Corneal Sensitivity in Tear Dysfunction and its Correlation With Clinical Parameters and Blink Rate

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• PURPOSE: To compare corneal sensitivity in tear dysfunction due to a variety of causes using contact and noncontact esthesiometers and to evaluate correlations between corneal sensitivity, blink rate, and clinical parameters.

• DESIGN: Comparative observational case series.

• METHODS: Ten normal and 33 subjects with tear dysfunction (meibomian gland disease [n = 11], aqueous tear deficiency [n = 10]—without (n = 7) and with (n = 3) Sjögren syndrome (SS)—and conjunctivochalasis [n = 12]) were evaluated. Corneal sensitivity was measured with Cochet-Bonnet and air jet esthesiometers and blink rate by electromyography. Eye irritation symptoms, tear meniscus height, tear break-up time (TBUT), and corneal and conjunctival dye staining were measured. Between-group means were compared and correlations calculated.

• RESULTS: Compared with control (Cochet-Bonnet 5.45 mm, air esthesiometer 3.62 mg), mean sensory thresholds were significantly higher in aqueous tear deficiency using either Cochet-Bonnet (3.6 mm; $P = .003$) or air (11.7 mg; $P = .046$) esthesiometers, but were not significantly different in the other groups. Reduced corneal sensitivity significantly correlated with more rapid TBUT and blink rate and greater irritation and ocular surface dye staining with 1 or both esthesiometers. Mean blink rates were significantly higher in both aqueous tear deficiency and conjunctivochalasis compared with control. Among all subjects, blink rate positively correlated with ocular surface staining and irritation and inversely correlated with TBUT.

• CONCLUSION: Among conditions causing tear dysfunction, reduced corneal sensitivity is associated with greater irritation, tear instability, ocular surface disease, and blink rate. Rapid blinking is associated with worse ocular surface disease and tear stability. (Am J Ophthalmol 2015;160(5):858–866. © 2015 by Elsevier Inc. All rights reserved.)

AJO.com Supplemental Material available at AJO.com.
Accepted for publication Aug 2, 2015.

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TEAR DYSFUNCTION IS A PREVALENT DISORDER caused by decreased tear production, excessive evaporation, or an altered distribution.[1] Patients with tear dysfunction often experience irritation symptoms such as dryness, foreign body sensation, and burning[2–4]; however, paradoxically, certain patients with moderate to severe ocular surface disease have a paucity of irritation symptoms.[5–15] Patients with tear dysfunction may also complain of blurred and fluctuating vision, photophobia, and frequent blinking. Increased frequency of blinking has been previously noted in patients with tear dysfunction[16]; however, the factors contributing to the increased blink rate have not been established and may be influenced by the source of tear dysfunction. Studies evaluating tear dysfunction following laser in situ keratomileusis (LASIK) have reported a decrease in blink rate.[15] Although LASIK is known to cause corneal hyposensitivity that is often transient, no reduction in corneal sensitivity was found in 1 study, while hyperesthesia was measured in subjects with concurrent dry eye disease after LASIK.[3,15,17]

Tear instability and epithelial disease can disrupt corneal epithelial barrier function, which can affect corneal sensitivity and nerve morphology.[2,5,6,10,18] Studies measuring corneal sensitivity in dry eye by contact and noncontact methods have reported conflicting results, with either increased, decreased, or no change in sensitivity.[2–12,15,17,19–21] However, none of these previously reported studies stratified dry eye subjects by cause of tear dysfunction. Because corneal epithelial disease is more severe in aqueous tear deficiency than in meibomian gland disease and conjunctivochalasis,[13,14] we hypothesized there may be differences in corneal sensitivity and blink rate between these subsets of tear dysfunction that may be related to severity of ocular surface epithelial disease. To our knowledge, corneal sensitivity and blink rate have not been compared between these distinct subsets of tear dysfunction. Evaluating corneal sensitivities among different subsets of tear dysfunction may prove to be important for stratifying patients for clinical trials, for determining the cause for ocular irritation/pain symptoms, and perhaps for making treatment recommendations. Furthermore, the relationship between sensitivities and blink rate may provide insight into the mechanisms for increased blinking in dry eye. Testing corneal sensitivity in defined subsets of

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0002-9394/$36.00
http://dx.doi.org/10.1016/j.ajo.2015.08.005

TABLE 1. Criteria Used to Define Tear Dysfunction Subsets and Normal Controls

Group	OSDI	TBUT ≤7 Seconds	Meibomian Gland Disease	TMH (μm)
Meibomian gland disease	>20	+	+	>220
Aqueous tear deficiency	>20	+	−	<220
Conjunctivochalasis	>20	+	−	CC
Normal	≤20	−	−	>220

OSDI = ocular surface disease index; TBUT = tear break-up time; TMH = tear meniscus height (measured by optical coherence tomography).

tear dysfunction may help to explain the conflicting results of previous studies that have reported both corneal hyposensitivity and hypersensitivity findings.

The objective of this study was to compare corneal sensitivity using contact and noncontact methods in 3 common subtypes of tear dysfunction (aqueous tear deficiency, meibomian gland disease, and conjunctivochalasis). The relationship between corneal sensitivity and irritation symptoms, blink rate, and clinical parameters was also assessed.

METHODS

• **STUDY OVERSIGHT:** The institutional review board (IRB) at Baylor College of Medicine approved the study protocol to conduct clinical assessments in a prospective manner in which normal, non–dry eye subjects and those with tear dysfunction were enrolled for research participation after written informed consent. No retrospective IRB approval was necessary. Our study complies with the Health Insurance Portability and Accountability Act.

• **STUDY DESIGN:** Data for this comparative observational case series were collected from April 1, 2012 to June 1, 2014 at the Alkek Eye Center at Baylor College of Medicine, Houston, Texas. Subjects underwent a standardized tear and ocular surface evaluation, in the following order, that included anterior segment optical coherence tomography (OCT) as a measure of tear production and volume, respectively; fluorescein tear break-up time (TBUT) as a measure of tear stability; and corneal fluorescein and conjunctival lissamine green dye staining as measures of ocular surface epithelial cell health. Corneal and conjunctival dye staining with fluorescein and lissamine green, respectively, were performed and graded as previously reported.[13] Severity of eye irritation symptoms was measured using validated questionnaires, including the Ocular Surface Disease Index (OSDI) and a 5-question visual analog scale (VAS). After standard clinical tests were performed, corneal sensitivity was measured by both Cochet-Bonnet and air jet esthesiometers, and blink rate was measured using electromyography (EMG) with signals detected by the NeuroSky MindBand Bluetooth device (NeuroSky, Silicon Valley, California, USA). Data from only 1 eye (with the worst corneal fluorescein staining) for each subject, and the right eye for normal control subjects, were included in the data analysis.

• **SUBJECTS:** Thirty-three subjects with tear dysfunction were classified into the following groups: aqueous tear deficiency, meibomian gland disease, and conjunctivochalasis (according to criteria listed in Table 1). The classifications were based on an OSDI score >20, TBUT <7 seconds, tear meniscus height measured by OCT, and the presence (or absence) of meibomian gland disease and conjunctivochalasis.[13]

Normal control subjects had an OSDI score ≤20, no history of contact lens or eye drop use, or prior ocular surgery. They also had a TBUT ≥8 seconds and absence of fluorescein and lissamine green staining, meibomian gland disease, and conjunctivochalasis on biomicroscopic examination.

Subjects were excluded if they had prior LASIK or corneal transplantation surgery, cataract surgery in the past year, punctal occlusion with plugs or cautery, a history of contact lens wear, use of topical medications other than preservative-free artificial tears, or chronic use of systemic medications known to reduce tear production. In addition, subjects were excluded if they had active ocular surface or corneal inflammation, infection, or eyelid disorders causing exposure of the ocular surface. Seventy-one patients were excluded owing to these criteria.

Subjects were recruited from patients presenting to the corneal service at the Alkek Eye Center and employees of Baylor College of Medicine.

• **OPTICAL COHERENCE TOMOGRAPHY:** OCT measurement of the height of the lower tear meniscus was performed as described previously.[13] All subjects underwent cross-sectional imaging of the lower tear meniscus prior to the instillation of drops or measurement of clinical parameters.

• **FLUORESCEIN TEAR BREAK-UP TIME AND CORNEAL FLUORESCEIN STAINING:** TBUT was measured by instilling fluorescein into the lower fornix with a fluorescein strip (BioGlo; HUB Pharmaceuticals, Rancho Cucamonga, California, USA) wetted with preservative-free saline (Unisol; Alcon, Fort Worth, Texas, USA). The patient was allowed to blink at a spontaneous rate, and the elapsed time from the last blink to the appearance of the first break in the continuous layer of fluorescein, as observed under cobalt blue light through a yellow filter,

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