Tear Osmolarity and Tear Film Parameters in Patients With Ocular Rosacea

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Objectives: The aim of this study was to evaluate tear osmolarity and tear film parameters in patients with ocular rosacea.

Methods: In a single center, 25 eyes of 25 patients with ocular rosacea (group 1), 25 eyes of 25 patients with rosacea without ocular involvement (group 2), and 20 eyes of 20 healthy individuals (group 3) were evaluated using the Ocular Surface Disease Index (OSDI) questionnaire, Schirmer I test, tear film break-up time (TBUT), scoring of ocular surface fluorescein staining using modified Oxford scale, and tear osmolarity.

Results: Tear osmolarity values, OSDI and Oxford scale scores were significantly higher in group 1 than in groups 2 and 3 ($P<0.001$ for all). Schirmer I test and TBUT in group 1 were significantly lower than in groups 2 and 3 ($P<0.001$ for all). There were no significant differences in OSDI, Schirmer I test, TBUT, Oxford scores, or tear osmolarity between groups 2 and 3 ($P=0.629$, $P=0.175$, $P=0.713$, $P=865$, and $P=0.388$, respectively).

Conclusions: This study showed that ocular rosacea is associated with tear hyperosmolarity and tear film dysfunction.

Key Words: Dry eye—Ocular surface—Meibomian gland dysfunction—Tear osmolarity—Ocular rosacea.

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Rosacea, which primarily affects blood vessels and pilosebaceous units of the central facial skin (i.e., cheeks, chin, nose, and central forehead), is a chronic cutaneous disorder.[1] The most common clinical findings are transient or persistent erythema, telangiectasias, papules, pustules, and phymatous changes.[2] Rosacea also causes eyelid and ocular surface inflammation and may involve the eyes in 58% to 72% of patients.[3]

Ocular rosacea may present with a watery or bloodshot appearance (interpalpebral conjunctival hyperemia), foreign body sensation, burning or stinging, dryness, itching, light sensitivity, blurred vision, telangiectasias of the conjunctiva and lid margin, and lid and periocular erythema. Anterior blepharitis, meibomian gland dysfunction, and eyelid margin irregularity may also be seen.[2–5]

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Insufficient tear production or excessive tear evaporation both cause tear hyperosmolarity.[6] The most common cause of increased evaporation is meibomian gland disease (MGD), which results in reduced oil delivery to the lid margin and tear film.[7] Individuals with MGD may also have hypersecretion of meibum. Some persons with ocular rosacea may actually have hypersecretory MGD. Abnormal meibum composition may also play a role in accelerated tear evaporation. Hyperosmolarity has been shown to provide proinflammatory stress to the ocular surface.[8] Some studies suggest that tear osmolarity measurement should be preferred over alternative subjective means as the gold standard to diagnose dry eye disease.[9] Despite its well-established importance, technology with good sensitivity and specificity to measure tear osmolarity in the evaluation of dry eye disease has only recently become available.[10,11]

The aim of our study was to evaluate tear osmolarity and other ocular surface parameters in subjects with ocular rosacea and to compare the results with those of subjects with rosacea without ocular involvement and with healthy controls.

MATERIALS AND METHODS

A total of 25 eyes of 25 patients with ocular rosacea (group 1), 25 eyes of 25 patients with rosacea without ocular involvement (group 2), and 25 eyes of 25 healthy individuals without signs or symptoms of dry eye disease or other ocular pathology (group 3) were included in this single-center, cross-sectional observational study. Right eye data for each patient were assessed.

Patients in groups 1 and 2 were diagnosed with rosacea by a specialist dermatologist (A.B.). Among those diagnosed with rosacea, ocular rosacea was diagnosed on detection of one or more of the following: watery or bloodshot appearance, foreign body sensation, burning or stinging, dryness, itching, light sensitivity, blurred vision, telangiectasias of the conjunctiva and lid margin, lid and periocular erythema, anterior blepharitis, MGD, or irregularity of eyelid margins.[12] Subjects were excluded if they had a history of smoking, current or recent drug use that could affect the lacrimal functional unit, active ocular infection or allergy, ocular surface scarring, previous eye surgery, or current contact lens use.

The study was reviewed and approved by the Istanbul Medipol University Ethics Committee, and written informed consent was obtained from each patient before enrollment. The study was conducted in accordance with the tenets of the Declaration of Helsinki.

Initially, patients completed the International Ocular Surface Disease Index (OSDI) survey. All subjects underwent a full

ophthalmological examination in the same order, including visual acuity assessment, standardized slitlamp examination, and fundus examination. Full ophthalmologic examination and evaluation of tear osmolarity were performed on the same day but at a different time.

Tear osmolarity measurements were evaluated using a TearLab osmometer (TearLab Co., San Diego, CA). Tears were collected from the inferior lateral tear meniscus. Three consecutive measurements were obtained, and their mean was used for statistical analysis. All eyes underwent corneal fluorescein staining scoring using the Oxford scheme.

Tear film break-up time (TBUT) was assessed after instillation of 2% fluorescein staining under a cobalt blue filter. The time interval between the last complete blink and the appearance of the first dry spot was recorded. The mean of three consecutive measurements was obtained. The Schirmer I test was performed with topical anesthesia using a standardized filter strip (Bio-Tech Vision Care, Ahmedabad, India). The amount of wetting was measured after 5 min.

The normality of the distribution of each of the parameters was checked using the Kolmogorov–Smirnov normality test. The tear osmolarity, Schirmer I test with anesthesia, TBUT values and OSDI scores among groups were compared using one-way analysis of variance. The differences were calculated using the multiple comparison Tukey's test. A P-value <0.05 was considered statistically significant.

RESULTS

The mean subject age was 46.7±8.5 years (range: 35–63 years) in group 1 (14 women and 11 men), 48.8±10.3 years (range: 32–69 years) in group 2 (12 women and 13 men), and 47.1±10.1 years (range: 33–63 years) in group 3 (13 women and 12 men). There were no significant differences among the three groups with respect to age or sex ($P=0.72$ and $P=0.852$, respectively). Summary statistics are shown in Table 1. The mean tear osmolarity was significantly higher in group 1 compared with groups 2 and 3 ($P<0.001$ for both). There was no significant difference in tear osmolarity between groups 2 and 3 ($P=0.388$).

The Schirmer I test values for group 1 were significantly lower than those for groups 2 and 3 ($P<0.001$ for both). There was no significant difference in Schirmer I test results between groups 2 and 3 ($P=0.175$). Tear film break-up time measurements for group 1 were significantly lower than those for groups 2 and 3 ($P<0.001$ for both). Tear film break-up time measurements did not differ between groups 2 and 3 ($P=0.713$).

The mean superficial punctate staining, as measured by the Oxford scale, differed significantly between group 1 and group 2, and between group 1 and group 3 ($P=0.016$ and $P=0.004$, respectively). There was no significant difference between groups 2 and 3 on the Oxford scale ($P=0.865$). The mean OSDI scores were significantly higher in group 1 than in groups 2 and 3 ($P<0.001$ for both). No significant difference in OSDI score was noted between groups 2 and 3 ($P=0.86$).

DISCUSSION

In this study, patients with ocular rosacea had significantly higher tear osmolarity levels, lower Schirmer I scores, and lower TBUT values than patients with rosacea without ocular involvement and controls. There was no difference between the patients with rosacea without ocular involvement and control patients.

Zengin et al.[13] compared 28 patients with ocular rosacea with 15 patients with dermatologic rosacea and their sex- and age-matched control subjects. They found that patients with ocular rosacea had significantly lower Schirmer I scores, TBUT, and meibomian gland function values than for those with cutaneous-limited rosacea and controls. Consistent with our study, they reported that test results for patients with dermatologic rosacea did not differ from those of age- and sex-matched controls. A study by Yaylali et al.[14] showed higher rose Bengal staining scores, lower TBUT values and lower Schirmer I test values for those with ocular rosacea than for patients in the control group. Kocak-Altintas et al.[15] found that patients with ocular rosacea had both decreased tear production and increased tear instability.

Based on the results of this study, we suggest that the tear hyperosmolarity believed to be the main pathogenic factor leading to ocular surface inflammation may decrease the number of goblet cells and alter ocular surface mucins to cause tear film instability.[9,16] This instability may trigger a cycle that perpetuates the inflammatory process.

Barton et al.[17] found a differential increase in the level of the inflammatory cytokine interleukin 1α in the tear fluid from patients with ocular rosacea compared with controls. They hypothesized two possible causes: (1) increased production or release by epithelial or inflammatory cells on the ocular surface or both; and (2) reduced tear drainage. Activation of the epithelial signaling molecules cascade induces damage to surface epithelium, release of proinflammatory mediators into tears, and cell death by apoptosis.

In this study, we found that patients with ocular rosacea have different tear film parameters compared with those with rosacea without ocular involvement and controls. Patients with ocular rosacea had dry eye symptoms but were unaware of a connection between their ocular symptoms and rosacea. Although patients with rosacea without ocular involvement also had elevated tear osmolarity values compared with controls, the difference was not statistically significant. This finding is remarkable because MGD, which causes evaporative dry eye, is present in up to of 92% of patients with rosacea.[4,18] It is common for patients with rosacea not to mention ocular symptoms in a dermatology clinic unless they are

TABLE 1. *Comparisons of the Mean Dry Eye Parameters Among Groups*

Parameter	Group 1	Group 2	Group 3	*P*
Tear osmolarity, mean±SD, mOsm/L	321±16.3	295.8±19.5	286.3±23.4	<0.001 (group 1 vs. groups 2 and 3)
Schirmer test, mean±SD, mm	10.5±3.2	18.3±4.7	20.4±4.2	<0.001 (group 1 vs. groups 2 and 3)
Oxford scale, mean±SD	0.56±0.7	0.12±0.33	0.04±0.2	0.016 (group 1 vs. group 2); 0.004 (group 1 vs. group 3)
TBUT, mean±SD, sec	9.8±3.5	21.6±4.3	22.5±4	<0.001 (group 1 vs. groups 2 and 3)
OSDI score, mean±SD	54.1±16.5	24.5±17.3	22.3±11.6	<0.001 (group 1 vs. groups 2 and 3)

OSDI, ocular surface disease index; SD, standard deviation; TBUT, tear film break-up time.

directly questioned. Therefore, we strongly encourage dermatologists to assess patients for ocular symptoms.

A major limitation of our study is that we were unable to perform further tests, including assessment of changes in mean goblet cell density, conjunctival impression cytology, and especially meibography. Further evaluation using these measures may provide more information about the relationship between ocular rosacea and dry eye disease.

In conclusion, this study showed that patients with ocular rosacea had higher osmolarity than patients with rosacea without ocular involvement and healthy individuals. They also had tear film dysfunction. Prospective studies are needed to evaluate the changes in tear function and dry eye disease during the course of ocular rosacea.

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