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Effect of cycloplegia on keratometric and biometric parameters in keratoconus and controls

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Purpose. *This study aimed to evaluate and compare the effect of cycloplegia on keratometric and biometric parameters in keratoconus patients and controls.* ***Materials and methods.*** *A pre- and post-interventional study was performed on 48 keratoconus (KC) patients diagnosed per Collaborative Longitudinal Evaluation of Keratoconus (CLEK's) Classification and 41 age-matched controls. Full ophthalmological evaluations included refractive, keratometric, and biometric measurements with an auto kerato-refractometer (Topcon KR-800) and IOL MASTER 700, using 1% cyclopentolate hydrochloride for cycloplegia.* ***Results.*** *The study compared ocular measurements in KC patients and a control group before and after cycloplegia. KC patients exhibited significant changes in flat keratometry K1 (47.52 to 47.34), steep keratometry K2 (52.67 to 52.13), spherical equivalent (SE) (-6.35 to -5.5), lens thickness (LT) (3.49 to 3.44), anterior chamber depth (ACD) (3.75 to 3.84), and central corneal thickness (CCT) (446.78 to 450.72), all significant ($p < 0.01$), while axial length (AL) remained unchanged (23.5). The control group showed no significant differences in K1, K2, or AL, but SE, LT, ACD, and CCT exhibited significant changes.* ***Conclusion.*** *KC patients have a greater susceptibility to changes in corneal parameters post-cycloplegia compared to controls. These findings highlight the importance of careful evaluation in KC patients due to their distinct ocular responses to cycloplegia.*

Keywords: axial lengths; cycloplegics; eye; keratoconus
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Влияние циклоплегии на кератометрические и биометрические параметры пациентов с кератоконусом и контрольной группы

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Цель *работы — оценка и сравнение влияния циклоплегии на кератометрические и биометрические параметры пациентов с кератоконусом (КК) и контрольной группы.* ***Материал и методы.*** *Проведено пред- и постинтервенционное исследование с участием 48 пациентов с КК, диагностированным по классификации CLEK (Collaborative Longitudinal Evaluation of Keratoconus), и 41 человека контрольной группы соответствующего возраста. Полное офтальмологическое обследование включало рефракционные, кератометрические и биометрические измерения с помощью авторефрактометра (Topcon KR-800) и IOL MASTER 700 с использованием для циклоплегии 1% раствора циклопентолата гидрохлорида.* ***Результаты.*** *Сравнение результатов измерений у пациентов с КК и контрольной группы до и после циклоплегии показало, что при КК статистически значимо изменяются данные кератометрии K1 (с 47,52 до 47,34 D) и K2 (с 52,67 до 52,13 D), сферический эквивалент (СЭ) (-6,35 до -5,5 D), толщина*

хрусталика (ТХ) (с 3,49 до 3,44 мм), глубина передней камеры (ГПК) (с 3,75 до 3,84 мм) и центральная толщина роговицы (ЦТР) (с 446,78 до 450,72 мк), (p < 0,01), в то время как длина переднезадней оси (ПЗО) глаза не изменяется. В контрольной группе не выявлено различий в К1, К2 или ПЗО, но СЭ, ТХ, ГПК и ЦТР показали значительные изменения. ***Заключение.*** *При КК параметры роговицы измененяются после циклоплегии значительней, чем в контрольной группе Полученные результаты подчеркивают важность тщательной оценки этих параметров у пациентов с КК из-за отличной от нормы реакции их глаз на циклоплегию.*

Ключевые слова: диабет; диабетическая ретинопатия; контрастная чувствительность; время восстановления после фотостресса
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Keratoconus (KC) is complex multifactorial ectatic corneal condition marked by corneal thinning and irregularity, leading to forward buldging of central or paracentral cornea, causing keratometric and aberrometric irregularities and hence decreased visual acuity. It presents commonly the during the ages of 20 to 39, it's usually bilateral or asymmetric but can be rarely unilateral [1]. The condition impacts individuals of all ethnicities and both genders. The estimated prevalence and incidence rates of KC range from 1.5 to 25 cases per 100,000 individuals per year, respectively, with the highest rates observed in individuals aged 20 to 30 years, particularly among Middle Eastern and Asian population [2].

Numerous environmental risk factors contribute to KC development, including eye rubbing, atopy, sunlight exposure, environmental toxins, age, family history, ethnic variations, and contact lens use [3]. Genetic factors also play a role, with evidence linking the VXX1 and SOD1 genes (1%) to the disease [4]. KC presents in four main types: round (nipple cone), oval (sagging cone), forme fruste (typically symptomless), and keratoglobus (entire corneal thinning). Symptoms include myopia, astigmatism, and blurred vision, with stages ranging from mild to advanced, which may require treatments like contact lenses or corneal transplants [5]. Staging is based on Collaborative Longitudinal Evaluation of Keratoconus (CLEK's) criteria, using steepest K-readings from corneal topography: mild (≤ 45.00 D), moderate(45.00–52.00 D), and advanced (≥ 52.00 D) [6, 7]. KC causes biomechanical alterations in the corneal stroma, primarily due to changes in collagen structure, extracellular matrix changes, and keratocyte apoptosis, although its exact cause remains unknown [8]. Early detection is challenging, as corneal topography alone is insufficient for diagnosis. Thus, corneal pachymetry and data on higher order aberrations are often used alongside topography for a more complete assessment. Accommodation refers to the the eye's capability to concentrate and focus on near objects by contracting the ciliary muscles, which makes the crystalline lens rounder and increases its optical power. Eyes accommodation is disturbed due to the weakness of the ciliary muscles and zonular fibers and lens is unable to adopt normal round shape. This tonic accomodational weakness plays a part in visual performance of kertoconus patients and that cannot be ignored. The biomechanical weakness of the cornea in KC indicates that it could be affected by the surrounding ciliary muscles. This interaction may result in alterations to the corneal structure, which can subsequently impact the eye's refractive characteristics.

This study investigates the effects of cycloplegics, such as atropine and cyclopentolate hydrochloride, on keratometric and biometric parameters in KC patients. While cycloplegics are commonly used to assess refractive errors, their impact on corneal responses is less understood. The findings aim to enhance knowledge of ocular biomechanics and inform management strategies, potentially improving treatment approaches and patient quality of life.

MATERIAL AND METHODS

This study employed a pre- and post-interventional design, including patients aged 12 to 35 years with KC, along with a control group of the same age with simple refractive errors, recruited from Al-Shifa Trust Eye Hospital. Conducted in the Cornea Department and general outpatient department (OPD), the research lasted 6 months from March to September 2024.

A sample size of 30 was determined using OpenEpi Version 3 software, maintaining a 95% confidence level, a 5% confidence limitt, and an 80% power, based on findings by N. Polat and A. Gunduz [8] Inclusion criteria specified that participants must be 12–35 years old, of both genders, and either have a diagnosis of KC or be healthy controls with simple refractive errors, with eyes free from other ocular pathologies. The computed sample size's subjects who satisfied the inclusion requirements were chosen using a non-probability convenient technique. Exclusion criteria ruled out individuals with a history of corneal or intraocular surgery,contact lens wear, or eye trauma, corneal scarring, as well as those currently pregnant, nursing, or having diabetes, hypertension, or collagen tissue diseases. This study design allowed a clear comparison between the KC patients and healthy controls, enhancing the study's relevance and accuracy.

Data was collected using various instruments, including a slit lamp, an autokerato-refractometer (Topcon; KR-800), IOL MASTER 700, and by administrating 1% cyclopentolate hydrochloride drops. KC diagnoses were made based on biomicroscopic findings and CLEK Study criteria. Initial demographic data, such as age and gender, were gathered, and participants were screened for specific medical histories. Comprehensive ophthalmological assessments included slit lamp and intraocular pressure measurements, with refractive and keratometric data collected using the autokerato-refractometer and IOL MASTER 700. Cycloplegia was induced with 1% cyclopentolate hydrochloride drops administrated twice, followed by examinations after 45 minutes.

The institute's research and ethical committee accepted the study's project during an IRB meeting. Approval was also obtained from the head of the Optometry Department. Additionally, the individuals were given assurance that their information would be kept confidential in accordance with

the Helsinki Declaration Data management involved coding and checking the data in SPSS, with secure storage measures in place.

Descriptive statistics were used in the analysis, calculating mean and standard deviation for quantitative variables and frequency distribution for qualitative variables. The Shapiro-Wilk test was employed to assess normality. Dependent variables included K1, K2, ACD, SE, AL, LT and CCT, while independent variables comprised age, gender and the cycloplegic drug. For comparisons of measurements before and after cycloplegia, paired t-test was used for parametric data, while Wilcoxon and Mann-Whitney tests were applied for non-parametric data.

Table 1. Age and gender of patients with keratoconus (cases) and control group (Mean ± SD)
Таблица 1. Возраст и пол пациентов с кератоконусом (случаи) и контрольной группы

	Cases Случаи		Controls Контроль	
	gender пол			
	male мужчины	female женщины	male мужчины	female женщины
	28 (58.33%)	20 (41.67%)	21 (51.22%)	20 (48.78%)
Age, yrs Возраст, лет	18.89 ± 5.46	20.9 ± 7.33	20.57 ± 5.40	24.05 ± 5.84
Min–Max	12–33	12–35	13–34	16–35

Table 2. Frequency distribution of stage of keratoconus (KC)
Таблица 2. Распределение частоты стадий кератоконуса (КК)

Frequency, % Частота, %	Stage of KC Стадия КК	
	moderate умеренная	advance развитая
	38 (52.78%)	34 (47.22%)
Kmax, D		
Mean ± SD	51.64 ± 2.17	57.95 ± 3.63
Min Мин	48.74	50.76
Max Макс	56.85	66.89

RESULTS

The study involved 89 patients: 48 with keratoconus (24 unilateral, 24 bilateral) and 41 controls (10 unilateral, 31 bilateral), total 144 eyes. The case group had 28 males and 20 females; the control group had 21 males and 20 females aged between 12 and 35 years for both groups (Table 1).

KC was further divided into stages. In this study staging of KC is done according to CLEK's criteria based upon the steepest K-Readings calculated from corneal topography test. According to which there are three stages of KC with steep K ranging from (≤ 45.00 D) in mild stage, (45.00–52.00 D) in moderate stage and (≥ 52.00 D) in advance stage. In this study there were total 72 eyes of 48 subjects with KC (Case) out of which 38 were falling under moderate category on the basis of steepest K reading and 34 were falling under the Advance category as described in Table 2.

Table 3 summarizes the effects of cycloplegia in KC based on descriptive statistics from 72 individuals. Key findings include changes SE, K1 and K2, LT, AL, ACD, and CCT. It also presents post-cycloplegia effects in control subjects, along with 95% confidence intervals, providing a comprehensive overview of how cycloplegia influences these ocular parameters in both groups.

The study employed the Wilcoxon test to analyze non-normally distributed variables, comparing corneal curvatures K1, K2, SE, LT, ACD, AL, and CCT in KC patients before and after cycloplegia.

The results indicate significant structural differences between the cases and controls, with cases showing steeper keratometry values (K1 and K2), greater myopia (negative spherical equivalent), deeper anterior chambers, and thinner corneas compared controls. Cycloplegia significantly influenced the SE, LT and ACD in both groups, suggesting that it induces accommodative changes. However, AL remained unchanged, indicating it is not affected by cycloplegic effects as indicated in

Table 3. Descriptive statistics for effect of cycloplegia (CP) in keratoconus (KC) and in controls
Таблица 3. Описательная статистика эффекта циклоплегии (ЦП) при кератоконусе (КК) и в группе контроля

Parameter Показатель	Mean ± SD	95% confidence interval of mean 95%-ный доверительный интервал среднего значения	Parameter Показатель	Mean ± SD	95% confidence interval of mean 95%-ный доверительный интервал среднего значения
	KC after CP КК после ЦП			controls контроль	
SE, D СЭ, D	5.5 ± 3.84	4.62 to 6.39	SE, D СЭ, D	1.91 ± 1.39	1.59 to 2.23
K1, D	47.34 ± 3.72	46.48 to 48.2	K1, D	43.45 ± 2.13	42.95 to 43.94
K2, D	52.13 ± 4.39	51.12 to 53.15	K2, D	44.41 ± 2.25	43.89 to 44.93
LT, mm ТХ, мм	3.44 ± 0.24	3.39 to 3.5	LT, mm ТХ, мм	3.5 ± 0.26	3.44 to 3.56
ACD, mm ГПК, мм	3.84 ± 0.28	3.7 to 3.9	ACD, mm ГПК, мм	3.65 ± 0.34	3.57 to 3.73
AL, mm ПЗО, мм	23.5 ± 0.88	23.3 to 23.7	AL, mm ПЗО, мм	23.63 ± 1.25	23.39 to 23.97
CCT, μm ЦТР, мкм	450.72 ± 45.22	440.28 to 461.17	CCT, μm ЦТР, мкм	528.67 ± 36.86	520.15 to 537.18

Note. Here and in the tables 4, 5: SE — spherical equivalent, K1 — flat meridian of the anterior corneal surface, K2 — steep meridian of anterior corneal surface, LT — lens thickness, ACD — anterior chamber depth, AL — axial length, CCT — central corneal thickness, D — diopter, mm — millimeter, μm — micrometer, (-) — negative value, SD (±) — standard deviation.
Примечание. Здесь и в таблицах 4, 5: СЭ — сферический эквивалент, K1 — слабый меридиан передней поверхности роговицы, K2 — сильный меридиан, ТХ — толщина хрусталика, ГПК — глубина передней камеры, ПЗО — переднезадняя ось, ЦТР — центральная толщина роговицы, D — диоптрии, мм — миллиметр, мкм — микрометр, (-) — отрицательное значение, SD (±) — стандартное отклонение.

Table 4 and 5. Overall, these findings highlight corneal curvature, ACD, and CCT as key distinguishing factors between the two groups, with cycloplegia prompting notable adjustments in refractive and structural parameters.

DISCUSSION

To our knowledge, this study is only the second to examine the effect of cycloplegia on ocular biometric and keratometric measurements, along with lens parameters, in KC patients. The first study on this topic was conducted by N. Polat and A. Gunduz in 2016 [8].

Research on how accommodation affects the cornea in individuals with KC is currently limited. Given the biomechanical fragility of the cornea in KC patients, ciliary muscle contraction may have a significant effect. This study found a notable decrease in K1 and K2 values following cycloplegia in the KC group, indicating a flattening of the cornea. It is suggested that the relaxation of ciliary muscles after cycloplegia accounts for the reduction in K1 and K2, while the control group did not exhibit this effect, likely due to the greater biomechanical stability of their corneas.

Research on the impact of accommodation on the cornea has yielded conflicting findings [9, 10]. Some research has indicated that corneal steepening takes place during ciliary contraction and flattening occurs with cycloplegia [11, 12] while other studies have found no evidence of these effects [13, 14]. Notably, many of these studies involved children and myopic individuals, suggesting that the lower rigidity of ocular tissues in these populations may account for the observed outcomes [15].

The considerable variation in SE values within and among groups suggests effective accommodation in patients. While it is traditionally believed that post-cycloplegia refractive changes result from blocked accommodation and a subsequent reduction in lens power, our findings offer an alternative perspective. It is plausible that changes in corneal power, ACD, and AL during this state contribute to refractive changes observed after cycloplegia [12]. This is supported by the idea that variations in ACD are linked to modifications in the lens, and alterations in corneal power can be calculated from K readings taken before and after cyclioplegia.The study shows that cycloplegia does not have a significant effect on AL in either the KC or control group. While there is limited research examining the effects of cycloplegia in KC patients specifically, other studies on diverse cohorts asserts that cycloplegia does not substantially impact AL [16].

KC patients often exhibit an increase in ACD compared to age-matched controls. N. Polat and A. Gunduz [8] observed a notable correlation between the advancement of KC stages and

Table 4. Comparison of pre-cycloplegia (Pre-CP) and post-cycloplegia (Post-CP) parameters in cases
Таблица 4. Сравнение параметров до и после циклоплегии (ЦП) при кератоконусе

Parameter Показатель	Pre-CP До ЦП Mean ± SD	Pre-CP До ЦП Median	Post-CP После ЦП Mean ± SD	Post-CP После ЦП Median	p-value	Normally distributed Нормальное распределение
K1, D	47.52 ± 3.72	46.93	47.34 ± 3.72	46.69	< 0.001*	–
K2, D	52.67 ± 4.64	51.95	52.13 ± 4.39	51.46	< 0.001*	0.26
SE, D СЭ, D	-6.35 ± 3.92	-5.38	-5.5 ± 3.85	-4.5	< 0.001*	–
LT, mm ТХ, мм	3.49 ± 0.24	3.49	3.44 ± 0.24	3.45	< 0.001*	0.03
ACD, mm ГПК, мм	3.75 ± 0.28	3.77	3.84 ± 0.28	3.88	< 0.001*	–
AL, mm ПЗО, мм	23.50 ± 0.88	23.38	23.5 ± 0.88	23.37	0.887	–
CCT, μm ЦТР, мкм	446.78 ± 45.35	454	450.72 ± 45.22	459	< 0.001*	4.34

Note. Here and in the table 5: * — the difference with the initial value is significant.
Примечание. Здесь и в таблице 5: * — различие с исходным значением достоверно.

Table 5. Comparison of pre-cycloplegia (Pre-CP) and post-cycloplegia (Post-CP) parameters in controls
Таблица 5. Сравнение параметров до и после циклоплегии (ЦП) у пациентов группы контроля

Parameter Показатель	Pre-CP До ЦП Mean±SD	Pre-CP До ЦП Median	Post-CP После ЦП Mean±SD	Post-CP После ЦП Median	p-value	Normally distributed Нормальное распределение	Degree of freedom Степень свободы
K1, D	43.44 ± 2.13	43.45	43.45 ± 2.13	43.45	0.717	–	–
K2, D	44.41 ± 2.26	44.73	44.41 ± 2.25	44.73	0.527	0.27	71
SE, D СЭ, D	-1.47 ± 1.78	-1.5	-1.23 ± 2.02	-1.25	0.006*	–	–
LT, mm ТХ, мм	3.56 ± 0.28	3.55	3.5 ± 0.26	3.5	<0.001*	0.03	71
ACD, mm ГПК, мм	3.57 ± 0.35	3.55	3.65 ± 0.34	3.63	<0.001*	–	–
AL, mm ПЗО, мм	23.68 ± 1.25	23.75	23.68 ± 1.25	23.74	0.16	–	–
CCT, μm ЦТР, мкм	526.94 ± 37.3	528.5	528.67 ± 36.86	528.5	0.002*	4.4	71

a significant increase in ACD, suggesting that this rise may be due to the forward bulging of the cornea. The current study similarly found a notable increase in ACD values in KC patients compared to the control group. Notably, when the accommodative effect was eliminated through cycloplegia, higher ACD values were observed in KC patients, with a similar trend seen in the control group. This increase in ACD after cycloplegia is thought to result from the backward movement and flattening of the lens. The lack of changes in AL during cycloplegia further supports the notion that the increase in ACD is due to lens alterations [12, 13].

Numerous studies have illustrated the impact of accommodation on ACD, consistently showing an increase in ACD after accommodating effects are nullified through cycloplegia [16]. This research highlights a similar link between accommodation and ACD in individuals with KC, as illustrated by N. Polat and A. Gunduz [8]. These alterations are significant since ACD is a crucial parameter in biometric formulas like W. Haigis, et al. [17] as well as for the insertion of phakic intraocular lenses (IOLs).

While there are conflicting reports about the backward displacement of the lens's posterior surface in relation to LT [18], this study found no substantial difference in LT between KC patients and control subjects after cycloplegia. Although a few studies reported differences in LT between KC patients and emmetropes [19] such differences may be due to variations in age and measurement devices. However, N. Polat and A. Gunduz [8] obtained similar results, as the inclusion criteria for age were comparable. Both groups showed a decrease in LT following cycloplegia, indicating a similar degree of response to cycloplegia.

The CCT of both KC patients and control subjects was measured and analyzed statistically. Previous studies have shown corneal curvatures decrease in KC patients [12], but CCT had not been measured specifically in KC subjects. Like corneal curvature, CCT is an important factor in calculations and planning for various ophthalmic procedures, including cataract and refractive surgeries, and is particularly crucial for KC patients undergoing collagen cross-linking. This study noted an increase in CCT in KC patients following cycloplegia. While a similar increase was observed in controls, the pre-cycloplegic CCT in KC subjects was 446.78 ± 45.35, compared to 526.94 ± 37.3 in controls. Following cycloplegia, post-cycloplegic CCT in KC subjects was 450.72 ± 45.22, and in controls, it was 528.67 ± 45.22. The statistically significant change ($p < 0.001$) demonstrates a larger rise in CCT after cycloplegia in KC patients compared to the control group, highlighting a positive outcome of this research.

Numerous studies exploring changes in biometric and lens parameters during accommodation have depended on low-resolution measurement instruments or subjective techniques, leading to inconsistent results [20]. Additionally, many of these studies induced accommodation, resulting in varying outcomes [21]. The credibility of results is compromised when measurements are taken from the contralateral eye after inducing accommodation. The present research obtained measurements following natural physiological accommodation and assessed changes in the same eye after cycloplegia. Notably, measurements were conducted using the IOL MASTER 700, a tool recognized for its accuracy and reliability [19].

This study has several limitations. Firstly, it focused solely on the impact of cyclopentolate hydrochloride 1% and did not explore the effects of other cycloplegic agents in both KC and control groups, which diminishes the generalizability of the findings. Secondly, the study did not differentiate effects on posterior and anterior KC subjects; a more nuanced examination of these subgroups could yield more tailored results. Thirdly, using the IOL Master 700 for both keratometric and biometric data might introduce variability; employing a topographer for measuring K1 and K2 could enhance precision. Incorporating the use of a keratograph in clinical diagnostics could enhance the reliability and accuracy of keratometric and biometric measurements in KC. Finally, the short duration of the study limited the sample size, and a longer timeframe could facilitate the inclusion of a larger and more diverse population, enhancing the accuracy and reliability of the study's outcomes.

CONCLUSIONS

The study found that KC patients showed a flattened corneal curvature, increased SE, and higher ACD and CCT after cycloplegia. While LT decreased significantly, AL remained unchanged. In contrast, controls had similar changes in SE, ACD, and CCT, but no change in corneal curvature. Notably, KC patients experienced a greater increase in corneal thickness, indicating a potential benefit in managing progressive corneal thinning.

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