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Effect of repeated peribulbar triamcinolone injection on corneal topography in patients with thyroid eye disease

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Abstract

Introduction

Studies have shown that repeated peribulbar triamcinolone injections reduce the inflammatory signs of moderate to severe thyroid eye disease (TED). Other studies found that TED was associated with greater with-the-rule corneal astigmatism owing to fibrosis of the soft tissue in the superolateral orbital region. This study aimed to detect the effect of repeated peribulbar triamcinolone injections in patients with moderate to severe TED on corneal topography and astigmatism.

Patients and methods

A prospective, controlled, and randomized study was conducted that included 30 eyes with moderate to severe TED who underwent repeated peribulbar triamcinolone injections in addition to pretreatment and posttreatment corneal topography using Occulus Pentacam. The patients received repeated peribulbar injections of 20-mg triamcinolone acetate (40 mg/ml) for four doses with a 1-week interval.

Results

On a comparison between pretreatment and posttreatment corneal topographic measures, it revealed a highly statistically significant difference between pretreatment and posttreatment results according to K-max and Pentacam astigmatism. In contrast, the Pentacam astigmatism axis and central corneal thickness by Pentacam show a statistically insignificant difference between preinjection and postinjection periods. A comparison between the mean difference of pretreatment and posttreatment refraction showed a statistically significant difference between both according to mean differences of the cylinder.

Conclusion

A significant change in corneal curvature occurs after repeated peribulbar injection of triamcinolone acetate in patients with TED. The amount of this change in corneal curvature is sufficient to change the posttreatment refraction of the eye.

Keywords: Corneal topography, repeated peribulbar triamcinolone injection, thyroid eye disease

Introduction

Thyroid eye disease (TED) refers to a pathological autoimmune condition, resulting in a pronounced thickening and orbital fat and fibrosis of extraocular muscles [1].

T helper 1-type CD4+ T cells are the dominant inflammatory cells and promote the recruitment of new fat cells [2].

Multiple surgical options are there for treatment. Elective orbital decompression surgery can be done in patients with cosmetically inappropriate proptosis, whereas emergency orbital decompression surgery may be required when blinding symptoms occur or are about to occur [3]. Each of these invasive tactics has its own threats and unforeseen complications [4].

Studies have shown that repeated peribulbar triamcinolone injections reduce the inflammatory signs of moderate to severe TED [5]. Besides, Mombaerts *et al.* [6] showed that TED was associated with greater with-the-rule corneal astigmatism.

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To the best of our knowledge, no reported study has evaluated changes in corneal astigmatism using corneal topography after repeated triamcinolone peribulbar injections as an alternative to surgery.

Aim

This study aimed to detect the effect of repeated peribulbar triamcinolone injections in patients with moderate to severe TED on corneal topography and astigmatism.

Patients and Methods

The population of study and disease condition

This is a prospective, controlled, and randomized study that included 30 eyes with moderate to severe TED who underwent repeated peribulbar triamcinolone injections in addition to pretreatment and posttreatment corneal topography using Occulus Pentacam. Corneal topographic parameters analyzed were total astigmatism, steepest axis, central corneal thickness (CCT), and anterior chamber depth.

Moderate TED was considered in patient's recent occurrence of motility dysfunction (diplopia) and/or increased proptosis, with computed tomography scan reported muscle enlargement, or in patients with active ophthalmopathy (clinical activity score: ≥4). Severe TED has been identified as a vision-threatening condition (optical neuropathy or corneal ulceration detected by eye examination).

The patients were allocated from the outpatient clinic. The study was revised and approved by the Ophthalmology Department, and tenets of the Declaration of Helsinki were respected.

All patients' demographic data were recorded: age, sex, and medical problems.

Age ranged from 20 to 46 years, with a mean ± SD of 29.80 ± 7.74. Concerning sex, eight (26.7%) of the eyes were for males, whereas 22 (73.3%) were for females (Fig. 1), and 53.3% of the eyes studied were right eyes and 46.7% were left (Fig. 2).

Inclusion criteria included the following:

(1) Moderate to severe TED.

Exclusion criteria included the following:

(1) Young patients less than 18 years of age.
(2) Previous ocular surgery.
(3) Corneal opacities or irregularities.
(4) Uncontrolled thyroid functions.

All patients were subjected to complete ophthalmological examination, including the following:

(1) Ophthalmic history.
(2) Refraction and assessment of best-corrected visual acuity (BCVA) using Autorefractometer and Snellen's letters at 6 m, respectively.
(3) Anterior segment evaluation using the slit lamp.
(4) Fundus examination using indirect ophthalmoscopy and slit-lamp biomicroscopy using +90 D Aspheric Volk Optical Lens.
(5) Assessment of intraocular pressure (IOP) using Goldmann's applanation tonometry before treatment and 3 months after treatment.
(6) Assessment of degree of proptosis using Hertel exophthalmometry before treatment and 3 months after treatment.
(7) Corneal topographic imaging using Occulus Pentacam (at least five scanning procedures were performed for each eye and the best quality images were chosen for analysis).
    (a) Total astigmatism amplitude in the 3- and 5-mm zone.
    (b) Steepest axis in the 3- and 5-mm zone.
    (c) CCT.

The related change in astigmatism was defined as a change in cylinder power of at least 0.2 D or a proper rotation of the axis, defined as a change of more than 10°, as smaller variations typically do not affect visual acuity. All eyes with TED were subjected to the following:

(1) Corneal topography before treatment and 3 months after treatment.
(2) Hertel exophthalmometry before treatment and 3 months after treatment.
(3) IOP measurement before treatment and 3 months after treatment.

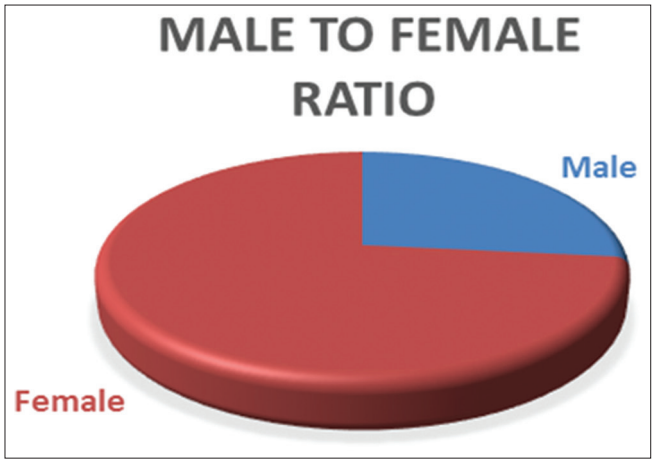

Figure 1: Pie chart showing sex incidence among the study group.

Figure 2: Pie chart showing laterality among the study group.

Method applied

The patients received repeated peribulbar injections of 20-mg triamcinolone acetate (40 mg/ml) for four doses with a 1-week interval.

The injections were carried out in the operation theater using 0.5 ml of a 40 mg/ml triamcinolone acetate solution applied in orbit at the inferolateral and superomedial quadrants injected using 23-G syringes, under topical anesthesia and complete sterile conditions (Fig. 3).

Patients had frequent ophthalmic tests during the follow-up analysis. Full pretreatment and posttreatment tests have been carried out and whenever appropriate. Thyroid drugs, regulated by our Department of Endocrinology, have not changed during the study period. Patients have been tracked for an average of 12 months, whereas our reports have been taken for 3 months following treatment.

Results

This study comprised 30 human eyes for 22 patients (22 women and eight men), with a mean ± SD age of 29.80 ± 7.74 years (range, 20–46 years). A total of 26 patients were considered to have a moderate disease and four to have severe Graves' ophthalmopathy.

Pretreatment complaint and signs

The main complaints of the patients were recorded to show 100% cosmetic appearance in the study group, in addition to diplopia, with 13.3% incidence, and corneal ulcers, with only 13.3% among the patients (Table 1).

Other signs such as EOM state (extra ocular muscles), corneal exposure, and optic neuropathy were reported for both study groups to reveal the following: concerning EOM state, two (6.7%) eyes showed medial rectus, whereas another two (6.7%) eyes showed both inferior and medial recti involvement.

Reported corneal exposure was found to include six (20.0%) eyes in the mild stage in the form of mild superficial corneal infiltrations, whereas only four (13.3%) were in the severe degree in the formation of corneal ulcerations and recurrent erosions.

None of our patients in this study had shown signs of optic neuropathy (Table 2).

Visual acuity

Patients showed to have mean ± SD BCVA before treatment of 0.56 ± 0.31 and after treatment of 0.62 ± 0.31, with a mean ± SD difference of 0.06 ± 0.05 (Fig. 4). Statistically insignificant values were recorded according to the mean differences between pretreatment and posttreatment BCVA (Table 3).

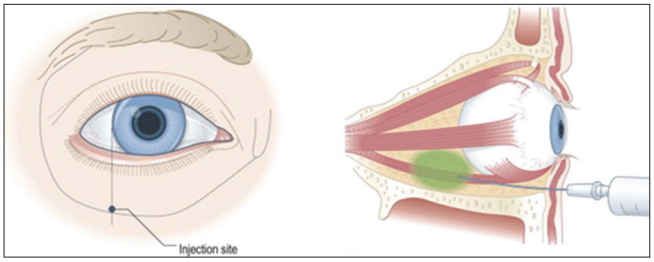

Figure 3: Technique for peribulbar injection of Triamcenolone Acetate.

Intraocular pressure

The patients showed a mean ± SD pretreatment IOP of 16.73 ± 3.45, whereas the mean ± SD postoperative IOP was 15.60 ± 3.11 (Fig. 5). A highly statistically significant difference ($P < 0.001$) was revealed for the difference between pretreatment and posttreatment IOP (Table 4).

Table 4 shows a highly statistically significant difference between pretreatment and posttreatment IOP.

Hertel's exophthalmometer

The mean degree of proptosis measured by Hertel's exophthalmometer before treatment showed a mean ± SD of 24.87 ± 1.85, whereas after treatment of 22.33 ± 2.02 (Figs. 6 and 7), with a highly statistically significant difference between pretreatment and posttreatment results according to Hertel's exophthalmometer ($P < 0.001$) (Table 5).

Refraction

Pretreatment refraction showed a mean ± SD sphere of 2.75 ± 3.17 and a cylinder of 2.03 ± 1.31 with axis of 58.0 ± 69.87 (Table 6). In contrast, posttreatment refraction showed a mean ± SD sphere of 2.50 ± 3.35 and cylinder of 1.20 ± 0.80, with axis of 68.57 ± 68.09 (Table 7).

Plotting the comparison between the mean difference of pretreatment and posttreatment refraction in each group showed a statistically significant difference between both according to mean differences of the cylinder. However, statistically

Table 1: Different complaints among the study group

Complaints	Patients (n=30) [n (%)]
Corneal ulcers	4 (13.3)
Diplopia	4 (13.3)
Cosmetic	30 (100.0)

Table 2: Pretreatment EOM state, corneal exposure, and optic neuropathy among the study group

Preoperative signs	Study group (n=30) [n (%)]
EOM state	
IR++	0
MR++	2 (6.7)
MR++IR++	2 (6.7)
None	26 (86.7)
Corneal exposure	
+	6 (20.0)
++	4 (13.3)
None	20 (66.7)
Optic neuropathy	
+	0
++	0
+++	0
None	30 (100.0)

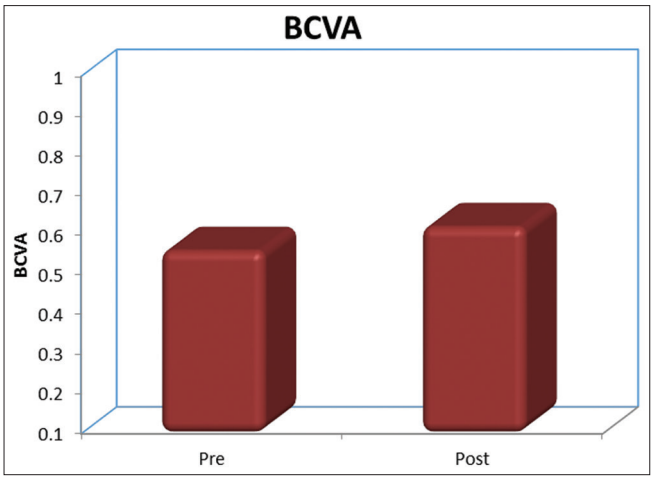

Figure 4: Bar chart between pre and postoperative according to BCVA.

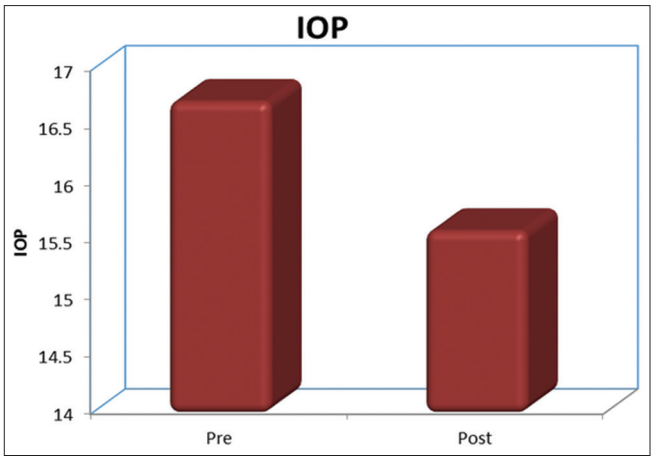

Figure 5: Bar chart between pre and postoperative according to IOP.

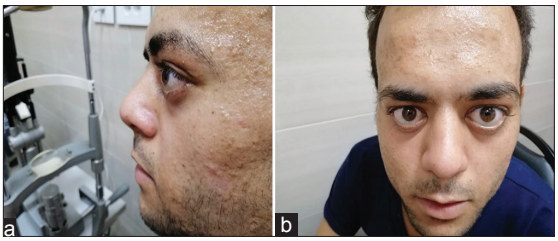

Figure 6: (A) and (B) showing a patient pre and post injection respectively.

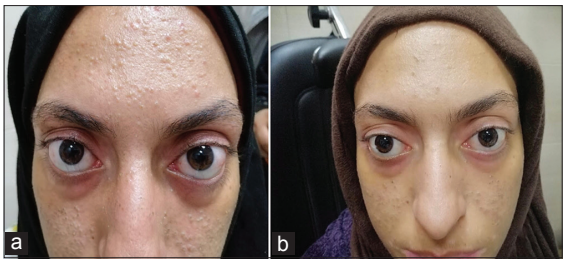

Figure 7: (A) and (B) showing a patient pre and post injection respectively.

Table 3: Comparison between pretreatment and posttreatment results according to best-corrected visual acuity (this table shows a statistically insignificant difference according to the mean difference between pretreatment and posttreatment best-corrected visual acuity)

BCVA	Study group ($n=30$)	*t* test	*P*
Pretreatment			
Mean±SD	0.56±0.31	27.666	
Range	0.2-1.0		
Posttreatment			
Mean±SD	0.62±0.31	26.565	
Range	0.2-1.0		
Difference			
Mean±SD	0.06±0.05	0.039	0.846
Range	0-0.1		

BCVA, best-corrected visual acuity; *t* test; *t* independent sample. $P>0.05$ (nonsignificant). $^{**}P<0.001$ (highly significant).

insignificant differences concerning the mean difference of sphere refraction and cylinder axis were revealed (Table 8).

Corneal topography

The K-max measured with Pentacam showed a mean ± SD of 43.87 ± 2.07 and 43.29 ± 1.99 before operatively and after operatively, respectively, whereas Pentacam astigmatism was 2.19 ± 1.40 before treatment and 1.41 ± 0.93 after treatment. However, astigmatism axis showed a mean of 79.67 ± 74.99 before treatment and 62.67 ± 65.87 after treatment. Moreover, the CCT was 522.93 ± 26.52 before treatment and 523.13 ± 26.71 after treatment (Table 9).

Table 9 shows a highly statistically significant difference between pretreatment and posttreatment findings according to K-max and Pentacam astigmatism. In contrast, the Pentacam astigmatism axis and CCT by Pentacam showed a statistically insignificant difference between before and after injection findings.

On the comparison between pretreatment and posttreatment corneal topographic measures, it revealed a highly statistically significant difference between pretreatment and posttreatment results according to K-max (Fig. 8) and Pentacam astigmatism (Fig. 9). In contrast, the Pentacam astigmatism axis and CCT by Pentacam showed a statistically insignificant difference between before and after injections.

Discussion

In this study, we compared the pretreatment and posttreatment corneal topographic measurements, reporting the effect of peribulbar repeated injections of triamcinolone acetate. However, little is known about the improvements in corneal astigmatism and topography following orbital decompression surgery. Furthermore, to the best of our knowledge, no recorded research studies have examined corneal astigmatism improvements using corneal topography following repeated injections of triamcinolone peribulbar as an alternative to surgery.

Table 4: Comparison between pretreatment and posttreatment results according to intraocular pressure in the study group

Study group	Pretreatment	Posttreatment	Difference	*t* test	*P*
IOP	16.73±3.45	15.60±3.11	1.13±0.92	4.795	<0.001**

IOP, intraocular pressure; *t* test; *t* paired sample. **P*<0.05 (significant). ***P*<0.001 (highly significant).

Table 5: Comparison between pretreatment and posttreatment results according to Hertel's exophthalmometer in the study group (this table shows a highly statistically significant difference between pretreatment and posttreatment results according to Hertel's exophthalmometer)

Study group	Pretreatment	Posttreatment	Difference	*t* test	*P*
Hertel's exophthalmometer	24.87±1.85	22.33±2.02	2.53±0.92	10.717	<0.001**

t test; *t* paired sample. **P*<0.05 (significant). ***P*<0.001 (highly significant).

Table 6: Pretreatment refraction among the study group

Prerefraction	Study group
Sphere	
Mean±SD	2.75±3.17
Range	0.25-10
Cylinder	
Mean±SD	2.03±1.31
Range	0.25-4.25
Axis	
Mean±SD	58.00±69.87
Range	0-180

Table 7: Posttreatment refraction among the study group

Posttreatment refraction	Group B (*n*=15)
Sphere	
Mean±SD	2.50±3.35
Range	0-11.25
Cylinder	
Mean±SD	1.20±0.80
Range	0.25-2.75
Axis	
Mean±SD	64.57±68.09
Range	5-180

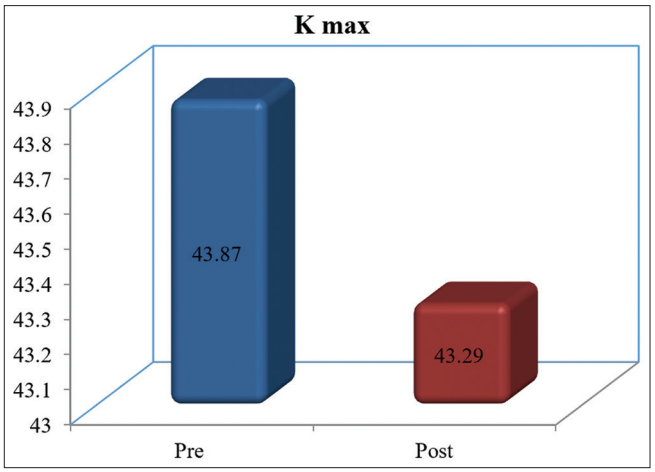

Figure 8: Bar chart between pre and post injection according to K max.

Our data clearly showed that repeated peribulbar injections of triamcinolone in patients with TED significantly affect corneal curvature, resulting in a significant change in corneal curvature after the injections. Furthermore, we showed that peribulbar injection as an alternative to surgery affected IOP and exophthalmometry values.

The cornea is considered to have strong elastic and viscoelastic properties. As a consequence, external forces or stress can affect corneal topography and astigmatism. Lieberman and Grierson [7] have shown that corneal topographical changes occur not only after surgery that affects the anterior portion of the eye, such as corneal surgery explicitly, but also after postpartum surgery, such as vitreoretinal surgery, including scleral folding or extraocular muscle surgery.

Similarly, Bordaberry *et al*. [5] concluded that repeated peribulbar triamcinolone injections reduce the inflammatory signs of moderate TED, as measured by the clinical activity score, and could also be used as an alternative treatment for surgery in TED, and subsequently, in 2015, Kim *et al*. [8] performed a study mapping the effect of TED orbital decompression surgery on corneal topography, finding that there were substantial improvements in corneal astigmatism following orbital decompression surgery. These changes were likely to influence the optical function of the cornea as there were significant changes in the steepest axis in the 3-mm region between the decompression group and the control group. A review of the related changes in astigmatism found that there was a prevailing tendency to incyclotor the steepest axis of the eyes undergoing decompression surgery. Thus, it was apparent that peribulbar injection may affect the corneal topography in a way just like its alternative (surgical decompression) does.

Similarly, our study concluded a highly statistically significant difference between pretreatment and posttreatment measurements according to K-max and Pentacam astigmatism, whereas Pentacam astigmatism axis and CCT by Pentacam

showed a statistically insignificant difference between pretreatment and posttreatment measurements, revealing significant changes in corneal astigmatism amplitude only but not axis, unlike the orbital decompression that was previously shown by Kim and colleagues to affect both amplitude and axis of astigmatism.

Ebner *et al.* [9], in a study to evaluate the efficacy of periocular triamcinolone acetate for the treatment of TED and the presence of systemic or ocular adverse effects, reported visual function improvement, documented as improvement of BCVA by two lines or more on Snellen's chart in 66% of their patients after peribulbar steroid injections.

To the best of our knowledge, our research was the first to use corneal topography to demonstrate the effect of peribulbar injections on the corneal form, recognizing the benefit of computerized corneal topography that allows the identification of subtle and minimal changes in corneal curvature.

Conclusion

We have shown that there is a significant improvement in corneal curvature following repeated peribulbar injection of triamcinolone acetate in patients with TED. The magnitude of this improvement in corneal curvature is sufficient to adjust the postoperative refraction of the eye, which, as is the case, would make any refractive operation better delayed until TED treatment for all patients. For all patients undergoing these injections, thorough preoperative therapy is also necessary.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Table 8: Comparison between pretreatment and posttreatment results according to mean difference of refraction (this table shows a statistically significant difference between both according to the mean difference of cylinder)

Mean difference refraction	Study group ($n=30$)	*t* test	*P*
Sphere			
Mean±SD	0.25±0.31	0.794	0.414
Range	0-1.25		
Cylinder			
Mean±SD	0.83±0.56	4.112	0.019*
Range	0-1.98		
Axis			
Mean±SD	6.57±4.55	1.635	0.198
Range	5-20		

t test, *t* independent sample. $P>0.05$ (nonsignificant). *$P<0.05$ (significant)

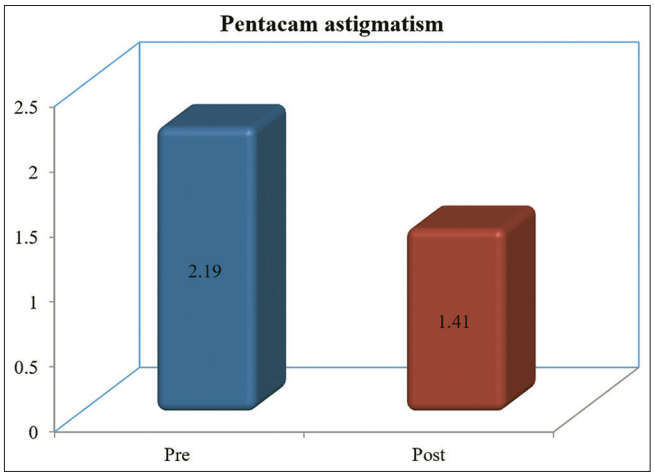

Figure 9: Bar chart between pre and post injection according to Pentacam astigmatism.

Table 9: Comparison between pretreatment and posttreatment results according to K-max, Pentacam astigmatism, Pentacam astigmatism axis, and central corneal thickness

	Pretreatment	Posttreatment	Difference	*t* test	*P*
K-max					
Range	40.8-47.9	40.4-47	0.58	4.862	<0.001**
Mean±SD	43.87±2.07	43.29±1.99			
Pentacam astigmatism					
Range	0.1-4.5	0.1-2.95	0.78	5.668	<0.001**
Mean±SD	2.19±1.40	1.41±0.93			
Pentacam astigmatism axis					
Range	5-175	5-175	17	1.066	0.304
Mean±SD	79.67±74.99	62.67±65.87			
CCT Pentacam					
Range	487-577	488-578	0.2	0.315	0.757
Mean±SD	522.93±26.52	523.13±26.71			

CCT, central corneal thickness; *t* test; *t* paired sample. $P>0.05$ (nonsignificant). *$P<0.05$ (significant). **$P<0.001$ (highly significant).

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Nil.

Conflicts of interest
There are no conflicts of interest.

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