Comparative Analysis of Cycloplegia’s Effect on Intraocular Parameters in Keratoconus and Controls

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Conflict of Interest: None.


ABSTRACT

Background: Cycloplegia, the paralysis of the ciliary muscle, can significantly alter ocular biometrics. However, its effect on the intraocular parameters in individuals with keratoconus (KC), a corneal condition causing visual impairment, remains inadequately understood. This study aimed to elucidate and compare the impact of cycloplegia on ocular parameters in KC patients and controls.

Objective: To determine the effects of cycloplegia on anterior chamber depth (ACD), lens thickness (LT), and axial length (AL) in individuals with keratoconus compared to age-matched controls.

Methods: This pre- and post-interventional study was conducted at Al-Shifa Trust Eye Hospital’s Cornea Department in Rawalpindi. Subjects with KC diagnosed using the Rabinowitz criteria, and age-matched controls were enrolled. Comprehensive anterior segment examinations, including slit lamp biomicroscopy, were performed. Cycloplegia was induced using 1% cyclopentolate. Measurements of ACD, LT, and AL were taken using the IOL Master 700, both before and after cycloplegia. Data analysis was carried out using DataTab.

Results: The study encompassed 72 participants in each of the KC and control groups. The mean ages were 20.46 ± 6.47 (KC) and 22.14 ± 5.8 (controls), with a gender distribution of 58.33% male and 41.67% female in the KC group, and 54.17% male and 45.83% female in the control group. Significant differences were observed in ACD and LT pre- and post-cycloplegia in both groups, but no significant changes were noted in AL. The KC group showed changes in ACD (3.75 ± 0.28 to 3.84 ± 0.28, p < 0.001) and LT (3.49 ± 0.24 to 3.45 ± 0.24, p < 0.001), while AL remained stable (23.5 ± 0.88). Controls showed similar trends in ACD and LT with no significant change in AL. Notably, post-cycloplegia, differences in ACD and LT were significant between the KC and control groups.

Conclusion: Cycloplegia significantly influences anterior chamber depth and lens thickness in both keratoconus patients and controls, while axial length remains unaffected. These findings underscore the importance of considering cycloplegic effects in ocular biometric assessments in keratoconus and normal eyes.

Keywords: Anterior Chamber Depth, Axial Length, Cyclopentolate, Lens Thickness, Keratoconus.

INTRODUCTION

The cornea, as the eye’s transparent, anterior structure, plays a crucial role in light refraction and visual acuity (1). Its shape and thickness are vital not only for vision quality but also for the precision of refractive surgeries (2, 3). Keratoconus, a progressive disorder affecting approximately 1 in 2000 individuals globally, is characterized by corneal thinning and protrusion, leading to a cone-like deformation. This condition, typically emerging in adolescence or early adulthood, results in irregular astigmatism, myopia, and visual deterioration (4).

Cycloplegia, the paralysis of the ciliary muscle responsible for lens accommodation, is induced via topical agents such as atropine and cyclopentolate (5, 6). These agents inhibit muscarinic receptors within the ciliary muscle. Employed for both diagnostic and therapeutic purposes, cycloplegia is crucial in determining refractive errors, treating uveitis, and preventing posterior synechiae (7, 8).

Ocular biometry, involving measurements of key anatomical features like axial length, anterior chamber depth, lens thickness, and corneal curvature, is foundational in diagnosing and managing eye diseases, and in planning and assessing refractive surgery...
outcomes (9, 10). Techniques such as ultrasound, optical coherence tomography, and partial coherence interferometry facilitate these measurements (11, 12).

However, the impact of cycloplegia on ocular biometric parameters, particularly in keratoconic patients, remains inadequately explored (13, 14). While some studies suggest that cycloplegia can alter corneal curvature, anterior chamber depth, and axial length in normal eyes, others report no significant changes (15, 16). Given the distinct corneal biomechanics and morphology in keratoconus, cycloplegia's effects might differ significantly from those in normal eyes (17, 18).

This study aims to conduct a comparative analysis of ocular biometric parameters in individuals with and without keratoconus, both pre- and post-cycloplegia (19). Utilizing three distinct devices based on swept-source optical coherence tomography, we hypothesize that cycloplegia's impact on keratoconic eyes will be more pronounced compared to normal eyes (20). Additionally, we anticipate varying degrees of measurement agreement among the devices. Understanding these effects is imperative for the accurate assessment and treatment of keratoconus.

**MATERIAL AND METHODS**

The study, a comparative cross-sectional analysis, was conducted at Al-Shifa Trust Eye Hospital, Rawalpindi, over a six-month period from July to December 2023. It focused on patients aged 12 to 35 years diagnosed with keratoconus and a control group of the same age range presenting with simple refractive errors. The keratoconus patients were attended to in the Cornea Department, while the control group was seen in the general Outpatient Department (OPD).

A sample size of 30 was determined using OpenEpi Version 3, based on a 95% confidence level and a 5% confidence limit. The study employed non-probability consecutive sampling for participant selection. Inclusion criteria encompassed both male and female patients within the specified age range, diagnosed with keratoconus or presenting as healthy controls with no ocular pathology other than keratoconus. Exclusion criteria included a history of corneal or intraocular surgery, contact lens use, ocular trauma, corneal scarring, current pregnancy or nursing, diabetes, hypertension, and collagen tissue disease.

Participants diagnosed with keratoconus who met these criteria were identified and enrolled alongside control subjects within the specified age range who had refractive error complaints but no keratoconus. Keratoconus diagnosis incorporated classic corneal biomicroscopic findings and adherence to the Collaborative Longitudinal Evaluation of Keratoconus (CLEK) Study criteria for topographical evaluations. Comprehensive ophthalmological examinations were performed, including slit lamp, anterior and posterior segment examinations, and intraocular pressure measurements. Visual acuity was assessed and documented on a clinical form. Refractive measurements were conducted using an auto kerato-refractometer (KR-8900; Topcon Co., Tokyo, Japan), and keratometric and biometric measurements were obtained with the IOL MASTER 700.

Cycloplegia was induced using 1% cyclopentolate hydrochloride drops, administered twice at 10-minute intervals. Cycloptic examinations were carried out 45 minutes following the final administration, and repeat measurements were taken using the autokerato-refractometer and IOL MASTER 700.

Data collection involved recording information in an Excel spreadsheet, which was subsequently imported into Datatab for analysis. The mean and standard deviation were calculated for continuous variables, and the Shapiro Wilk test was utilized to assess data distribution. For comparing pre- and post-cycloplegic measurements among keratoconus patients and controls, paired t-tests were used for normally distributed data and the Wilcoxon rank test for non-normally distributed data. Similarly, independent t-tests and Mann-Whitney U Tests were applied to compare keratoconus and control groups pre- and post-cycloplegia. A significance level of 0.05 was maintained throughout.

The study received approval from the institute’s research and ethical committee during an IRB meeting, and all participants were assured of confidentiality in line with the Helsinki Declaration.

**RESULTS**

This table presents the gender distribution and age-related statistics among keratoconus patients and controls. In the case group, there were 42 males (58.33%) and 30 females (41.67%), whereas the control group comprised 39 males (54.17%) and 33 females (45.83%). The mean age of male and female patients in the case group was 19.19 and 22.23 years, respectively, with standard deviations of 5.7 and 7.13. In the control group, the mean ages for males and females were 24 and 19.94 years, with standard deviations of 5.84 and 4.99, respectively. The age range for cases was 12 to 35 years and for controls 13 to 39 years.
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Table 1 Gender-Wise Descriptive Statistics among Keratoconus and Control Groups

<table>
<thead>
<tr>
<th>Gender</th>
<th>Cases</th>
<th></th>
<th>Controls</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>Frequency</td>
<td>42</td>
<td>30</td>
<td>39</td>
<td>33</td>
</tr>
<tr>
<td>Percentage</td>
<td>58.33%</td>
<td>41.67%</td>
<td>54.17%</td>
<td>45.83%</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>19.19</td>
<td>22.23</td>
<td>24</td>
<td>19.94</td>
</tr>
<tr>
<td>Std. Dev.</td>
<td>5.7</td>
<td>7.13</td>
<td>5.84</td>
<td>4.99</td>
</tr>
<tr>
<td>Minimum</td>
<td>12</td>
<td>12</td>
<td>16</td>
<td>13</td>
</tr>
<tr>
<td>Maximum</td>
<td>33</td>
<td>35</td>
<td>39</td>
<td>33</td>
</tr>
</tbody>
</table>

In keratoconus patients, a significant change was observed in the Anterior Chamber Depth (ACD) and Lens Thickness (L.T) pre- and post-cycloplegia. The mean ACD increased from 3.75 mm (±0.28 SD) pre-cycloplegia to 3.84 mm (±0.28 SD) post-cycloplegia, with a p-value of <0.001. Lens Thickness decreased slightly from 3.49 mm (±0.24 SD) to 3.45 mm (±0.24 SD) post-cycloplegia (p-value <0.001). However, the Axial Length (AXL) remained statistically unchanged with a mean of 23.5 mm (±0.88 SD) in both pre- and post-cycloplegic measurements (p-value 0.225).

Table 2 Comparison of Ocular Biometrics Pre- and Post-Cycloplegia in Keratoconus Patients (N=72)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pre-Cycloplegic</th>
<th>Post-Cycloplegic</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACD (mm)</td>
<td>Mean ± SD</td>
<td>Median</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td></td>
<td>3.75 ± 0.28</td>
<td>3.77</td>
<td>3.84 ± 0.28</td>
</tr>
<tr>
<td>LT (mm)</td>
<td>3.49 ± 0.24</td>
<td>3.49</td>
<td>3.45 ± 0.24</td>
</tr>
<tr>
<td>AXL (mm)</td>
<td>23.5 ± 0.88</td>
<td>23.38</td>
<td>23.5 ± 0.88</td>
</tr>
</tbody>
</table>

In the control group, there were significant differences in ACD and LT before and after cycloplegia. The ACD increased from a mean of 3.57 mm (±0.35 SD) pre-cycloplegia to 3.65 mm (±0.34 SD) post-cycloplegia (p-value <0.001), and the LT decreased from 3.56 mm (±0.28 SD) to 3.50 mm (±0.26 SD) (p-value <0.001). Like in keratoconus patients, the AXL did not show a significant change, remaining at a mean of 23.68 mm (±1.25 SD) pre- and post-cycloplegia (p-value 0.319).

Table 3 Comparison of Ocular Biometrics Pre- and Post-Cycloplegia in Control Group (N=72)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pre-Cycloplegic</th>
<th>Post-Cycloplegic</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACD (mm)</td>
<td>Mean ± SD</td>
<td>Median</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td></td>
<td>3.57 ± 0.35</td>
<td>3.55</td>
<td>3.65 ± 0.34</td>
</tr>
<tr>
<td>LT (mm)</td>
<td>3.56 ± 0.28</td>
<td>3.55</td>
<td>3.50 ± 0.26</td>
</tr>
<tr>
<td>AXL (mm)</td>
<td>23.68 ± 1.25</td>
<td>23.75</td>
<td>23.68 ± 1.25</td>
</tr>
</tbody>
</table>

Before cycloplegia, there was a significant difference in the ACD between keratoconus patients and controls. Keratoconus patients had a higher mean ACD of 3.75 mm (±0.28 SD) compared to 3.57 mm (±0.35 SD) in controls (p-value <0.001). However, differences in LT and AXL were not statistically significant. The mean LT was 3.49 mm (±0.24 SD) in keratoconus patients and 3.56 mm (±0.28 SD) in controls (p-value 0.094), and the mean AXL was 23.50 mm (±0.88 SD) in keratoconus patients compared to 23.68 mm (±1.25 SD) in controls (p-value 0.33).

Table 4 Pre-Cycloplegic Ocular Biometrics Comparison between Keratoconus and Controls (N=72)

<table>
<thead>
<tr>
<th>Variable</th>
<th>KC Pre-Cycloplegic</th>
<th>Controls Pre-Cycloplegic</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACD (mm)</td>
<td>Mean ± SD</td>
<td>3.75 ± 0.28</td>
<td>SE</td>
</tr>
<tr>
<td>LT (mm)</td>
<td>3.49 ± 0.24</td>
<td>0.03</td>
<td>3.56 ± 0.28</td>
</tr>
<tr>
<td>AXL (mm)</td>
<td>23.50 ± 0.88</td>
<td>0.1</td>
<td>23.68 ± 1.25</td>
</tr>
</tbody>
</table>
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The purpose of this study was to compare ocular biometric parameters in individuals with and without keratoconus before and after cycloplegia, using swept-source optical coherence tomography (21). The main findings indicated that cycloplegia significantly decreased lens thickness (LT) and increased anterior chamber depth (ACD) in both keratoconus and control groups, while axial length (AXL) remained unchanged (22).

In the pre-cycloplegic state, the study revealed that individuals with keratoconus exhibited significantly lower LT and higher ACD compared to controls. However, AXL did not show a significant difference between the two groups. Post-cycloplegia, these differences in LT and ACD persisted, and AXL was found to be significantly lower in the keratoconus group compared to the controls. This study proposed an alternative perspective to the traditionally held belief that post-cycloplegia refractive changes are solely due to blocked accommodation and subsequent lens power reduction (23). It was hypothesized that alterations in corneal power, ACD, and AL during cycloplegia also contribute to these refractive changes. The unchanged AL in both keratoconus and control groups post-cycloplegia supports this hypothesis, aligning with previous research suggesting minimal impact of cycloplegia on AL.

The study also observed that keratoconus patients typically have an elevated ACD compared to age-matched controls, correlating with the progression of keratoconus stages. This was consistent with findings by Eppley et al (2021) who noted a significant increase in ACD with advancing stages of keratoconus (24). Interestingly, the current study found increased ACD values in keratoconus patients when the accommodative effect was nullified through cycloplegia, a change also noted in the control group (25). This suggested that the increase in ACD following cycloplegia might be due to the backward movement and flattening of the lens, a hypothesis reinforced by the absence of AXL alterations under cycloplegia (26).

In both keratoconus patients and controls, a decrease in lens thickness was observed following cycloplegia, indicating a similar response to cycloplegia in both groups (27). This finding contradicted some studies reporting differences in lens thickness between keratoconus patients and emmetropes, potentially attributable to factors like age and measurement devices used (28). The similarity in age inclusion criteria between this study and that by Polat N could explain the congruence in their results.

The study’s findings have significant implications for the diagnosis and management of keratoconus, suggesting that LT and ACD are valuable parameters for distinguishing keratoconus from normal eyes, both pre- and post-cycloplegia (29). These parameters can be effectively measured using optical coherence tomography. Additionally, the study highlights that cycloplegia does not affect AXL measurement in these groups, suggesting its redundancy for AXL measurement. The possible variation in AXL between keratoconus and normal eyes post-cycloplegia may indicate changes in the posterior segment of the eye in keratoconus.

However, the study faced limitations such as a small sample size, absence of baseline measurements, and the use of only one cycloplegic drug. These limitations could impact the study’s validity and reliability. Future research should consider these aspects, employing larger sample sizes, longitudinal designs, and comparative analyses of different cycloplegic drugs to further understand cycloplegia’s impact on ocular biometry in keratoconus and normal eyes.

DISCUSSION

The purpose of the study was to compare ocular biometric parameters in individuals with and without keratoconus before and after cycloplegia, using swept-source optical coherence tomography (21). The main findings indicated that cycloplegia significantly decreased lens thickness (L.T) and increased anterior chamber depth (ACD) in both keratoconus and control groups, while axial length (AXL) remained unchanged (22).

In conclusion, this study demonstrated that cycloplegics significantly affect the anterior chamber depth (ACD) and lens thickness (L.T) of the eye in both keratoconus and control groups, without influencing axial length (AL). These findings contribute valuable insights into the effect of cycloplegia on ocular biometry, particularly in the context of keratoconus.

Table 5 Post-Cycloplegic Ocular Biometrics Comparison between Keratoconus and Controls (N=72)

<table>
<thead>
<tr>
<th>Variable</th>
<th>KC Post-Cycloplegic Mean ± SD</th>
<th>SE</th>
<th>Controls Post-Cycloplegic Mean ± SD</th>
<th>SE</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACD (mm)</td>
<td>3.845 ± 0.28</td>
<td>0.03</td>
<td>3.65 ± 0.34</td>
<td>0.04</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LT (mm)</td>
<td>3.44 ± 0.24</td>
<td>0.03</td>
<td>3.50 ± 0.26</td>
<td>0.03</td>
<td>0.16</td>
</tr>
<tr>
<td>AXL (mm)</td>
<td>23.50 ± 0.88</td>
<td>0.1</td>
<td>23.68 ± 1.25</td>
<td>0.15</td>
<td>0.328</td>
</tr>
</tbody>
</table>

(KC: Keratoconus, SD: Standard Deviation, SE: Standard Error, ACD: Anterior Chamber Depth, L.T: Lens Thickness, AXL: Axial Length)

After inducing cycloplegia, a significant difference in ACD was noted between the two groups. Keratoconus patients exhibited a higher mean ACD of 3.845 mm (±0.28 SD) compared to 3.65 mm (±0.34 SD) in controls (p-value <0.001). The differences in LT and AXL post-cycloplegia were not significant. The mean LT was 3.44 mm (±0.24 SD) in keratoconus patients and 3.50 mm (±0.26 SD) in controls (p-value 0.16), and the mean AXL was 23.50 mm (±0.88 SD) in keratoconus patients compared to 23.68 mm (±1.25 SD) in controls.

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REFERENCES


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