Original Article

# Intraocular lens power calculation changes before and after isotonic collagen cross-linking in keratoconus patients

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**Purpose:** To find the intraocular lens (IOL) power calculation changes before and after isotonic collagen cross-linking (CXL) in keratoconus patients. **Methods**: Thirty-five eyes of 25 patients who underwent isotonic CXL were included. The cases included conventional CXL (n = 16), accelerated CXL (n = 7), contact lens-assisted CXL (CACXL) (n = 9), accelerated CACXL (n = 3). All underwent ocular biometry (IOL master), corneal topography (Orbscan II), and simulated keratometry (Orbscan II) preoperatively and 1-year post CXL. Change in best-corrected visual acuity (BCVA), axial length (AL), simulated keratometry (Sim K), anterior chamber depth (ACD), and IOL power were analyzed in the overall data and then grouped based on flattening (Group A) and no flattening (Group B) of Sim K value post CXL procedure. **Results:** For the overall data, there was no significant change in IOL power ($P = 0.05$) at the end of 1 year, BCVA showed a significant increase ($P < 0.01$), and Sim K reading showed a statistically significant flattening ($P = 0.001$); ACD and AL showed insignificant change. In intergroup comparison, there was no statistically significant change in IOL power. However, in Group A, a significant change in BCVA and Sim K values was observed. In both groups (Group A and Group B), IOL power was found to be negatively correlated with AL and Sim K values. **Conclusion:** Isotonic CXL did not affect IOL power calculation at the end of 1 year. However, significant change in BCVA and sim K reading was noted.

Access this article online
Website:
www.ijo.in
DOI:
10.4103/ijo.IJO_395_21
Quick Response Code:

**Key words:** Collagen cross-linking, IOL power, Keratoconus

Keratoconus is a noninflammatory degenerative disorder of the cornea and is associated with corneal steepening, irregular astigmatism, and reduced visual acuity. It begins in puberty and progresses until about 40 years with an incidence of 50–130/100,000.[1,2] Collagen cross-linking (CXL) is a treatment procedure that targets the disease pathology and helps in halting the disease's progression.[3-8] It strengthens the cornea by photo-polymerization of collagen fibers in the stroma using ultraviolet-A (UV-A) light and riboflavin. The most consistent finding of observational and randomized controlled studies has been that corneal collagen cross-linking induces a reduction in keratometry values, which tend to be maintained over at least a year.

However, there are only a few studies that document post-CXL changes in the anterior chamber depth (ACD) and axial length (AL). These parameters are the cornerstone of intraocular lens (IOL) power calculation. When patients who have undergone the CXL procedure earlier in their lives develop cataract after 20–30 years, will one need to calculate IOL power using a technique that applies corrections for CXL post keratoconus? This study aims to answer the first part of that question by analyzing the probable dioptric change after CXL in young patients (aged 18–31) using IOL biometry (IOL Master, Carl Zeiss, IOL Master Advanced Technology V.5.2.1).

## Methods

This prospective observational study was conducted for a period of 2 years (June 2015–May 2017) and adhered to the tenets of the Declaration of Helsinki. Prior institutional review board approval and ethical committee clearance was obtained on 03-june-2015 and written informed consent forms were taken. Thirty-five eyes of 25 patients with ages above 18 years with progressive keratoconus were selected. Keratoconus was confirmed by clinical examination and by corneal topography (ORBSCAN II, Bausch and Lomb, Rochester, NY) with a minimum corneal thickness of >350 microns after excluding the epithelium. Patients with scarred cornea, central corneal dystrophy, those who are pregnant, and those who had intraoperative or postoperative complications were excluded. All patients underwent best-corrected visual acuity (BCVA by Snellen's decimal equivalent), manifest refraction, anterior segment, and posterior segment evaluation. Corneal topography was recorded by Orbscan (OrbscanIIz; Bausch and Lomb, Rochester, NY), and ultrasound-guided pachymetry (Pachette; DCHTechnology, Exton, PA) was used to measure the corneal thickness. Based on the above mentioned investigations, we determined suitable candidates for the procedure. These candidates were subjected to IOL Master (Carl Zeiss IOL Master Advanced Technology V.5.2.1). During the procedure, for all the candidates whose eyes had an axial length of <22 mm, we used Hoffer Q, 22-26.5 mm - SRK/T, and >26.5 – Holladay I formula. For all the patients, an ultrasound A constant of 118 was used and emmetropic IOL

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Received: 15-Feb-2021 Revision: 06-Jul-2021
Accepted: 24-Aug-2021 Published: 23-Dec-2021



**Cite this article as:** Namitha VG, Kumar DA. Intraocular lens power calculation changes before and after isotonic collagen cross-linking in keratoconus patients. Indian J Ophthalmol 2022;70:114-7.

power was determined in phakic mode. From the IOL Master, axial length (AL), anterior chamber depth (ACD), and IOL power were analyzed. Simulated keratometry (Sim K) value was determined using Orbscan. Ethical committee clearance was obtained.

After topical anesthesia using proparacaine hydrochloride 0.5% eye drops, the epithelium was abraded using a blunt spatula in a 9.0-mm diameter area. Riboflavin drops of 0.1% in 20% dextran (Ribolink; Aurolab, Madurai, India) were applied at intervals of 1–5 minutes for 15–30 minutes until riboflavin was seen in the anterior chamber of the eye using a blue filter on slit-lamp examinations.

In conventional CXL, using an ultraviolet-A meter, an intended radiance of 3.0 mW/cm$^2$ was calibrated, which was supplied with the ultraviolet-A light source of 370 nm (CL-UVR; Appasamy Associates), was applied for 30 minutes (cumulative dose of 5.4 J/cm$^2$). Throughout the procedure, riboflavin drops were instilled every 2–3 minutes to prevent the corneal surface from getting dry and to make the corneal stromal bed more than 400-micron thick.[9] In an accelerated CXL, instead of following the Dresden protocol,[10] an overall cumulative dose of 5.4 J/cm$^2$ was achieved by using 10 mW/cm$^2$ of irradiance for 9 minutes.

Patients whose thinnest pachymetry was <400 microns after epithelial removal were subjected to contact lens-assisted collagen cross-linking.[11] After epithelial removal, isotonic riboflavin 0.1% in dextran T500 was applied every 3 minutes for 30 minutes. At the same time, a daily disposable soft contact lens (14-mm diameter and 8.6-mm basal curvature - Bausch And Lomb of 90-µm thickness made of Hilafilcon B without UV filter) was immersed in 0.1% riboflavin in dextran for 30 minutes. The riboflavin-soaked contact lens was then applied to the surface of the cornea and the thickness was measured. Once pachymetry was confirmed to be more than 400 µm, the treatment was continued as per the conventional protocol or accelerated protocol.[12] A bandage contact lens was applied at the end of the procedure. The patients were instructed to use 0.5% moxifloxacin eye drops four times a day till the epithelial healing and followed by fluorometholone 1% drops in a tapering dose for 2 weeks along with tear substitutes, and followed up.

### Statistical analysis

Statistical analysis was carried out using a computer-based statistical program, Microsoft Excel 2007, and statistical package, SPSS v. 20. All categorical data were summarized using frequency and percentages. All continuous data were described using mean and standard deviation. To study the difference of clinical parameters within the group Paired sample *t*-test was used after checking the normality assumption. The difference in means of parameters between groups was analyzed using Mann–Whitney U test. Pearson correlation analysis was used to find the relationship between the two parameters. $P$ <0.05 was considered significant.

## Results

Thirty-five eyes of 25 patients were studied out of which 18 were males (25 eyes) and 7 were females (10 eyes). The mean age at the time of presentation was 22.22 years (range: 18–30 years). Ten patients had bilateral involvement; thus, both their eyes have been included in the study. However, the remaining 15 had unilateral involvement. Among the total 35 eyes that were included in this study, standard CXL was done for 16 eyes (45.72%), contact lens-assisted CACXL was performed for 9 eyes (25.71%), accelerated CXL was done in 7 eyes (20%), and accelerated CACXL was done for 3 (8.57%) eyes. The mean preoperative BCVA in decimal equivalent was 0.16 ± 0.15. Mean preoperative axial length, Sim K value, anterior chamber depth (ACD), and IOL power were 23.9 ± 1.44 mm, 48.83 ± 2.99 D, 3.49 ± 0.28 mm, and 14.01 ± 4.78 D, respectively.

At 1 year postoperatively, BCVA was 0.09 ± 0.10. Axial length, Sim K ACD, and IOL power were 24.00 ± 1.52 mm, 48.15 ± 2.90 D, 3.49 ± 0.25 mm, and 13.27 ± 5.67 D, respectively.

### BCVA

We found a statistically significant improvement in BCVA ($P$ = 0.0058) at the end of 1 year (n = 35). Mean preoperative BCVA increased from 0.137 ± 0.11 to 0.091 ± 0.10 one year after the procedure [Table 1].

### Sim K

The Sim K reading (n = 35) measured was found to be statistically significant ($P$ = 0.0010) with a change from 48.83 ± 2.99 D to 48.15 ± 2.91 D [Table 1].

### Anterior chamber depth (ACD)

The change in the ACD (n = 35) was found to be statistically insignificant with a change from 3.492 ± 0.280 mm to 3.498 ± 0.25 mm ($P$ = 0.747) in our study [Table 1].

### Axial length

The change in the axial length (n = 35) was found to be statistically insignificant (23.90 ± 1.44 mm to 24.00 ± 1.51 mm) ($P$ = 0.26) [Table 1].

### IOL power

The change in IOL power for the overall data (n = 35) was found to be statistically insignificant ($P$ = 0.08) at the end of 1-year post procedure (14.01 ± 4.77 D to 13.27 ± 5.67 D) [Table 1].

The change in IOL power using SRK/T formula (n = 31) was found to be not statistically significant ($P$ > 0.05) from preoperative (14.73 ± 3.78 D; 95%CI: 13.4–16.11) and at the end of one-year post-follow-up (13.96 ± 5.05 D; 95%CI: 12.10–15.81) [Table 2].

The change in IOL power was calculated using Hoffer Q formula in 2 eyes. In both the patients, the percentage change between the preoperative IOL power in diopters (20.50D, 7.00D) and the one year post-operative value (19.50D, 7.50 D) was negligible. Pre- and post-operative percentage difference was 4.88 and 7.14 for the first and second patient, respectively [Table 3].

**Table 1: Analysis of Parameters pre and post CXL**

| Parameter | Period | Mean | Standard deviation | P* |
|---|---|---|---|---|
| BCVA | Preop | 0.137 | 0.11 | 0.00580* |
| | Postop 1 year | 0.091 | 0.10 | |
| K | Preop | 48.83 | 2.99 | 0.00100* |
| | Postop 1 year | 48.15 | 2.91 | |
| ACD | Preop | 3.492 | 0.28 | 0.747 |
| | Postop 1 year | 3.498 | 0.253 | |
| Axial length | Preop | 23.9 | 1.44 | 0.26 |
| | Postop 1 year | 24 | 1.51 | |
| IOL Power | Preop | 14.01D | 4.78 | 0.08 |
| | Postop 1 year | 13.27D | 5.67 | |

*$P$<0.05 (paired sample *t* test). Number of Patients, *n*=35. CXL=Collagen Cross-linking; BVCA=Best-Corrected Visual Acuity; K=Keratometry. ACD=Anterior Chamber Depth; IOL Power=Intraocular Lens Power

The change in IOL power was determined using Holladay I formula in 2 eyes. We found that both patients' post-operative IOL power was decreased (i.e., preoperative (5.10 D, 1.32 D) and postoperative (4.40 D, 0.50 D)). Pre- and postoperative percentage differences were 13.73 and 62.12 for the first and second patient, respectively [Table 3].

### Intergroup analysis

An intergroup analysis was carried between those who exhibited flattening of Sim K value post CXL (Group A) procedure versus those who did not exhibit flattening/worsening of Sim K value (Group B). Among the 35 eyes that had undergone CXL, 26 eyes (74.3%) had shown flattening in K value and 9 eyes (25.7%) showed worsening or no flattening.

Evaluation of postoperative parameters between group A and group B showed a statistically significant difference in the mean ($P < 0.05$) for BCVA and Sim K, but for AL, ACD, and IOL power, the difference in mean was statistically insignificant ($P > 0.05$) [Table 4].

In Group A at the end of 1 year, the change in BCVA and Sim K was found to be statistically significant ($P < 0.05$), but no significant change in AL, ACD, and IOL power ($P > 0.05$) was observed. By contrast, in group B, there was a statistically significant increase in Sim K value at the end of 1 year. However, all the other parameters were found to be statistically insignificant [Table 5].

Correlation analysis carried out between post-op parameters in Group A and Group B showed that the IOL dioptric power was negatively correlated with AL and Sim K values. Also, the change in Sim K value was found to be negatively correlated with BCVA in group B.

**Table 2: Analysis of IOL Power using SRK/T formula**

| Variable | Obs (*n*) | Mean | SE | SD | [95% CI] | |
|---|---|---|---|---|---|---|
| Preop | 31 | 14.73 | 0.68 | 3.78 | 13.34 | 16.11 |
| Postop 1 year | 31 | 13.96 | 0.91 | 5.05 | 12.10 | 15.81 |
| Diff | 31 | 0.77 | 0.47 | 2.62 | -0.19 | 1.73 |

No significant between groups ($P$=0.112); $P$>0.05. SE=Standard Error; SD=Standard Deviation; CI=Confidence Interval

**Table 3: Analysis of IOL power using HofferQ and Holladay I formula**

| Sample. No | Group | Preop | Postop 1 year | % Difference |
|---|---|---|---|---|
| 1 | HofferQ | 20.50 | 19.50 | 4.88 |
| 2 | HofferQ | 7.00 | 7.50 | -7.14 |
| | ±SD | 9.55 | 8.49 | |
| 1 | Holladay I | 5.10 | 4.40 | 13.73 |
| 2 | Holladay I | 1.32 | 0.50 | 62.12 |
| | ±SD | 2.67 | 2.76 | |

SD=Standard Deviation; preop=Pre-operative IOL Power; Postop 1 year=Postoperative IOL Power 1 year after procedure

**Table 4: Evaluation postop parameters between groups**

| | Group | Mean | SD | Mann-Whitney | *P* |
|---|---|---|---|---|---|
| BCVA | Group A | 0.06 | 0.097 | 66.500 | 0.027* |
| | Group B | 0.16 | 0.088 | | |
| AL (mm) | Group A | 24.13 | 1.579 | 91.000 | 0.326 |
| | Group B | 23.61 | 1.335 | | |
| SIM K | Group A | 47.65 | 2.783 | 58.000 | 0.026* |
| | Group B | 49.58 | 2.929 | | |
| ACD (mm) | Group A | 3.50 | 0.269 | 111.500 | 0.835 |
| | Group B | 3.48 | 0.214 | | |
| IOL power (D) | Group A | 13.22 | 5.509 | 108.000 | 0.734 |
| | Group B | 13.40 | 6.479 | | |

*$P$<0.05, (Mann-Whitney U test)

## Discussion

The outcome of a cataract surgery is highly dependent on accurate IOL power calculation. The formula for IOL power calculation has been modified over years from the first Fyodorovs formula to the late Hill RBF formula.[12] Collagen cross-linking is a revolutionary technique that was introduced in late 1998 by Theo Seilor to address the problems of progressive corneal ectasia.[3] We analyzed the changes in the variables required for IOL power calculation, and IOL power 1 year after the CXL procedure.

In the overall data as well as those in Group A, at the end of 1 year, BCVA and Sim K values improved significantly, supporting the findings on other studies[5,6,7,8,9,13] done till date on CXL. It was reported that the maximum corneal curvature regression is observed one year post CXL. We found a statistically significant change at the end of one year with a decrease in Sim K by 0.7 D. However, in the case of Group B (25.7%), we found that there was a statistically significant increase in the Sim K value. This could be attributed to the progressive nature of the pathology in keratoconus in moderate to advanced disease conditions as previously established.[5,14]

In our study group, mean axial length did not show any statistically significant change at the end of one year. This finding remained the same in the intergroup analysis as well. This can be explained as most of our study patients had an inferiorly displaced cone; thus, the flattening effect was most remarkable in the inferior cornea rather than on the central cornea. Hence, the AL measured using IOL master along the visual axis (from the back of cornea to the retinal pigment epithelium) did not show any significant change. A similar finding was noted in a study conducted by Bernado *et al*.[15] and Goldich *et al*.,[16] where they showed no statistically significant change at the end of year 1.

We found at the end of one year the change in ACD was statistically not significant in the overall nor in the intergroup analysis, which correlated well with the AL results. This was substantiated in a study conducted by Toprak *et al*.[17] and Yildrim *et al*., where they found a statistically insignificant change from baseline at the end of 6 months. Another study by Bernado *et al*.[15] showed similar results in a 2-year follow-up study. On the contrary, a study done by Polat *et al*.[18] had shown a significant increase in anterior chamber depth at the end of 1 year.

We found there was no statistically significant change in IOL power ($P$ = 0.08) in the overall data and in the grouped data at end of one year. On group analysis based on the IOL power calculation formula used, we found a similar observation with SRK/T formula where IOL power change at year 1 from preoperative value was found to be not significant. The important variables required for IOL power calculations include the A constant, ACD, AL, and Sim K values. In our study, we

**Table 5: Evaluation of parameters between post-op and pre-op based on groups**

| Group | Operative status | Mean | SD | Mean difference | *P* |
|---|---|---|---|---|---|
| Group A | | | | | |
| BCVA | Pre-op | 0.13 | 0.11 | 0.062 | 0.036* |
| | Post-op | 0.07 | 0.10 | | |
| AL (mm) | Pre-op | 24.04 | 1.50 | -0.095 | 0.825 |
| | Post-op | 24.14 | 1.58 | | |
| SIM K (D) | Pre-op | 48.85 | 2.97 | 1.194 | 0.000** |
| | Post-op | 47.66 | 2.78 | | |
| ACD (mm) | Pre-op | 3.49 | 0.30 | -0.008 | 0.915 |
| | Post-op | 3.50 | 0.27 | | |
| IOL power (D) | Pre-op | 13.60 | 4.80 | 0.374 | 0.795 |
| | Post-op | 13.23 | 5.51 | | |
| Group B | | | | | |
| BCVA | Pre-op | 0.16 | 0.12 | 0.000 | 1.000 |
| | Post-op | 0.16 | 0.09 | | |
| AL (mm) | Pre-op | 23.51 | 1.25 | −0.108 | 0.862 |
| | Post-op | 23.61 | 1.34 | | |
| SIM K (D) | Pre-op | 48.78 | 3.21 | −0.801 | 0.022* |
| | Post-op | 49.58 | 2.93 | | |
| ACD (mm) | Pre-op | 3.49 | 0.24 | 0.001 | 0.992 |
| | Post-op | 3.49 | 0.21 | | |
| IOL power (D) | Pre-op | 15.20 | 4.77 | 1.797 | 0.513 |
| | Post-op | 13.4 | 6.47 | | |

**$P<0.01$, *$P<0.05$ (paired sample *t* test)

used a uniform A constant and the results showed a statistically significant decrease in Sim K value and an insignificant change in ACD and AL. Though there was a statistically significant change in Sim K value, the contribution of it toward IOL calculation is remarkably less compared to AL, which explains our study result. Thus, the fall in Sim K was clinically not sufficient to affect the IOL power in our study group.

Though the results obtained using Hoffer Q and Holladay I formulas showed a minimal decrease in IOL power at end of 1 year, further evaluation with a large number of observations is required.

In our study, we also found a negative correlation between IOL power with Sim K value and axial length.[19]

Biometry in keratoconus is a very challenging situation due to the irregular corneal surface, changing refraction, and tear film abnormality; therefore, traditional biometric formulas may not be accurate in predicting IOL power calculation irrespective of CXL. One has to understand this, and it is accepted that it is a totally different focus of discussion, which is still under continuous research.

Limitations of our study include small sample size and short term follow-up. The comparison was between nonuniform procedures (CXL, accelerated CXL, CACXL, and accelerated CACXL), although it has been done for the same disease.

We recommend that our study is continued further over a larger population and followed up over a longer duration to further comment on the change in IOL power calculation after CXL.

## Conclusion

In conclusion, we found that despite there being a statistically significant change in mean karetometry, there was no statistically significant change in IOL power at the end of one year post isotonic collagen cross-linking in keratoconus eyes .

### Financial support and sponsorship

Nil.

### Conflicts of interest

There are no conflicts of interest.

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