

Comparison of effects of mydriatic drops (1% cyclopentolate and 0.5% tropicamide) on anterior segment parameters

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Purpose: The purpose of this study is to investigate and compare the effects of cyclopentolate and tropicamide drops on anterior segment parameters in healthy individuals. **Methods:** Two hundred and fifty-eight eyes of 129 healthy volunteers were included in this randomized clinical study. Cyclopentolate 1% drop was applied to 75 (58%) participants (group 1) and tropicamide 0.5% drop was applied to 54 (42%) participants (group 2). Flat keratometry (K1), steep keratometry (K2), axial length (AL), central corneal thickness (CCT), anterior chamber depth (ACD), white-to-white (WTW) distance, pupil diameter, total pupil offset and intraocular lens (IOL) power were measured before and after drops, using Lenstar 900 optical biometry. **Results:** The increase in CCT, ACD, pupil diameter, and pupil offset was significant in group 1 after the drop ($P < 0.05$), while the increase in ACD, pupil diameter, and pupil offset was significant in group 2 ($P < 0.05$). When the two groups were compared, there was no significant difference in K1, K2, CCT, ACD, WTW, pupil diameter, pupil offset, and IOL power (using Sanders–Retzlaff–Kraff T formula) changes after drops ($P > 0.05$), whereas the change in AL was significant ($P = 0.01$). **Conclusion:** The effects of cyclopentolate and tropicamide drops on anterior segment parameters were similar; they did not make significant changes in K1, K2, AL, WTW, and third-generation IOL power calculation. However, ACD values significantly changed after these drops; thus, measuring anterior segment parameters before mydriatic agents should be taken into account particularly for fourth-generation IOL formulas and phakic IOL implantation. The change in pupil offset, which can be important in excimer laser and multifocal IOL applications, was not clinically significant.

Key words: Anterior segment parameters, cyclopentolate, pupil offset, tropicamide

Mydriatic and cycloplegic drops are indispensable preparations used in ophthalmology clinic. They are often used to determine the refractive errors in pediatric patients and pupillary dilation for routine examinations. Today, the most commonly used mydriatic agents in the clinic are cyclopentolate and tropicamide. Cyclopentolate is a muscarinic receptor antagonist as atropine. It inhibits cholinergic stimulation of the sphincter muscle and ciliary muscle in the iris, causing pupil dilation and cycloplegia.^[1] Compared to atropine, effect of cyclopentolate starts and ends faster, and it has less side effects.^[1,2] The cycloplegia effect of topically used 1% cyclopentolate is seen after 30–45 min after application and continues for up to 24 h.^[3,4] Tropicamide also causes mydriasis and cycloplegia, since it is a muscarinic receptor antagonist like cyclopentolate. Although the cycloplegic effect of tropicamide is not as effective as cyclopentolate, it is used frequently for pupillary dilatation due to acting in a shorter time and having fewer side effects.^[5-7]

When the circular ciliary muscles contract during the accommodation, the zonules relax and the iris lens diaphragm comes forward, the thickness of the lens increases, and consequently the refractivity of the lens increases. In a study by Yuan *et al.*,^[8] changes in anterior segment parameters were observed due to the change in lens thickness and anterior

curvature of the lens during accommodation. When cycloplegic agents inhibited accommodation, it was observed that the lens thickness decreased, the lens moved backward, and anterior chamber depth (ACD) increased.^[9] Today, parallel to the developments in modern cataract surgery, the importance of anterior segment parameters and their accurate measurement are gaining importance. Therefore, the effects of mydriatics on the anterior segment parameters have been investigated in many studies. However, there is no study comparing pharmacological effects of these mydriatics (including topical cyclopentolate and tropicamide) on anterior segment parameters. On the other hand, with the advancement of technology and increase in the demand of achieving excellent results with the excimer laser and multifocal intraocular lenses (IOLs), the importance of pupil offset, another anterior segment parameter, has emerged. Yet, there is no study in the literature evaluating the effect of mydriatics agents on pupillary offset.

In this study, as a first in the literature, we aimed to investigate and compare the effects of 1% cyclopentolate and 0.5% tropicamide application on anterior segment parameters using Lenstar 900 optical biometry.

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Methods

This study was conducted in accordance with the rules of the Declaration of Helsinki and informed consent forms were obtained from the patients. Prior to the study, an institutional ethical approval was obtained.

The subjects included in the study were randomly selected from healthy subjects who applied to the outpatient clinic due to routine eye examination. Patients with refractive error between (−4.00) and (+2.00) D spherical power, (−3.00) and (+3.00) D cylindrical power and patients with 20/20 best-corrected visual acuity (BCVA) were included. Patients with previous history of ocular surgery, ocular surface problem, dry eye, pterygium, corneal scarring, keratoconus, primary open-angle glaucoma, closed-angle glaucoma, topical drug use, cataract, difficult fixation, rheumatoid arthritis, connective tissue disease, diabetes mellitus, thyroid disease, and systemic drug use were not included in the study.

Refraction, BCVA, anterior segment, and fundus examination were performed in all participants included in this study. Either cyclopentolate hydrochloride 1% (Sikloplejin, Abdi Ibrahim, Istanbul, Turkey) (group 1) or tropicamide 0.5% (Tropamid, Bilim, Istanbul, Turkey) (group 2) drops were applied to both eyes of the participants three times at 10-min intervals. Before and 45 min after the last drops, flat keratometry (K1), steep keratometry (K2), axial length (AL), central corneal thickness (CCT), ACD, white-to-white (WTW) distance, pupil diameter, IOL power according to SRK-T (Sanders–Retzlaff–Kraff T) formula, and total pupil offset values were examined using Lenstar LS 900 optical biometry (Haag-Streit AG, Switzerland). The measurements were taken three times by the same operator for each participant and the most reliable was selected according to Lenstar outcome. The total pupil offset value was calculated by taking the square root of the sum of the squares of the pupil offset values on the X and Y-axis [(total pupil offset = $\sqrt{X^2 + Y^2}$), where X is the horizontal pupil offset and Y is the vertical pupil offset].

For statistical evaluation, data were recorded to SPSS 21.0 (Statistical Package for the Social Sciences, IBM) and MedCalc (MedCalc Software version 12.3 bvba, Inc.). The normal distribution of the data was evaluated by Kolmogorov–Smirnov test. To compare the obtained data, Chi-square, paired-samples *t*, Mann–Whitney *U*, and Kruskal–Wallis tests were used. The correlation between the measurements was evaluated by the Pearson correlation analysis. Evaluations were made within 95% confidence interval and *P* value less than 0.05 was considered statistically significant. Power analysis was performed using G* Power 3.1 program^[10] to determine the sample size necessary to give statistical reliability.

Results

In this study, 258 eyes of 129 healthy volunteers were included. Cyclopentolate drops were applied to 75 (58%) participants (group 1) and tropicamide drops were applied to 54 (42%) participants (group 2). The mean age of group 1 and group 2 participants was 34.71 ± 17.1 (10–63) and 30.67 ± 16.9 (10–66) years, respectively. Group 1 included 21 male (28%) and 54 female (72%) participants (ratio: 1:2.6) and group 2 included 18 male (33%) and 36 female (67%) participants (ratio: 1:2). There was no statistically significant difference between the two groups in terms of age and sex ($P = 0.05$, $P = 0.21$). Significant power was demonstrated for all groups ($P > 0.9$).

Tables 1 and 2 show the average K1, K2, AL, CCT, ACD, WTW distance, pupil diameter and total pupil offset values

before and after drops in groups 1 and 2, respectively. After drop, CCT, ACD, pupil diameter, and total pupil offset values were significantly increased in group 1 ($P < 0.05$), whereas in group 2, ACD, pupil diameter, and total pupil offset values were significantly increased ($P < 0.05$). The comparison of the change in anterior segment values between the two groups after the drop is given in Table 3. While there was no significant difference between K1, K2, CCT, ACD, WTW distance, pupil diameter, and total pupil offset changes in both groups after drop ($P > 0.05$, Table 3), AL was significantly lower after drop in group 2 compared to group 1 [$P = 0.014$, Table 3]. When we investigated the effects of both drops on IOL calculation, we found no significant change in IOL after drop in both groups according to SRK-T formula [$P > 0.05$, Table 4], and also no significant difference was observed between groups [$P = 0.79$, Table 5]. The 0.50-D change according to SRK-T formula was 34 (23%) eyes and 18 (17%) eyes in groups 1 and 2, respectively. None of the patients had a 1-D or greater change in IOL calculation after drop.

Table 6 shows the comparison of the changes in the anterior segment parameters of the patients after drops according to the decades between group 1 and group 2. There was no difference between the two groups in K1, K2, AL, CCT, ACD, WTW distance, and pupil offset changes in all decades. The pupillary dilatation was more in group 2 than in group 1 in the first and third decades ($P < 0.05$); however, the dilatation was similar between the groups in the second, fourth, and fifth decades ($P > 0.05$).

Discussion

In modern cataract and refractive surgery applications, anterior segment parameters have a critical importance in determining the indication and results of surgery. Therefore, accurate measurement of anterior segment parameters, repeatability of these measurements, or determination of the factors affecting these measurements has always been a subject of research. In this study, we aimed to show the effects of 1% cyclopentolate and 0.5% tropicamide drops on the K1, K2, AL, CCT, ACD, WTW, PD, total pupil offset, and IOL power measured by Lenstar 900 biometry device. Besides, we compared the effects of the two drops on these parameters.

Optical biometry devices such as Lenstar and IOL Master have been shown to be accurate, reliable, and reproducible.^[11–13] Anterior segment measurements of cataract patients are usually performed when the pupil is dilated on the same first examination day. There are many studies investigating the effect of pupillary dilatation on biometric parameters. Huang *et al.*^[14] showed that cycloplegia affects ACD and WTW distance but does not affect AL and keratometric values. In a study by Ozcaliskan *et al.*,^[15] there was no significant change in AL, K1, K2, and WTW distance values after pupil dilatation; however, ACD, aqueous depth, and increase in CCT were significantly changed. Higashiyama *et al.*^[16] observed an increase in ACD and lens thickness in pediatric patients after cycloplegia via SS-OCT biometric measurements. On the other hand, Ferrer-Blasco *et al.*^[13] did not observe a change in AL, CCT, WTW distance, K1, and K2 values in biometric measurements during accommodation, while the lens thickness increased and the ACD decreased. In accordance with most of these studies in the literature, in our study, there was no significant change in K1, K2, AL, WTW distance after cyclopentolate drop, and K1, K2, AL, CCT, WTW distance after tropicamide drop; whereas CCT and ACD increase after cyclopentolate drop and ACD increase after tropicamide drop were significant. When the effects of both drops were compared, the mean AL measured after tropicamide was significantly lower.

Table 1: Anterior segment parameters of group 1 before and after drop

	Before drop	After drop	P
K1 (D)	43.10±1.6 (39-47)	43.10±1.5 (39-47)	0.77
K2 (D)	44.06±1.6 (40-47)	44.07±1.6 (40-47)	0.23
AL (mm)	23.39±0.86 (21.7-25.6)	23.39±0.87 (21.7-25.6)	0.50
CCT (µm)	541±31 (476-633)	543±31 (479-608)	<0.001
ACD (mm)	2.92±0.37 (2.18-3.74)	3.04±0.35 (2.30-3.95)	<0.001
WTW (mm)	12.05±0.44 (11.04-13.49)	12.06±0.44 (11.05-13.17)	0.54
Pupil diameter (mm)	4.99±0.96 (3.29-7.27)	7.65±0.84 (4.36-9.55)	<0.001
Pupil offset	0.28±0.13 (0.04-0.91)	0.33±0.14 (0.11-0.87)	<0.001

K1: Flat keratometry, K2: Steep keratometry, D: Diopter, AL: Axial length, CCT: Central corneal thickness, ACD: Anterior chamber depth, WTW: White-to-white measurement. Bold number indicates a statistically significant difference with a p-value less than 0.05

Table 2: Anterior segment parameters of group 2 before and after drop

	Before drop	After drop	P
K1 (D)	44.02±1.4 (40-46)	43.16±1.4 (39-46)	0.05
K2 (D)	44.02±1.4 (40-46)	43.98±1.4 (40-46)	0.16
AL (mm)	23.63±0.89 (21.9-26.17)	23.61±0.89 (21.9-26.17)	0.08
CCT (µm)	549±31 (483-617)	550±31 (489-620)	0.24
ACD (mm)	2.99±0.37 (2.17-3.93)	3.07±0.38 (2.25-3.96)	<0.001
WTW (mm)	12.14±0.42 (10.93-13.03)	12.15±0.43 (10.92-13.05)	0.72
Pupil diameter (mm)	4.90±0.85 (3.21-6.91)	7.76±0.86 (5.98-9.40)	<0.001
Pupil offset	0.22±0.09 (0.04-0.45)	0.28±0.08 (0.05-0.57)	<0.001

K1: Flat keratometry, K2: Steep keratometry, D: Diopter, AL: Axial length, CCT: Central corneal thickness, ACD: Anterior chamber depth, WTW: White-to-white measurement. Bold number indicates a statistically significant difference with a p-value less than 0.05

Table 3: Change in anterior segment values of group 1 and group 2 before and after drop

	Group 1	Group 2	P
ΔK1 (D)	0.04±0.18	-0.04±0.24	0.75
ΔK2 (D)	-0.02±0.2	-0.03±0.21	0.56
ΔAL (mm)	0.005±0.09	-0.02±0.11	0.014
ΔCCT (µm)	2.39±4.64	1.28±10.67	0.27
ΔACD (mm)	0.12±0.13	0.08±0.12	0.05
ΔWTW (mm)	0.006±0.12	0.003±0.09	0.66
ΔPupil diameter (mm)	2.65±0.76	2.85±0.86	0.06
ΔPupil offset (mm)	0.05±0.09	0.05±0.09	0.506

Group 1: Cyclopentolate applied eyes, Group 2: Tropicamide applied eyes, K1: Flat keratometry, K2: Steep keratometry, D: Diopter, AL: Axial length, CCT: Central corneal thickness, ACD: Anterior chamber depth, WTW: White-to-white measurement. Bold number indicates a statistically significant difference with a p-value less than 0.05

Table 4: IOL power calculated according to SRK-T before and after drops in group 1 and group 2

Groups	Calculation method	Before drop	After drop	P
Group 1	SRK-T	20.48±3.15 (18.00-24.50)	20.78±1.99 (17.50-24.50)	0.86
Group 2	SRK-T	20.20±1.85 (17.00-24.00)	20.20±1.85 (17.50-24.00)	0.99

SRK-T: Sanders-Retzlaff-Kraff T

In our study, the significant increase in CCT after cyclopentolate drop was 2 µm, which was not clinically

important. In contrast to our study, a previous study with using IOL Master 700 showed a significant increase in CCT after tropicamide application,^[17] whereas in another study, there was no significant change in CCT after mydriatics drops.^[18] Zeng *et al.*^[19] explained the increase in CCT after phenylephrine drops by the damaging effect of the drop to the epithelial integrity causing corneal edema. In our study, we can also explain the increase in CCT after cyclopentolate drop by this mechanism.

In our study, the other anterior segment parameter that significantly changed after cyclopentolate or tropicamide drop application was ACD, which is an important parameter particularly in anterior or posterior chamber phakic IOL implantations.^[20,21] Therefore, with this study, it can be concluded that it is important to perform ACD measurements before pupil dilatation in patients who are planned to undergo phakic IOL implantation.

In a previous study, there was no significant change in WTW distance values after pupil dilation with cyclopentolate.^[15] Differently, Arriola-Villalobos *et al.*^[17] demonstrated a significant change in WTW distance values before and after pupil dilatation with tropicamide. WTW distance can be measured on digital photo images obtained with the Lenstar 900 and the IOL Master 700. They give us the WTW distance value by taking advantage of the rapid contrast difference between limbus in pale color appearance and cornea in dark color appearance. Therefore, the quality and brightness of the image may affect the measurement.^[15] In our study, no significant change in WTW distance values was observed after pupil dilatation with both cyclopentolate and tropicamide.

Besides the above measurements, in our study, the effect of pupil dilatation on pupil offset was evaluated for the first time in the literature. Pupillary offset is the parameter that

indirectly gives us the lambda angle between the pupillary axis and the visual axis. Pupil offset is the value of how much

the pupil center deviates from the patient’s point of view while the patient is looking at the center point of the topography device.^[22] As the general approach in the excimer laser, the corneal vertex is taken as the reference to the ablation center, while the pupil center is the reference in the wavefront-guided laser system.^[22] In multifocal IOL implantation, pupil offset is generally preferred to be lower than 0.4 mm.^[23,24] In our study, total pupil offset increased significantly in both cyclopentolate and tropicamide applied eyes; however, the change can be acceptable not clinically significant.

Table 5: Change in IOL according to SRK-T before and after drop of group 1 and group 2

	Group 1	Group 2	P
ΔSRK-T	0.003±0.24 (-0.50)-(+0.50)	0.007±0.26 (-0.50)-(+0.50)	0.79

SRK-T: Sanders-Retzlaff-Kraff T

Table 6: Change in anterior segment parameters after drop according to age decades

Decades	Parameters	Group 1	Group 2	P
First decade (10-20 years), n=80	ΔK1 (D)	-0.02±0.13	-0.05±0.25	0.575
	ΔK2 (D)	0.02±0.17	-0.02±0.25	0.382
	ΔAL (mm)	0.004±0.02	-0.004±0.02	0.112
	ΔCCT (μm)	1.15±2.70	1.66±3.47	0.475
	ΔACD (mm)	0.09±0.05	0.08±0.06	0.608
	ΔWTW (mm)	0.02±0.14	0.019±0.09	0.884
	ΔPupil diameter (mm)	2.4±0.79	3.06±0.97	0.004
	ΔPupil offset	0.01±0.09	0.04±0.07	0.275
Second decade (20-30 years), n=42	ΔK1 (D)	-0.03±0.13	0.01±0.10	0.168
	ΔK2 (D)	-0.05±0.20	-0.01±0.16	0.582
	ΔAL (mm)	-0.004±0.01	-0.01±0.02	0.299
	ΔCCT (μm)	2.09±5.70	1.22±3.13	0.567
	ΔACD (mm)	0.14±0.06	0.12±0.07	0.584
	ΔWTW (mm)	-0.02±0.08	0.016±0.07	0.648
	ΔPupil diameter (mm)	2.63±0.93	2.75±0.64	0.131
	ΔPupil offset	0.07±0.14	0.03±0.09	0.140
Third decade (30-40 years), n=30	ΔK1 (D)	-0.05±0.10	0.005±0.12	0.185
	ΔK2 (D)	-0.03±0.15	-0.02±0.13	0.728
	ΔAL (mm)	-0.02±0.06	-0.001±0.04	0.980
	ΔCCT (μm)	3.31±4.25	3.66±3.65	0.888
	ΔACD (mm)	0.17±0.16	0.14±0.07	0.594
	ΔWTW (mm)	-0.04±0.06	-0.02±0.11	0.592
	ΔPupil diameter (mm)	2.61±0.87	3.25±0.75	0.048
	ΔPupil offset	0.05±0.10	0.12±0.11	0.280
Fourth decade (40-50 years), n=48	ΔK1 (D)	0.06±0.25	-0.05±0.14	0.184
	ΔK2 (D)	0.03±0.28	-0.04±0.13	0.464
	ΔAL (mm)	-0.002±0.02	-0.01±0.01	0.186
	ΔCCT (μm)	3.04±3.79	2.46±3.46	0.804
	ΔACD (mm)	0.12±0.16	0.06±0.11	0.339
	ΔWTW (mm)	-0.01±0.07	0.02±0.08	0.275
	ΔPupil diameter (mm)	4.30±0.50	4.37±0.71	0.562
	ΔPupil offset	0.07±0.08	0.05±0.06	0.539
Fifth decade and above (50-66 years), n=58	ΔK1 (D)	-0.01±0.08	-0.001±0.10	0.815
	ΔK2 (D)	-0.06±0.17	0.03±0.34	0.938
	ΔAL (mm)	0.04±0.02	-0.003±0.01	0.771
	ΔCCT (μm)	2.82±4.49	0±4.51	0.246
	ΔACD (mm)	0.12±0.15	0.07±0.08	0.697
	ΔWTW (mm)	0.01±0.14	0.01±0.07	0.836
	ΔPupil diameter (mm)	2.77±0.59	2.70±0.55	0.195
	ΔPupil offset	0.05±0.07	0.08±0.10	0.324

Group 1: Cyclopentolate applied eyes, Group 2: Tropicamide applied eyes, K1: Flat keratometry, K2: Steep keratometry, D: Diopter, AL: Axial length, CCT: Central corneal thickness, ACD: Anterior chamber depth, WTW: White-to-white measurement. Bold number indicates a statistically significant difference with a p-value less than 0.05

The main parameters of third-generation formulas commonly used in IOL calculation are K1, K2, and AL.^[25,26] In our study, since pupil dilatation did not affect these parameters, there was no significant change in IOL power calculated by SRK-T (≤ 0.5 D). In cyclopentolate and tropicamide applied eyes, the 0.5-D change after drop was 23%, 17% according to SRK-T formula. In accordance with our study, in other studies, it was observed that there was no significant change in K1, K2, and AL after pupillary dilatation and therefore did not affect third-generation IOL formulas.^[15,17] In a study by Heatley *et al.*,^[27] the calculation of IOL with IOL Master after pupil dilation showed a 12% change between 0.50 and 1.0 D and a 4% change between 1.0 and 2.0 D according to the SRK-T formula. According to SRK-T formula in the IOL calculation measured with Lenstar after pupil dilatation, the change between 0.50 and 1.0 D was 9.1%,^[28] however, Arriola-Villalobos *et al.*^[18] showed no change of 1.0 D and above, and the change between 0.50 and 1.0 D was 6.9%. In another study, it was found that there were no significant changes in the thickness of the ACD, WTW distance, and lens thickness after pupil dilation; however, the change between 1 and 2 D was 5% and between 0.50 and 1.0 D was 27%, according to the formula Holladay 2.^[17] In the light of all these results, it can be concluded that pupil dilation does not have a significant effect in the IOL calculation when third-generation formulas, such as SRK-T, are used; however, it may affect the results when fourth-generation formulas, such as Holladay 2, are used. In our study, Holladay 2 formula could not be calculated due to the inability to measure the lens thickness, which can be considered as a limitation of our study.

The comparison of the effects of cyclopentolate and tropicamide drops was investigated as a first time in our study and it was shown that the effects of these two drops in anterior segment measurements (other than AL) and pupil diameter were similar. The difference in AL has also no significant clinical effect. Therefore, 0.5% tropicamide, which has less systemic side effects and shorter duration compared to 1% cyclopentolate, could be preferred for pupillary dilatation.

Conclusion

In conclusion, it was observed that cyclopentolate and tropicamide did not make a significant change in most of the anterior segment parameters (K1, K2, AL, CCT, WTW) and therefore did not affect the third-generation IOL calculation; however, there was a significant change in ACD. For this reason, in the phakic IOL implantation and use of fourth-generation IOL formulas, anterior segment measurements should be performed before the mydriatic drop application. On the other hand, the change in pupil offset, which can be important in excimer laser and multifocal IOL applications, was not clinically significant.

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Conflicts of interest

There are no conflicts of interest.

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