Comparison of Autorefraction, Cyclorefraction, and Subjective Manifest Refraction in Keratoconic Eyes

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Abstract

Purpose: This study aimed to estimate the agreement of astigmatism between an autorefractor (Topcon), cycloplegic refraction, subjective manifest refraction, front and back corneal astigmatism. Moreover, this study aimed to investigate which factors influence the difference between cycloplegic refraction and subjective manifest refraction in these keratonic eyes.

Methods: subjective manifest refraction, Autorefractometer were measured in 64 keratonic eyes of 43 patients (21-45 years old) before and after using cycloplegic drop. We measured Corneal values by using Scheimpflug tomography. Astigmatic power was converted to vectors. The agreement of astigmatism between an autorefractor (Topcon), cycloplegic refraction, subjective manifest refraction, front and back corneal astigmatism was measured overall and in each vector. The difference between Cycloplegic refraction and subjective manifest refraction was calculated in each vector axis. Factors were anticipated associated with discrepancy by using Multivariable Regression Analysis.

Results: The maximum estimations of agreement were found between autorefractometer and subjective manifest refraction in cylindrical power (lcc:0.703, $P<0.026$), cylindrical axis (lcc:0.943, $P<0.0001$) and astigmatic vectors of J0 (lcc:0.972, $P<0.0001$) and J45 (lcc:0.827, $P=0.006$). The significant factors Associated With discrepancy between cyclorefraction and subjective manifest refraction in both vectors (J0 and J45) were Q-value (B Coefficient= -4.91, $P<0.0001$) (B Coefficient=1.01, $P<0.0001$), corneal astigmatism (B Coefficient= 0.66, $P=0.001$) (B Coefficient=0.11, $P=0.001$), Kmax (B Coefficient= -0.52, $P<0.0001$) (B Coefficient=0.07, $P=0.02$), IHA (B Coefficient=0.04, $P=0.005$) (B Coefficient= -0.03, $P<0.0001$). The significant associated factors for axis changes between cycloplegic refraction and subjective manifest refraction were cone location (B Coefficient= -33.34, $P=0.001$) and corneal astigmatism (B Coefficient= -0.1, $P=0.04$).

Conclusion: Maximum agreement of subjective manifest refraction astigmatism is with auto refractometer in keratoconus patients, so it could be said that the result of the auto refractometer is the most appropriate starting point during subjective refraction in these patients. It can be predicted that the closer the keratoconus cone location relative to the center of the cornea and the lower the keratoconus patient's corneal astigmatism, the more the probability of axis changes by cycloplegic drop.

Introduction:

Keratoconus is the most common primary ectasia, along with degeneration and localized thinning in the cornea, usually leading to reduced quality of vision[1]. The most critically important factor in deciding on the keratoconus treatment is the best-corrected visual acuity. An accurate best-corrected visual acuity during subjective manifest refraction plays an essential clinical role in assessing visual performance and disease progression. The first information we need at the beginning of subjective manifest refraction in a keratoconus patient to obtain the best visual acuity is an auto refractometer and manual retinoscopy. The previous study showed that the difference between subjective manifest refraction and autorefraction was increased where the cornea had been steepened[2]. Furthermore, manual retinoscopy requires more skill to neutralize corneal scissor motion reflex result from keratonic properties. During subjective manifest refraction, accommodative relaxation is the crucial factor. Keratonic patients are often much more likely to change accommodation because of the excessive amount of corneal aberrations and lack of clear vision[3]. Subjective manifest refraction in keratoconic subjects usually causes concern about accommodative fluctuation. Keratoconic subjective manifest refraction is often based on patient responses, and achieving the best-corrected visual acuity in these patients with poor collaboration is so difficult. During keratoconic subjective manifest refraction, precise determination of axis takes a long time, and astigmatism is usually high in these eyes. In people with poor cooperation or low detection of clear vision, this step is very time-consuming. In this study, we consider subjective manifest refraction as the gold standard[4]. We tried to get the best starting point in subjective manifest refraction based on different cornea information because high astigmatism in these patients usually results from the cornea. In this study, we want to estimate the subjective manifest refraction agreement with autorefractor (Topcon), cycloplegic refraction, anterior and posterior corneal astigmatism. Moreover this study aimed to investigate which factors influence the difference between cycloplegic refraction and subjective manifest refraction in these keratonic eyes.

Material And Method:

Study Design:

This study included 64 eyes of 43 patients aged from 21 to 45 years old who were diagnosed as keratoconus in optometric evaluation at Poostchi ophthalmology center for two years, from October 2016 to October 2018. This study followed the tenets of the Declaration of Helsinki, and informed consent was obtained from each subject after an explanation of the nature and possible consequences of the study. This research was approved by the ethical board of shiraz university of medical sciences. The initial diagnosis of keratoconus was made based on scissor motion in the retinoscopic reflex. After More detailed diagnostic examinations for keratoconus, 64 eyes of 43 Patients with more severe keratoconus (stage III to Amsler criteria[5]) were selected and enrolled in the study. According to the Amsler-krumeich grading scale, there should be no scarring KCN stage III. If scarring is present, it could be a stage IV. Also, assessing scarring is crucial in this kind of works, as scarring (and possible opacities) will influence refraction, so we only enrolled stage III keratonic eyes in the study. Keratoconus stage assessed by the mean keratometry value of the Pentacam Keratometry . pachymetry and scarring. The Ophthalmic Research Centers' ethics committee at Shiraz University of Medical Sciences approved the study protocol. Methods and objectives of the study are described for the patients, and Informed consent was obtained from each patient. Inclusion criteria included best-corrected visual acuity 20/50 or better, Having unchanged refraction for at least six months, Not using the contact lens for at least a month before examination, and normal intraocular pressure (10mmHg < IOP < 20mmHg). At least six months have passed if crosslinking is done. Exclusion criteria were any systemic disease, history of trauma, or corneal injury. Each subject was refracted twice, from 7 to 10 days apart, by two optometrists. Each refraction was recorded as a sphere (diopter (D), negative cylinder (D) × axis (degree). If the difference between the two subjective refractions in the power of sphere or cylinder was more than 0.50 D or the astigmatism axis between two examinations was more than 5 degrees, the third examination was checked the patient' patients

eye and the best axis and power for $f \in d \in \text{the best - c or rected visual acuity was not checked, so } \leq \text{cted and rec or ded. If the } \Rightarrow \text{ence be}$

mean was recorded as the final subjective refraction axis. If performing an autorefraction was not possible because of keratoconic corneal abnormalities, the patient was excluded from the study. Topcon auto refractometer result was the starting point in subjective manifest refraction. The back vertex distance in the trial frame was adjusted to 12mm. The endpoint of refraction was the maximum positive lens with which the patient could see the best. Standard subjective techniques were used. In patients with lower visual acuity, the optometrists used larger steps of the lens in subjective refraction. In determining the astigmatism axis, higher power Jackson cross-cylinder and manual axis adjustment by the patient were used. During manual axis adjustment by the patient, we ask the patient to rotate the axis and hold the axis when the best vision is achieved. Cycloplegia was induced with three drops of Mydrax 1 % (tropicamide) within five minutes apart. Cycloplegia and pupil dilation were evaluated after 20 minutes. If the cycloplegia effect was not enough, a drop was administered again, and the patient rechecked 15 minutes later. Autorefraction was done by Topcon RM-8900 following complete cycloplegia. Autorefractometer repeated three times in each eye, and their mean was recorded as the final result. If an auto refractometer was not possible in the patient or the difference between repeated measurements was over 0.50D (in sphere and cylinder power) or more than 5 degrees in axis, the patient was excluded. Pentacam topographic photos were conducted with the patient's natural pupils under scotopic conditions by The Pentacam HR (Oculus; Optikgeräte GmbH, Wetzlar, Germany). During the repeated measurements, Participants remained positioned. The patients' eyes should be open and looked directly at the fixation target. Scans were performed in automatic mode. Only approved quality scans (quality specification graded as "OK") were saved. Two power and axis in astigmatism (front cornea and back cornea keratometry reading) were recorded from Pentacam data. In order to avoid the effect of cylinder axis when comparing refraction data from different optometrists, the following equations were used to convert spherocylindrical refraction to vector notation (M, J0, and J45)

$$J0 = -\frac{c}{2} \cos(2\alpha)$$

$$J45 = -\frac{c}{2} \sin(2\alpha)$$

$$M = S + \frac{c}{2}$$

Where M is the spherical lens equal to the spherical equivalent; S is the sphere; C is the negative cylindrical power; α is the axis; J0 is the Jackson cross-cylinder, axes at 180 degrees and 90 degrees; and J45 is the Jackson cross-cylinder, axes at 45 degrees and 135 degrees, representing oblique astigmatism.

Statistical Analysis:

Descriptive statistics were used to analyze qualitative and quantitative data. The Kolmogorov–Smirnov test was used to assess the normality of quantitative variables. Comparison of means from J0, J45, and M between manifest subjective refraction and cyclorefraction was performed by paired t-test. The agreement between other refraction measurements with subjective refraction as the gold-standard procedure was evaluated using intra-class correlation coefficient (ICC) for J0, J45, M, cylindrical power, and cylindrical axis. If two eyes of one person had keratoconus, we would select only one eye randomly. So only one eye from each individual was included in the ICC analysis. A correlation is considered excellent when the ICC values are between 0.8 to 1.00, good when the ICC values are between 0.61 to .80, moderate when the ICC values are between 0.41 to 0.6, and fair when the ICC values are below 0.40.

A generalized estimated equation (GEE) procedure was used to estimate the parameters of a generalized linear model between correlated outcomes. In this study, 64 eyes from 43 individuals were included, and the GEE method was used to evaluate which factors had a significant influence on the Discrepancy Between J0, J45, and Axis of Cyclorefraction and subjective Manifest Refraction. In order to calculate the degree of change in the cylindrical axis between Cyclorefraction and subjective Manifest Refraction, we reduced the astigmatism axis (cylindrical axis in cyclorefraction- cylindrical axis in subjective manifest refraction), and the absolute value was taken. If this value was below 90 degrees, it was recorded. If it was more than 90 degrees, it was subtracted from 180 degrees (180-|cylindrical axis in cyclorefraction- cylindrical axis in subjective manifest refraction) and recorded as cylindrical axis changes. The included factors were gender, age, cone location, Kmax, VAsc, VAcc, pupil diameter, Q-value, index of height asymmetry (IHA), and Center keratoconus-index (CK). The analysis of the data was carried out using SPSS software (Ver. 18.0). P-values less than 0.05 were regarded as statistically significant.

Results:

This study was performed on 43 patients (24 male, 19 female) by the mean age of 32 years old. Table 1 displays the mean (SD) of the cylinder, axis, J0, and J45 components with the autorefractor, cyclorefraction, subjective manifest refraction, anterior and posterior corneal astigmatism measured with Pentacam corneal topography. All 64 eyes in the study group were in stage III of keratoconus without scarring (staging classified according to the mean keratometry value of the Pentacam). The agreement analysis results between an autorefractor (Topcon) cycloplegic refraction, anterior and posterior cornea astigmatism with the subjective refraction, only one eye from each individual are shown in Table 2. 43 eyes from 43 keratoconus patients were enrolled in the agreement analysis. In order to avoid the effect of cylinder axis when comparing refraction data from two methods, we used vector analysis. As represented by subjective manifest refraction, spherical equivalent ranged from - 9.25 to + 0.50 D (mean SD, -2.93 2.49D). Excellent ICC values were found between auto refractometer and subjective refraction for cylindrical axis, J0, and J45 (Table 2). Based on these results, an excellent agreement was found between the astigmatism axis of subjective manifest refraction and auto refractometer (ICC: 0.943 P < 0.0001) compared to cycloplegic refraction (ICC: 0.710 P < 0.0001). Comparison of means from J0, J45, and M between manifest subjective refraction and cyclorefraction was performed by paired t-test. Data showed significant mean differences of J0 and J45 between manifest subjective refraction and cyclorefraction (mean difference: -0.62 P = 0.001) (mean difference: -0.39 P = 0.005). The mean dioptric difference of M between the cyclorefraction and manifest subjective refraction was not significant (P = 0.217). Gender, age, cone location, Kmax, VAsc,

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VAcc, pupil diameter, Q-value, index of height asymmetry (IHA), and Center keratoconus-index (CKI) were factors that were included in the multivariable analysis of J0, J45, and axis. The results of GEE analysis revealed that Corneal astigmatism, Q-value, IHA were detected as variables associated with both dioptric differences in J0, J45, and axis (Table3, Table4, Table5).

Table 1
Descriptive Statistics of Mean (SD) Values of demographic and pentacam topographic values

Type of measurement	Value(mean ± SD)
Age	31.96 ± 6.56
Gender	24 males (56 %) 19 females (44%)
VAsc	0.70 ± 0.36
VAcc	0.11 ± 0.13
Kmean	46.24 ± 3.18
Kmax	52.83 ± 5.58
Cone location (mm)	0.82 ± 0.32
Front correal astigmatism	4.98 ± 2.39
Pupil Diameter	4.28 ± 1.46
Q-value	-0.52 ± 0.45
Maximum front corneal keratometry	52.83 ± 5.58
IHA	23.39 ± 23.63
CKI	1.02 ± 0.03
VAsc: Visual Acuity without Correction ,VAcc: visual acuity with correction, Kmean: mean corneal keratometry, kmax:maximum corneal keratometry, Q-value: corneal aspherisity, IHA: index of height asymmetry, CKI:Center keratoconus-index	

Table 2
Intraclass-correlation coefficient between subjective refraction and cyclorefraction,front corneal astigmatism,back corneal astigmatism for cylindrical power, axis and the vector components of refraction J0 and J45

	Sub R & cyclo R	Sub R & Dry Auto	Sub R & front corneal ast	Sub R & back corneal ast
Cylinder Power	lcc:0.556 P < 0.0001	lcc:0.703 P < 0.026	lcc:0.513 P < 0.0001	lcc:0.06 P < 0.334
Cylinder Axis	lcc:0.710 P < 0.0001	lcc:0.943 P < 0.0001	lcc:0.543 P < 0.0001	lcc:0.480 P < 0.001
J0	lcc:0.809 P < 0.0001	lcc:0.972 P < 0.0001	lcc:0.543 P < 0.0001	lcc:0.153 P < 0.179
J45	lcc:0.832 P < 0.0001	lcc:0.827 P = 0.006	lcc:0.310 P < 0.029	lcc:0.225 P < 0.126
Sub R: Subjective refraction, cyclo R: cycloplegic Refraction, Dry Auto:Dry Autorefraction, front corneal ast: front corneal astigmatism, back corneal ast: back corneal astigmatism				

Table 3
Factors Associated With the Discrepancy Between J0 of Cyclorefraction and Manifest Refraction in Keratoconus Using Multivariable Regression Analysis

variable	B Coefficient	Chi Square	P
Gender as male	-0.46	0.06	0.80
Age	0.13	1.14	0.28
Corneal Astigmatism	0.66	10.17	0.001
VAcc	0.65	0.06	0.80
Cone location	0.68	0.37	0.54
Pupil diameter	2.10	9.40	0.002
Q-value	-4.91	47.78	P < 0.0001
Kmax	-0.52	14.37	P < 0.0001
IHA	0.04	8.02	0.005
VAcc: visual acuity with correction, Q-value: corneal asphericity, K-max: maximum corneal keratometry, IHA: index of height asymmetry			

Table 4
Factors Associated With the Discrepancy Between J45 of Cyclorefraction and Manifest Refraction in Keratoconus Using Multivariable Regression Analysis

variable	B Coefficient	Chi Square	P
Gender as male	0.39	4.86	0.02
Age	0.005	0.16	0.68
Corneal Astigmatism	0.11	10.76	0.001
VAcc	0.85	3.23	0.07
Cone location	0.66	1.03	0.31
Pupil diameter	-0.05	0.91	0.33
Q-value	1.01	33.77	P < 0.0001
Kmax	0.07	4.91	0.02
IHA	-0.03	106.76	P < 0.0001
VAcc: visual acuity with correction, Q-value: corneal asphericity, K-max: maximum corneal keratometry, IHA: index of height asymmetry			

Table 5
Factors Associated With the Discrepancy Between Axis of Cyclorefraction and Manifest Refraction in Keratoconus Using Multivariable Regression Analysis

variable	B Coefficient	Chi Square	P
Gender as male	-3.63	0.10	0.74
Age	-0.05	0.01	0.90
Corneal Astigmatism	-0.10	0.003	0.04
VAcc	-54.10	4.15	0.229
Cone location	-33.37	10.76	0.001
Pupil diameter	-7.41	1.81	0.17
Q-value	-3.73	0.19	0.65
Kmax	0.72	0.32	0.57
IHA	0.03	0.04	0.82
VAcc: visual acuity with correction, Q-value: corneal asphericity, K-max: maximum corneal keratometry, IHA: index of height asymmetry			

Discussion:

It was estimated that the best start point for the cylindrical part of refraction in the subjective test could be an auto refractometer in keratoconic patients. Cyclorefraction and manifest refraction lead to significantly different J0 and J45 results, and this difference increases as corneal astigmatism and Q-value increases.

In the estimation of the agreement between an autorefractor (Topcon), cycloplegic autorefractor, anterior and posterior corneal astigmatism with the subjective refraction, It can be seen from data that the maximum estimations of the agreement were found between the cylindrical measurement of an auto refractometer and subjective manifest refraction in cylindrical power(Icc:0.703, $P < 0.026$, cylindrical axis(Icc:0.943, $P < 0.0001$) and astigmatism vector analysis of J0(Icc:0.972, $P < 0.0001$) and J45(Icc:0.827, $P = 0.006$). Excellent ICC coefficient between cycloplegic autorefractor and subjective refraction was obtained for J0(Icc:0.809, $P < 0.0001$) and J45(Icc:0.832, $P < 0.0001$). Cycloplegic refraction usually plays an important role in the control of accommodation in clinical practice. A previous study reported that higher-order aberrations and pupil size play a significant role in the Accommodation stimulus-response function[6]. Some studies indicated that cycloplegic drops caused a statistically significant J0 vector astigmatic shift[7, 8]. The study showed that Cycloplegice cylindrical axis could not be a good starting point for refraction. It seems that corneal abnormality makes an effective Contribution to final astigmatism in keratonic patients. But according to our data, ICC coefficients for cylindrical power, axis, J0, and J45 between anterior corneal astigmatism and subjective refraction were not excellent. This could be caused by the sampling of keratoconus patients between possible candidates for intracorneal ring segment implantation. Most of them had asymmetrical cones, and the mean of their cone location was $0.82\text{mm} \pm 0.32$. Cyclorefraction and manifest refraction lead to significantly different J0 and J45 results.^[2] The previous study showed that the repeatability of refraction in keratoconus patients was substantially worse than in normal myopes[9]; this was probably due to further accommodative fluctuations or the additional blur resulting from corneal irregularities in keratoconic patients. Although accommodative fluctuations were controlled by cyclorefraction in our study, the difference between subjective manifest refraction and cyclorefraction was significant for astigmatic components (J0 and J45). These differences could be associated with corneal and pupillary changes for cycloplegic effects. We investigated which factors were associated with the difference between cycloplegic refraction and manifest refraction for J0 and J45. Front corneal astigmatism was associated for both J0 difference (B coefficient = 0.68, $P < 0.0001$) and J45 different (B coefficient = 0.89, $P < 0.0001$). If front corneal astigmatism was more, the dioptric difference was more J0 and J45. The values of asphericity (Q-value) described the geometry of the cornea. The studies reported that the normal anterior corneal Q-value ranges from -0.01 to -0.80[10]. Keratoconic patients usually showed more negative asphericity [11]. We found negative association between Q-value and J0 difference (B Coefficient = -3.42, $P = 0.004$) and positive association between Q-value and J45 difference (B Coefficient = 0.81, $P < 0.0001$). Our study showed that a negative association between Kmax and J0 difference was found (B coefficient = -0.37, $P = 0.025$), meaning that J0 difference was decreased with keratoconus severity. The previous study measured a significant M difference between auto refractometer and manifest refraction in keratoconic patients and showed Kmax was the only variable associated with M dioptric difference[2]. Positive association was found between best corrected visual acuity and J45 difference (B coefficient = 1.24 $P < 0.0001$).

corneal astigmatism (B Coefficient = 0.68), pupil diameter (B Coefficient = 1.64), Q-value (B Coefficient = -3.45), Kmax (B Coefficient = -0.37) and IHA (B coefficient + 0.04) were found to be variables associated with J0-difference and Gender (B Coefficient = 0.89), corneal astigmatism (B Coefficient = 0.15), VAsc (B Coefficient = 1.24), Q-value (B Coefficient = 0.81) and IHA (B Coefficient = -0.02) were found to be factors associated with J45 difference. If front corneal astigmatism was more, the dioptric difference was more in J0 and J45.

Cone location (B Coefficient = -33.37) and corneal astigmatism (B coefficient = -0.1) were found to be variables associated with axis-difference between Cyclorefraction and subjective manifest refraction. It can be predicted that the closer the keratoconus cone location relative to the center of the cornea and the lower the keratoconus patient's corneal astigmatism, the more the probability of axis changes by cycloplegic drop.

Declarations:

Funding:

None

Conflicts of interest/Competing interests:

None

Availability of data and material:

Data available upon reasonable request

Ethics approval:

This research was approved by the ethical board of shiraz university of medical sciences

Consent to participate:

informed consent was obtained from each subject after an explanation of the nature and possible consequences of the study.

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