Temperatures of the Ocular Surface, Lid, and Periorbital Regions of Sjögren's, Evaporative, and Aqueous-Deficient Dry Eyes Relative to Normals

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ABSTRACT **Purpose: To compare the temperatures of the ocular surface, eyelid, and periorbital skin in normal eyes with Sjögren's syndrome (SS) eyes, evaporative dry eyes (EDE), and aqueous deficient dry eyes (ADDE). Methods: 10 eyes were analyzed in each age-matched group (normal, SS, EDE, and ADDE). A noninvasive infrared thermal camera captured two-dimensional images in three regions of interest (ROI) in each of three areas: the ocular surface, the upper eyelid, and the periorbital skin within a controlled environmental chamber. Mean temperatures in each ROI were calculated from the videos. Ocular surface time-segmented cooling rates were calculated over a 5-s blink interval. Results: Relative to normal eyes, dry eyes had lower initial central OSTs (SS −0.71°C, EDE −0.55°C, ADDE −0.95°C, KW $P<.0001$) and lower central upper lid temperatures (SS −0.24°C, ADDE −0.51°C, and EDE −0.54°C, KW $P<.0001$). ADDE eyes had the lowest initial central OST ($P<.0001$), while EDE eyes had the lowest central lid temperature and lower periorbital temperatures ($P<.0001$). Over the 5-s interblink interval, the greatest rate of temperature loss occurred following eyelid opening, but varied by group (normals −0.52, SS −0.73, EDE −0.63, and ADDE −0.75°C/s). The ADDE group also had the most substantial heat loss over the 5-s interblink interval (−0.97°C). Conclusions: Differences in OST may be related to thermal differences in lids and periorbita along with an altered tear film. Thermography of the ocular surface, lids, and surrounding tissues may help to differentiate between different etiologies of dry eye.**

KEY WORDS **dry eye, eye lid temperature, infrared thermography, ocular surface temperature, periorbital temperature, thermal measurements**

I. INTRODUCTION

Dry eye disease has been identified as a multifactorial disease of the tears and ocular surface.[1] Identification of the etiologic causes of dry eye can help providers in the approach to and care of their patients. Broadly, dry eye can be classified into aqueous deficient dry eye (**ADDE**), evaporative dry eye (**EDE**), and combination dry eye (demonstrating features of both ADDE and EDE).[1] Sjögren syndrome (**SS**) is an autoimmune-mediated inflammatory disorder that occurs in 0.1-3% of the population and results in hypofunction of the salivary and lacrimal glands.[2-7] In SS patients, inflammation of the lacrimal gland can lead to decreased tear production. Recent research has also suggested that within SS, some forms of EDE are caused by meibomian gland dysfunction (**MGD**),[3,8] so patients with SS may have combination dry eye.[9] Ultimately, SS patients have decreased tear production and/or an excessive tear film evaporation rates resulting in tear film instability, which can cause damage to the ocular surface and discomfort. According to a 2012 expert consensus, SS can be diagnosed by the presence of two of three objective features specified in Section II.A.[10,11]

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OUTLINE

Two other frequently used tests to diagnose and differentiate between dry eye etiologies are the tear film breakup time test (TFBUT) and Schirmer test.[12] Although both ADDE and EDE can have decreased TFBUT, ADDE can also be identified by decreased tear production (<10 mm wetting of Schirmer strip with anesthesia). Unfortunately, these tests, like most methods to detect dry eye, are semi-invasive and provide challenges for accurate diagnosis.[13-15] Fluorescein dye instillation, used for determination of TFBUT and ocular surface staining, can induce ocular irritation leading to reflex tearing and change in the tear film stability, thereby significantly altering the tear film's natural characteristics. Furthermore, TFBUT, as determined with fluorescein instillation, does not correlate with noninvasive studies of TFBUT.[16] The fluorescein concentration and volume are difficult to control and can impact accuracy and repeatability of the tear turnover and tear film breakup measures. Within the clinic, TFBUT typically requires subjective timing, which can result in inter-examiner variability.

Similarly, the filter papers used in Schirmer tests can cause irritation resulting in reflex tearing and overestimation of tear production. This may explain the high variability in Schirmer test results.[17] When anesthesia is used in Schirmer testing, excess fluid needs to be carefully removed or it can confound the results of the Schirmer test. Schirmer tests have not correlated with patients' symptoms or corneal staining.[18,19]

The utility of infrared thermography for understanding the ocular surface and dry eye is being explored, as this imaging device is noninvasive and provides an objective quantitative output.[20-22] IR imaging has been used to assess the ocular surface temperatures (**OST**) in patients with and without dry eye disease.[20,23] Studies have consistently demonstrated that dry eye patients have cooler ocular surfaces when compared to asymptomatic normal subjects.[21,22,24] Additionally, a recent report demonstrated altered thermal profiles of the periorbita of subjects with Graves' ophthalmopathy, an autoimmune disease.[25]

Currently, knowledge is incomplete with regard to temperature of the lids and periorbital tissues and its influence on the ocular surface temperatures in dry eye and normal eyes. In our laboratory, we have demonstrated the importance of the blink for providing a thermal pulse to the ocular surface temperature, thus demonstrating that the temperature of the eyelid and replenished tears influence ocular surface temperatures.[26] The aims of the current study are two-fold: 1) to quantitatively compare ocular surface, upper eyelid, and periorbital skin temperatures in SS, EDE, ADDE, and asymptomatic non-dry eye patients to understand the relationship between ocular surface temperatures and the lids and periorbita, and 2) to assess whether the systemic autoimmune disease, SS, alters the thermal profile of the lids and periorbita.

II. METHODS

This study used retrospectively collected data from studies approved by the University of Rochester Institutional Review Board. The research adhered to the tenets of the Declaration of Helsinki. Informed consent was obtained from all subjects after the potential consequences of the study were fully explained. This research was conducted in our environmentally controlled chamber located in the Flaum Eye Institute's Ocular Surface Laboratory. Data from prior studies were reviewed, and eyes were included in the study if they met the criteria outlined for inclusion in each of the groups. Eyes were not included if they met exclusionary criteria.

A. Subjects

Data were analyzed from 10 eyes in each of the groups described below. Assignment of an eye to a group was based solely on the following objective inclusion criteria with matching performed by age across groups:

Group 1: Normal, asymptomatic eyes. The asymptomatic, normal group was comprised of eyes of individuals who reported no subjective dry eye symptoms and lacked objective findings of dry eye. Subjects were excluded from the normal group if they had Schirmer test wetting <10 mm or fluorescein TFBUT <10 s.

Group 2: Eyes of patients with SS. To be included in this group, subjects had to have two of the three following objective criteria: 1) positive serum anti-SSA/Ro and/or anti-SSB or (positive rheumatoid factor and ANA titer ≥1:320); 2) labial salivary gland biopsy exhibiting focal lymphocytic sialadenitis with a focus score ≥ 1 focus/4mm^2; or 3) keratoconjunctivitis sicca with ocular staining score ≥3[10] (assuming no glaucoma drops or recent corneal or eyelid surgery).[11] Criteria 1 and 2 were established by our colleagues in the Department of Rheumatology/Immunology or Oral Surgery. Ocular surface staining was performed by trained clinicians within the Ocular Surface Laboratory at the Flaum Eye Institute. There were no Schirmer test or fluorescein TFBUT criteria for inclusion in this group.