Effect of Dry Eye Disease on Central Corneal Thickness and Corneal Topometric Indices Measured by Scheimpflug Tomography

Masoud Siyahkamari[1], Amir Asharlous[2], Ali Mirzajani[1], Hassan Koohian[1], Ebrahim Jafarzadepour[2], Hadi Ostadimoghaddam[3], Nazereh Babaei[2], Abbasali Yekta[3], Mehdi Khabazkhoob[4]

[1] Department of Optometry, School of Rehabilitation Sciences, Iran University of Medical Sciences, Tehran, Iran

[2] Noor Ophthalmology Research Center, Noor Eye Hospital, Tehran, Iran

[3] Refractive Errors Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

[4] Department of Basic Sciences, School of Nursing and Midwifery, Shahid Beheshti University of Medical Sciences, Tehran, Iran

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Abstract- To evaluate the effect of dry eye disease (DED) on the central corneal thickness and anterior corneal surface irregularity parameters using Scheimpflug tomography. In this study, the central corneal thickness and topometric indices of the anterior corneal surface were compared between the right eyes of 43 subjects with dry eye (DE group) and the right eyes of 35 non-dry eye individuals (NDE group). The central corneal thickness (CCT) and the topometric indices of the anterior corneal surface, including IVA, IHA, ISV, and IHD, were measured using the Pentacam HR (Pentacam-HR, Oculus, Wetzlar, Germany). Dry eye was diagnosed using a symptom questionnaire, TBUT, and Schirmer's test without anesthesia. The mean ISV, IVA, IHA, and IHD were 17.02 ± 3.43, 0.114 ± 0.04, 5.82 ± 4.82, and 0.011 ± 0.01 in the DE group and 14.65 ± 3.10, 0.086 ± 0.03, 3.70 ± 3.23, and 0.007 ± 0.00 in the NDE group, respectively. All of the above corneal irregularity indices were significantly higher in the DE group (P<0.05). The mean CCT was 531.19 µ (±34.88 µ) and 540.66 µ (±27.13 µ) in the DE and NDE group, respectively. Based on linear regression analysis, ISV, IVA, IHA, and IHD had a significant association with DED (P<0.05), while CCT had no significant association with DED (P=0.148). DED significantly increases corneal surface irregularity, but it has no significant effects on CCT measured by the Pentacam.

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Keywords: Dry eye; Corneal topometric indices; Pentacam; Tomography; Tear film

Introduction

The pre-corneal tear film is a very thin fluid layer covering the anterior corneal surface and has an important role in maintaining a healthy corneal and ocular surface and forming a regular optical surface (1). Tears lubricate and nourish the surface of the eye and provide physical and immune protection against infection. Aqueous deficiency and/or excessive tear evaporation can lead to dry eye disease (DED). Based on the TFOS DEWS II definition and classification report, "dry eye is a multifactorial disease of the ocular surface that is characterized by a loss of tear film homeostasis and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles" (2). The normal structure and thickness of the tear film alter in DED, and patients with tear film disorders usually experience a variety of symptoms, such as grittiness, irritation, photophobia, and blurred or fluctuating vision (3). This disorder can significantly reduce the quality of life (4). Millions of people suffer from DED across the world, and its prevalence ranges from 5% to 50% in different populations (5).

Some previous studies found that corneal surface irregularity detected by Placido disc corneal videokeratoscopy indices significantly increased in DED

Corresponding Author: E. Jafarzadepour
Noor Ophthalmology Rsearch Center, Noor Eye Hospital, Tehran, Iran
Tel: +98 2182401615, Fax: +98 2182401615, E-mail address: jafarzadehpour.e@iums.ac.ir

(6-8); however, a review of the literature found no studies investigating topometric indices in DED patients by the Pentacam. Furthermore, there is controversy about the effect of DED on central corneal thickness (CCT). Some studies showed decreased CCT in DED, and some studies found no difference in CCT between dry and normal eyes (9-11).

The Pentacam is one of the widely used elevation-based topographers used for corneal evaluation, especially prior to refractive surgery or for keratoconus screening. Pentacam measurements are based on the backscattering light from the corneal tissue, and, according to the manufacturer, the tear film has no effect on CCT and anterior corneal surface measurements (12,13). Therefore, it seems that the Pentacam is a reliable system for the evaluation of DED effects on the corneal tissue; therefore, the Pentacam was used in this study to evaluate whether or not DED causes any difference in CCT or corneal topometric indices. The purpose of this study was to evaluate the effect of DED on CCT and corneal topometric indices.

Materials and Methods

In this study, the right eyes of 43 subjects with DED (DE group) were compared with the right eyes of 35 normal NDE subjects (NDE group). Two groups were statistically matched in terms of sex and age. The study was performed according to the Declaration of Helsinki and was approved by the Ethics Committees of the Iran University of Medical Sciences. Written informed consent was obtained from all subjects prior to participation in the study. All participants underwent the following ocular examinations: objective refraction (Heine Beta 200 retinoscope, HEINE Optotechnic, Germany), visual acuity measurement, slit lamp biomicroscopy (Haag Streit Biomicroscope 900; Haag Streit, Bern, Switzerland), corneal tomography (Pentacam-HR, Oculus, Wetzlar, Germany), DED evaluation using a symptom questionnaire, tear break-up time test (TBUT), and Schirmer I test (S I) without anesthesia (Schirmer tear test, Optitech Eye Care, India), intraocular pressure measurement, and funduscopic examination. The subjects with any systemic or ocular pathology except DED were excluded from the study.

During the Pentacam imaging, the subjects were comfortably positioned at the instrument with the chin and the forehead properly placed on the chinrest and forehead strap. The participants were asked to blink several times and then open both eyes and look directly at the fixation target. The data of CCT and corneal topometric indices were collected from Pentacam tomography.

For DED diagnosis, a symptom questionnaire was completed by patients, and then TBUT and Schirmer I tests was performed. The participants who had DED symptoms, a TBUT less than 10 seconds (s), and S I test less than 10 millimeters (mm) in 5 minutes were considered as DED patients. The subjects in the NDE group had no DED symptoms, had a TBUT above 10 s, and the Schirmer result was above 10 mm in 5 minutes. The subjects were selected from patients who presented to "……." Hospital for a refractive surgery consultation.

After Pentacam tomography, TBUT was done in the right eyes of the participants. For this purpose, the subjects were asked to sit at the slit lamp. A strip impregnated with fluorescein was moisturized with a drop of normal saline, and the inferior bulbar conjunctiva was gently touched with the stripped tip without touching the corneal surface. The cornea was examined under a cobalt blue filter on the slit lamp using 10X magnification. The patient was instructed to blink 2-3 times and then avoid blinking until told otherwise. The time between the last blink and the appearance of a dry spot was measured in seconds. This test was done in triplicate for each eye, and the mean value was recorded as the tear break-up time. After TBUT, a 30-minute rest was considered for the tear film to resume its normal state; then, Schirmer's test was done without anesthesia. For this test, the patient was asked to look up, and a Schirmer strip was placed in the conjunctival fornix. The wet portion was recorded in millimeters after 5 minutes

Data were analyzed using the SPSS software version 22.0 (SPSS, Chicago, Illinois, USA). The data normality was assessed using the Shapiro-Wilk test. The difference between the two groups was evaluated using the independent t-test or Mann-Whitney U test, depending on the data normality. *P* less than 0.05 were considered significant.

Ethical issues

The Ethics Committee of "…." the University of Medical Sciences approved the study protocol. The study was conducted in accordance with the tenets of the Helsinki Declaration, and informed consent was obtained from all participants.

Results

There was no statistical difference in age and gender

between DE and NDE groups, while a significant difference was found in TBUT and SI results between the two groups. The demographic and DED data of the subjects in DE and NDE groups are summarized in Table 1.

CCT values were lower in the DE group, but the difference was not statistically significant (P=0.193). ISV, IVA, IHA, and IHD were significantly higher in the DE group (P<0.05). The results of CCT and corneal topometric indices are summarized in Table 2.

Linear regression analysis (Table 3) showed a significant association between DED and corneal topometric indices, including ISV, IHA, IVA, and IHD. There was no significant association between DED and CCT, according to linear regression analysis.

Table 1. Comparison of demographic and dry eye data between dry eye patients and control group

Parameter	DE	NDE	*P*
	Mean±SD	Mean±SD	
Age	27.44±5.79	28.94±5.51	0.248
Gender Female/Male	27(62.8%)/16(37.2%)	23(65.7%) /12(34.3%)	0.789
TBUT	5.53±1.61	13.63±3.51	<0.001
Schirmer I	6.16±2.48	24.46±6.98	<0.001

Abbreviations DE: Dry eye group, NDE: Non dry eye group, SD: Standard deviation, TBUT: tear break up time

Table 2. Comparison of central corneal thickness and corneal topometric indices between two groups

Parameter	DE	NDE	*P*
	Mean±SD	Mean±SD	
CCT	531.19 ± 34.88	540.66 ± 27.13	0.193*
ISV	17.02 ± 3.43	14.65 ± 3.10	0.002*
IVA	0.114 ± 0.04	0.086 ± 0.03	0.002**
IHA	5.82 ± 4.82	3.70 ± 3.23	0.039**
IHD	0.011 ± 0.01	0.007 ± 0.00	<0.001**

Abbreviations DE: dry eye group, NDE: non dry eye group, CCT: central corneal thickness, ISV: index of surface variance, IVA: index of vertical asymmetry, IHA: index of height asymmetry, IHD: index of height decentration

*the independent sample t-test was used

**the Mann-Whitney U test was used

Table 3. Linear regression analysis results

	CCT	IHD	ISV	IHA	IVA
	Coef; *P*	Coef; *P*	Coef; *P*	Coef; *P*	Coef; *P*
Age	-1.279; 0.045	0; 0.454	-0.08; 0.213	-0.088; 0.310	0; 0.566
Sex	-9.486; 0.206	-0.001;0.615	-2.097;0.007	0.297;0.77	-0.013;0.166
Spherical Equivalent	-0.971; 0.657	0; 0.306	-0.199; 0.368	-0.402; 0.179	0.003; 0.257
Mean keratometry	-2.289; 0.412	0; 0.522	0.446; 0.115	-0.189; 0.618	-0.002; 0.516
Dry Eye	10.651; 0.148	-0.003;0.001	-2.225;<0.001	-2.278; 0.025	-0.026; <0.001

Abbreviations: CCT: central corneal thickness, ISV: index of surface variance, IVA: index of vertical asymmetry, IHA: index of height asymmetry, IHD: index of height decentration

Discussion

This study was conducted to evaluate the effect of DED on CCT and corneal topographic indices. Most of the studies evaluating the effect of dry eye on the corneal surface have used reflection-based instruments, and because these systems are based on tear film reflection, it seems that their data are more affected by the tear film than the corneal tissue. On the other hand, due to the importance of the dry eye in corneal health and visual quality, this study can add to the existing knowledge of DED and its effects on the corneal surface. As mentioned in the Results section, the Pentacam results showed markedly more irregularity in the corneal surface of DED patients, which was consistent with the results of studies using reflection-based systems.

Previous studies using videokeratoscopy found that

corneal surface irregularity indices increased significantly in patients with DED compared to normal subjects (6,7). Goto *et al*., concluded that poor tear film stability could increase corneal surface irregularity indices (14). De Paiva *et al.,* found that surface regularity index (SRI) and surface asymmetry index (15) derived from reflection-based corneal videokeratoscopy could be used as objective diagnostic indices for DED (6). According to the finding of the present study, the topometric data of the Pentacam also showed increased irregularity of the anterior corneal surface. The higher corneal surface irregularity values in DED could be one of the reasons for blurred and fluctuating vision, decreased contrast sensitivity, and photophobia experienced by patients with aqueous tear deficiency (7).

The suggested reasons for the increased corneal surface irregularity in DED include tear film abnormalities and diseased corneal epithelium. Tear deficiency can damage the ocular surface, leading to epithelial disruption (8). Some previous studies found irregular and opaque superficial epithelial cells in DED (16). These epithelial layer changes can increase irregularity in the anterior corneal surface. Although corneal epitheliopathy was not evaluated in this study, due to the minor effects of the tear film on the backscattering light from the cornea, it seems that corneal surface pathologies such as corneal punctate epitheliopathy may be the major cause of higher topometric indices measured by the Pentacam (17).

The results showed that the mean CCT value was 9 µ thinner in the DE group, although the difference was not statistically significant. The literature is controversial regarding the effect of DED on CCT. Some studies showed decreased CCT in DED subjects (10,18,19), whereas some other studies found no significant differences in CCT between dry and non–dry eye patients (9,11). However, almost all studies reported lower CCT values in DED.

Various factors have been proposed for the effect of DED on corneal thickness. One of the proposed factors is reduced tear film thickness due to excessive evaporation (18,20). Tear film thickness normally ranges from 3 to 40 µ (15,21,22). Na Hee Kang *et al*., found reduced precorneal tear film thickness in dry eyes versus normal eyes using Scheimpflug imaging (23), and Dayanir *et al*., found that corneal drying reduced the corneal thickness. In their study, after one minute without blinking, the mean CCT measured by ultrasound decreased by about 16 µ (24). Other factors contributing to a decreased CCT in dry eyes include generalized corneal thinning induced by chronic exposure to hyperosmotic tear film in dry eyes (25), apoptosis of ocular surface cells as a consequence of an inflammatory process in DE (26), and corneal stromal thinning due to apoptosis as well as increased proteolytic activity at the stromal level (27).

Among these reasons, tear film thickness could be easily affected by the CCT measurement method. If we accept that reduced tear film thickness can decrease the measured corneal thickness, different methods could produce different results depending on the effect of the tear film on the measurement. In ultrasonic pachymetry, the precorneal tear film may be pushed away easily by the applanation force of the probe (28), so tear film thickness has a minor effect on CCT measured by ultrasonic pachymetry. However, some optical devices, such as the Orbscan, include the tear film thickness in CCT measurement. The Orbscan assesses the corneal thickness by calculating the distance between the anterior and posterior corneal surfaces. The anterior corneal surface is, in fact, the air/tear film interface, not the surface of the corneal epithelium (18). Therefore, the Orbscan usually produces higher CCT values compared to ultrasound pachymetry (29). Similarly, Han YS *et al.*, concluded that the corneal thickness measured by Orbscan pachymetry was more affected by DE compared to ultrasonic pachymetry measurements (30). The Pentacam system measures the corneal thickness from the backscattered light from the corneal tissue, and corneal thickness is calculated from the epithelium to the endothelium. More importantly, it does not measure the tear film (12,31). Consequently, by excluding the tear film thickness, the difference in CCT between normal and dry eyes may be lower in the Pentacam compared to other methods like the Orbscan.

Overall, it can be concluded that dry eye increases corneal surface irregularity, but it has no effects on CCT. It is suggested that corneal layer imaging, like confocal microscopy, be used for the more accurate evaluation of the effect of dry eye on the corneal tissue. Because this study had a cross-sectional design, the post-treatment data of DED were not available. It is suggested that changes in the CCT and the topometric parameters be investigated before and after DED treatment in future studies.

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