preparations were carried out for every patient. The skin of a patient in the region of the eyes was wiped with 10% povidone-iodine solution (Betadine 10%; El-Nile Co., Cairo, Egypt). The patient's eye was topically deadened with proparacaine hydrochloride 0.5%, and a lid speculum was used to open the eye during the procedure. A topical anesthetic eye drops with BAC preservative (0.01%) was installed to enhance the permeability of

riboflavin into the eye through the epithelium. Installation of 0.1% riboflavin was continued for 30 minutes after every 2 minutes interval. Then 8mm cornea of each subject was exposed to UVA radiation for 5 minutes at the wavelength of 370 nm to give a total dose of 5.4J/cm2 through the accelerated protocol (18mW/cm2 for 5min). After finishing the UVA procedure, riboflavin solution was washed out from the corneal surface and conjunctival sac with a balanced salt solution. The surgical procedure was ended with the installation of topical broad-spectrum antibiotic eye drops e.g., Moxifloxacin (Vigamox; Alcon). Intraocular pressure (IOP) measurements of every participant were taken with a Goldman Applanation tonometer 15 minutes after the procedure to check the immediate effect of corneal cross-linkage (CXL) on intraocular pressure (IOP) measurements. Patients were called on follow-up on the 2nd day, 1 month, and 3 months for postoperative examinations.

Results

A total of 60 eyes of 36 subjects with progressive keratoconus who underwent the corneal cross linkage at Al Ibrahim Eye Hospital during the study period were fulfilled the criteria of study with the age range of 15 to 35 years. The mean age of patients was 21.55±4.711 years. There was a statistically significant decrease in IOP measurements immediately after CXL on the same day. The average preoperative measured IOP was 20.22 +/- 3.9 mm Hg and the average postoperative measured IOP was 18.96 +/- 3.73 mmHg immediately after the procedure on the same day (P 0.001). The pre- and post-operative mean difference of intraocular pressure (IOP) measurements on the same day was 1.259 +/-0.24 mmHg (Table 1). Relative to the pre-operative IOP measurement, there was no statistically significant change in intraocular pressure (IOP) on post-operative visits on the 2nd day, 1 month, and 3 months. The average post-operative measured IOP was 19.61+/- 3.47 mmHg on the 2nd day, 19.67 +/- 3.14 mmHg on 1 month, and 19.33 +/- 3.64 mmHg at 3 months respectively (Table 2).

Table 1 Demonstrates the mean IOP, standard deviation and P-value, for the pre CXL IOP compared to the post-CXL measurements immediately. There was a statistically significant decrease post-CXL IOP measurements compared to the pre-CXL IOP measurement immediately on the same day

	Pre-op IOP	Post-op IOP on the same day after CXL
Mean IOP	20.22	18.96
Std Dev	3.97	3.73
P-values		0.001

Relative to the pre-operative IOP measurement, there was no statistically significant change in intraocular pressure (IOP) on post-operative visits on the 2nd day, 1 month, and 3 months. The average post-operative measured IOP was 19.61+/- 3.47 mmHg on the 2nd day, 19.67 +/- 3.14 mmHg on 1 month, and 19.33 +/- 3.64 mmHg at 3 months respectively (P 0.468)

Table 2 Demonstrates the mean IOP, standard deviation, and P-value, for the pre-CXL IOP compared to the post-CXL measurements on the 2nd day 1 month, and 3 months. There was no statistically significant change between all post-CXL, IOP measurements compared to the pre-CXL IOP measurement on different follow-ups

	Pre-op IOP	post IOP on the 2nd day after CXL	Post-op IOP 1month after CXL	Post-op IOP 3months after CXL
Mean IOP	20.22	19.61	19.67	19.33
Std Dev	3.97	3.47	3.14	3.64
P-value		0.468		

Discussion

Keratoconus is the most common progressive condition of the eyes. It mostly causes visual disturbance and glaring problems in patients. Corneal Cross Linkage (CXL) is a standard treatment option for halting the progression in keratoconus patients.[9] It also reduces the need for penetrating keratoplasty.[10]

The corneal cross-linkage (CXL) method, introduced in recent years, is the understudy for the management of numerous eye diseases. This process helps to return suitable curvature and formation of the cornea and makes it feasible for most subjects with progressive keratoconus, who want to wear rigid contact lenses once more.[11] This study showed that there was a statistically significant decrease (P=0.001) in intraocular pressure (IOP) measurements immediately after corneal cross-linkage (CXL). To our knowledge, no other study has been published to check the immediate response of corneal cross-linkage (CXL) on intraocular pressure (IOP) measurements on the same day.

Since the advent of CXL, several studies have secondarily assessed effects on measured IOP, though most have had measured IOP on different follow-ups and the results were varied. The reason for decreased intraocular pressure (IOP) readings on the immediate response of corneal cross-linkage (CXL) might be biomechanical alterations in the corneal structures due to the process of corneal cross-linkage (CXL). It has been noted that the decrease in central corneal thickness (CCT) can cause lower readings of intraocular pressure (IOP). Holopainen et al found a significant decrease in corneal thickness during the procedure of corneal cross-linkage (CXL).[12,13]

In this study, intraocular pressure (IOP) was also measured on different follow-ups after corneal cross-linkage (CXL) to evaluate the effect of CXL on intraocular pressure (IOP) measurements. There was no statistically significant change was observed in intraocular pressure (IOP) after corneal cross-linkage (CXL) on the 2nd day, 1 month, and 3 months after corneal cross-linkage (CXL) induced with riboflavin and UVA radiations. A cohort study by Kymionis et al., at the University of Greece also looked at measured intraocular pressure (IOP) after corneal cross linkage (CXL). Their results found a statistically significant increase in measured intra ocular pressure (IOP) at 6 and 12 months after corneal cross linkage (CXL) procedure due to corneal rigidity that affects the corneal thickness.[14] They have noticed the effect of CXL on IOP after the 1-year period, which showed that corneal rigidity increases with time whilst in current study; there was only 3 months follow-up and showed no effect on corneal health because time duration of was short.

Wollensak et al.[15] study on riboflavin with ultraviolet-A-induced corneal cross-linkage (CXL) on 15 subjects did not find statistically significant changes in measured intraocular pressure (IOP) with Goldman Applanation Tonometer (GAT) after corneal cross-linkage (CXL).[15] In an animal experimental study on adult albino rabbits, there was no statistically significant difference noted in intraocular pressure (IOP) measurements before and after corneal cross-linkage (CXL) procedure.[16] In a safety and efficacy study for CXL from Italy, no significant changes in measured IOP with Tonopen were noted in a group of 10 subjects at one and three-month follow-up.[17]

Conclusion

This study concluded that corneal cross-linkage (CXL) is a harmless and effective treatment method for keratoconus patients to halt the progression of the disease without influencing the intraocular pressure

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(IOP). There was no significant effect of corneal cross-linkage (CXL) noted on intraocular pressure (IOP) readings at different follow-ups, on the other hand, a reduction in intraocular pressure (IOP) readings were observed on the immediate response to corneal cross-linkage (CXL) on the same day. This change might be due to immediate alteration in the biomechanics of cornea during corneal cross-linkage. These changes return to the normal position later.

Limitations of study

i. The limitation of the study is that intraocular pressure was measured one time at each visit rather than averaging measurements due to a shortage of time.

ii. Sample size chosen for this study was very small consisting of patients who underwent CXL and there was no control group of patients to compare the effect of intraocular pressure within the groups.

iii. Shorter postoperative follow-up period was also limited to the results of the study.

Recommendations

a) Further multicenter studies desired to explore the proper and immediate response of corneal cross-linkage (CXL) on intraocular pressure (IOP) measurements.

b) Randomized and non-randomized clinical trials are needed to understand the mechanism of this therapy on the cornea by changing some parameters of treatment.

c) More advanced technologies are required to assess the exact effect of corneal cross-linkage (CXL) on intraocular pressure measurements.

d) Larger sample sizes are necessary to obtain good results for the study

e) Long post-operative follow-up periods are also recommended for the better evaluation of intraocular pressure (IOP) after corneal cross-linkage (CXL) which provide valuable results.

f) Immediate measurements of intraocular pressure (IOP) after corneal cross-linkage (CXL) are highly preferred to find out the exact effect.

g) Intraocular pressure (IOP) should be measured with different tonometers to measure the effect after the corneal cross-linkage (CXL) procedure.

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Conflicts of Interset

None.

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