Dynamic Changes in the Tear Film in Dry Eyes

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PURPOSE. To examine the dynamics of the tear film in patients with dry eye by measuring the wavefront aberrations of the anterior surface of the film.

METHODS. Anterior surface aberrations for a 7-mm pupil were determined in 13 patients with dry eye at 1-second time intervals, for 15 seconds after a blink. The aberrations were calculated from the elevations provided by corneal topography. All data were decomposed using Zernike polynomials. Total, spherical, and comalike aberrations terms were studied separately. Results were compared with those in normal eyes. Outcome measures included comparison with clinical tear breakup time measurements.

RESULTS. The total root mean square (RMS) wavefront aberration in patients with dry eye passed through in a minimum of 2.9 ± 0.4 seconds after a blink in comparison to the minimum at 6.1 ± 0.5 seconds in normal patients. In both groups, the minimum in total aberration appeared to be associated with similar changes in comalike aberrations, rather than in spherical aberrations, which increased monotonically with time. The time at which minimum RMS aberration occurred correlated reasonably well with the measured tear breakup times.

CONCLUSIONS. Measurements of the dynamic changes in the optical aberrations introduced by the anterior tear film surface give valuable insights into tear film changes and may provide a convenient objective method for the diagnosis of dry eye.

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Over the past few years, there has been increased interest in the study of the optical quality of the eye. The overall optical quality depends on the combined effect of each isolated refractive component of the eye, principally the cornea and lens. However, the tear film also plays an important role, but has received less attention. The front surface of the precorneal tear film is the most anterior optical surface of the eye and hence the most powerful, as it is associated with the largest change in refractive index. Changes in the local tear film surface radius associated with tear film irregularity produces local changes in the surface power—that is, aberrations (a 0.2-mm variation in radius causes a 1.3-D change in power, approximately).

Montés-Micó et al. 1,2 have recently found that, in normal eyes, after a blink there is initially a fairly rapid decrease in the aberrations associated with the anterior surface of the tear film as the tear film stabilizes and becomes smoother, followed by a gradual increase as evaporation and other effects cause the tear film to become more irregular and to start to break up. Minimal aberrations are typically found to occur approximately 6 seconds after a blink. 2

Eyes with abnormal tear film function have been found to show larger optical aberrations than normal eyes, 3 presumably because of the greater degree of irregularity in the tear film. This fact is supported by the finding that instillation of artificial tears in dry eyes reduces the optical aberrations and increases the optical quality of the retinal image. 4 The artificial tears reduce the irregularity of the tear film and increase tear breakup time (TBUT). As yet, however, there appear to have been no studies in which investigators have examined in detail the temporal changes that occur in the optical aberrations of the anterior surface of the tear film in patients with dry eye after a blink, although it is well known that TBUTs are shorter in such patients. 5

Thus, the purpose of the present study was to investigate the temporal changes in the higher-order aberrations associated with the anterior tear film surface of patients with dry eye during the first 15 seconds after a blink and to compare them with those found in normal control eyes.

METHODS

Patients

Thirteen patients with dry eye, 11 men and 2 women, participated in this study. Diagnosis of dry eye was made on the basis of signs of dry eye used in previous studies 5–7: Schirmer I test result of <10 mm without anesthesia and TBUT of <5 seconds. The normal interblink interval for each patient was determined by counting the number of blinks over a 2-minute interval while they sat in a normally lit area under relaxed conditions. Exclusion criteria included ocular trauma within the past 4 months, abnormality of the nasolacrimal drainage apparatus, and permanent occlusion of lacrimal puncta or a temporary punctal plug within 2 months. Mean TBUT in these patients was 3.5 ± 1.0 seconds, and mean interblink interval was 2.2 ± 0.6 seconds. None of the enrolled patient used artificial tears during the study. Their ages ranged from 34 to 52 years (45.3 ± 5 years). The study adhered to the tenets of the Declaration of Helsinki. Informed consent was obtained from all patients after the nature and possible consequences of the study had been explained.

Mean dynamic tear film data for an approximately sex- and age-matched group of 15 normal healthy subjects (13 men, 2 women; mean age, 36 ± 1.7 years) were obtained from a previous study 1 in which the same methodology had been used and which was directly comparable.

Aberrations of the Anterior Tear Film Surface from Corneal Topography

Topographic data were obtained with a videokeratoscope (model TMS-2N; Tomey Corp., Nagoya, Japan). The anterior surface of the tear
Mean pupil diameter during the measurements was 3.4 mm, obtained at 1-second time intervals from 1 to 15 seconds after a blink. VISSUM Instituto Oftalmológico de Alicante.

The Zernike coefficients were used to determine image quality when the pupil diameters are large, although in normal eyes the changing aberrations are likely to have the greatest effects on image coma when the pupil diameters are large.1 The Zernike coefficients were used to calculate the total higher-order monochromatic anterior tear-film surface aberration, and the aberration contributed by spherical aberration ($Z_0^s$ and $Z_0^c$) and comalike aberrations ($Z_1^s$ and $Z_1^c$). Wavefront aberrations were calculated relative to the pupil center instead of the normal vertex (videokeratoscope axis), since this point is more relevant to visual acuity.

The point-spread function (PSF), which is defined as the light distribution in the image of a point source, was also calculated for each time after a blink and in normal eyes at 6.1 ± 0.5 seconds. Minimal aberration values were lower in the normal group.

Data Analysis

The videokeratographic data were fitted with Zernike polynomials up to the sixth order to determine aberration coefficients. The calculation of the “corneal” wavefront aberration was performed on computer (CT-View, ver. 6.32; Sarver & Associates, Inc., Merritt Island, FL) for one pupil diameter: 7 mm. This pupil diameter was chosen because the point-spread function (PSF) for a 7-mm pupil diameters as a function of time (seconds) after blinking in normal (black) and dry (gray) eyes. Continuous lines represent the best polynomial trend equation (cubic) for normal and dry eyes. Data for normal eyes come from Montés-Micó et al.1

The temporal changes in the total amount in the higher-order (third to sixth) root mean square (RMS) wavefront aberration for a 7-mm pupil diameter are shown in Figure 1 for normal and dry eyes (averaged across all subjects in each group). The RMS values shown were fitted with a third-order polynomial equation using the least-squares fitting method (SigmaPlot, ver. 8.0; SPSS Inc.). There was an initial improvement (lower values) and subsequent worsening (higher values) of the total corneal wavefront aberrations in the first 15 seconds after a complete blink in both groups of patients. RMS error value reached its minimum level in dry eyes, on average, at 2.9 ± 0.4 seconds after a blink and in normal eyes at 6.1 ± 0.5 seconds. Minimal aberration values were lower in the normal group. A one-way ANOVA revealed statistically significant differences between the patient groups in corneal wavefront aberration versus time after blinking ($P < 0.01$).

Dry eyes showed larger values than normal subjects for measurements at all postblink times except for the first 4 seconds in which both groups of values were similar ($P > 0.01$).

Figure 2 shows mean values of the RMS spherical ($Z_0^s$ and $Z_0^c$) and comalike ($Z_1^s$ and $Z_1^c$) aberrations, for a 7-mm pupil diameter, as a function of time after blinking. Open symbols represent data for dry eyes and filled symbols data for normal subjects. Solid and dashed lines represent the best third-order polynomial trend equations for spherical and comalike aberrations, respectively. For both the spherical and comalike aberrations in dry eyes there was a gradual increase in the RMS error versus time after blinking ($P < 0.01$), with the values increasing by similar amounts (from 0.21 to 0.55 μm) and from 0.26 to 0.57 μm, respectively. Dry eyes showed larger values than normal subjects for all measurements except those in the blink. Statistical analysis was performed on computer (SPSS ver. 11.0.1; SPSS Inc., Chicago, IL). The statistical significance of postblink changes was evaluated using a one-way analysis of variance (ANOVA). Appropriate post hoc Bonferroni correction for multiple comparisons was used. For the comparison between results for dry eyes and normal subjects a Student’s $t$-test was used. $P < 0.01$ was regarded as statistically significant.

RESULTS

Higher-Order Wavefront Aberrations of the Anterior Tear Film Surface in Dry-Eye and Normal Subjects

Temporal changes in the total amount in the higher-order (third to sixth) root mean square (RMS) wavefront aberration for a 7-mm pupil diameter are shown in Figure 1 for normal and dry eyes (averaged across all subjects in each group). The RMS values shown were fitted with a third-order polynomial equation using the least-squares fitting method (SigmaPlot, ver. 8.0; SPSS Inc.). There was an initial improvement (lower values) and subsequent worsening (higher values) of the total corneal wavefront aberrations in the first 15 seconds after a complete blink in both groups of patients. RMS error value reached its minimum level in dry eyes, on average, at 2.9 ± 0.4 seconds after a blink and in normal eyes at 6.1 ± 0.5 seconds. Minimal aberration values were lower in the normal group. A one-way ANOVA revealed statistically significant differences between the patient groups in corneal wavefront aberration versus time after blinking ($P < 0.01$).

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first 4 seconds, in which both group of values were similar \( (P > 0.01) \).

**Retinal PSFs and Relationship between RMS Wavefront Error and TBUT in Dry Eyes**

The retinal PSFs corresponding to the mean anterior tear film surface aberrations for a typical patient with dry eye are shown in Figure 3. PSFs showed a time variation similar to that described in Figure 1. They confirm the relatively poor optical quality of the anterior cornea of this eye immediately after a blink and finally at 15 seconds after blinking. Best contrast and minimal size of the PSF were obtained at approximately 3 seconds after blinking. Normal subjects showed better PSFs (data not shown; see Montés-Micó et al.\(^1\) for a comparison) than those in dry eyes. Larger values of optical aberrations (Fig. 1) degrade the retinal image to a greater extent. Note that many of the PSFs tended to be more elongated in the vertical direction.

**Relation between TBUT and Time at which the Minimum Aberration Was Observed**

The results of the temporal aberrometric analysis can be compared with the corresponding results for the TBUT by plotting the time at which an aberration minimum occurred in each patient against the corresponding TBUT (Fig. 4). The minimum was found to occur earlier in those subjects with shorter TBUT \( (R = 0.43; P = 0.008) \). Figure 4 also includes data for normal eyes, to allow comparison with the results found in dry eyes. It can be seen that the results in both normal subjects and patients with dry eye can be approximated quite well as lying on a single straight line:

\[
\text{Time}_{\text{RMS minimum}}(\text{seconds}) = 0.49 \times \text{TBUT}(\text{seconds}) + 1.46.
\]

**DISCUSSION**

Not surprisingly, the results of this study suggest that the dynamics of the tear film differ in normal subjects and patients with dry eye: the dynamics of tear film change are accelerated in dry eye. The mean times at which minimum RMS value occurred \((2.9 \pm 0.4 \text{ seconds} \text{ after blinking for dry eyes versus } 6.1 \pm 0.5 \text{ seconds} \text{ for normal eyes})\) differed significantly \( (P < 0.01) \). This confirms that the tear film in dry eye becomes unstable earlier than in normal eyes. Stabilization of the tear film is reflected in the finding that the best PSF obtained in this eye occurred 3 seconds after blinking.

Considering now the reasons why the dynamic changes observed in patients with dry eye occur faster than in normal subjects, previous studies\(^1,6–8\) performed on normal patients suggest that after a blink the tear film needs a period to reach its most regular state \( (\text{approximately } 6 \text{ seconds} \text{ after a blink}) \). The tear film builds up quickly, although not uniformly, after the eyelids are opened.\(^9\) Capillary flow, evaporation, and other redistributive processes then start. The tear film becomes more uniform, gradually thins, and finally breaks up. The general temporal characteristics of tear film deposition and thinning have been modeled in some detail by Wong et al.\(^9\)

In the present study of patients with dry eye, the minimum RMS value, which correlates with the most regular tear film state, was achieved at earlier times \( (\text{around } 3 \text{ seconds}) \). Goto and Tseng,\(^10,11\) using kinetic analysis of tear interference images, found that although the tear lipid film spread time in normal eyes is short \((0.3 \pm 0.2 \text{ seconds})\), it is much longer in dry eyes with lipid and aqueous tear deficiency \((3.5 \pm 1.8 \text{ seconds} \text{ and } 2.2 \pm 1.1 \text{ seconds}, \text{ respectively})\). As the time resolution in our earlier study of normal subjects was only 1 second, the lipid film spreading time in normal subjects could not be detected. However, it is interesting to note that the lipid film stabilization in patients with dry eye occurred more slowly. We did not differentiate the type of dry eye among our patients. However, the data of Goto and Tseng suggest that the mean lipid spreading time in dry eyes with either aqueous or lipid deficiency is \( \sim 2.9 \text{ seconds} \). This value surprisingly agrees very well with the mean value at which the minimum RMS occurred. Considering this fact, it seems reasonable to hypothesize that the temporal minimum in corneal wavefront aberration found in dry eyes may relate to the time for lipid film stabilization. It would obviously be of interest to measure the lipid film at different times after stabilization in individual patients with dry eye to assess the time at which the lipid film becomes unstable again and to explore the extent to which this correlates with increasing wavefront aberrations. We may speculate that lipid film stabilization continues at least up to the time at which wavefront aberration starts to increase. This would explain the dynamic wavefront pattern found in dry eyes. In contrast, it is clear that there can be no such link in the case of normal eyes, whereas Goto and Tseng’s lipid film spreading time of 0.3 seconds is much shorter than the 5 to 7 seconds time taken for the tear film aberration to reach a minimum.\(^1\) Therefore, either...
the link between the two times is coincidental in the case of dry eyes, or different factors must play a more important role in the normal eye, perhaps the characteristics of the relatively thicker aqueous layer, since a thicker layer is known to increase TBUT.9

Turning to the temporal changes in the individual aberrations, in an earlier study,1 we suggested that the behavior of the total RMS wavefront error in normal patients could be accounted for by changes in the component aberrations. Spherical aberration terms (Z_0^6 and Z_5^6) tended to increase monotonically with time after a blink, whereas the comalike, third- and fifth-order aberrations passed through a minimum (see Fig. 2). Thus, the minimum for the total aberration was due to the changes in comalike aberration.

Dry eyes showed a similar pattern (Fig. 2). Spherical aberration increased monotonically with time, there being no evidence for any minimum. The values of the spherical aberration coefficients became more negative with time (suggesting that the air-tear film surface changes from a prolate toward an oblate shape). This behavior probably derives from the greater rate of evaporation at the center of the palpebral aperture in both types of eye, which causes the tear film to thin more rapidly at the center than peripherally.12 The alternative possibility, that the underlying cornea is changing shape as a result of short-term biomechanical changes associated with variations in local lid pressure,13 seems unlikely, since it is difficult to see how such changes could be rotationally symmetrical about the pupil center. As with normal eyes, the absence of any temporal minimum in spherical aberration in the patients with dry eye implies that the temporal minimum in total RMS aberration can probably be attributed to changes in aberrations without rotational symmetry—that is to comalike aberrations (Fig. 2).

Differences between vertical and horizontal comalike aberrations in normal eyes would be expected due to the directional characteristics of lid movement, the effects of gravity on the tear movement, the uneven local rates of evaporation associated with the shape of the palpebral aperture, and, perhaps, dynamic change in the contour of the underlying cornea after lid pressure.13 These effects produce asymmetry, primarily in the vertical meridian of the anterior cornea.1 The results found in dry eyes correlate well with this hypothesis (see e.g., the PSFs in Fig. 3). This suggestion is supported by the fact that we have found in a previous study5 that dry eyes show larger values of vertical coma than horizontal coma (Z_3^6: 0.43 μm and Z_5^6: 0.24 μm; and Z_3^6: 0.16 μm and Z_5^6: 0.09 μm, for a 6.0-mm pupil). Normal eyes also show different vertical and horizontal coma, but the differences were smaller (Z_3^6: 0.17 μm and Z_5^6: 0.14 μm; and Z_3^6: 0.06 μm and Z_5^6: 0.05 μm, for a 6.0-mm pupil). Dry-eye aberration maps have shown that the wavefront is more advanced in the superior than in the inferior cornea, which indicates a relative thinning of the tear film in the superior cornea.5 In addition, Goto and Tseng,10,11 have found that in eyes with aqueous and lipid tear deficiency, the lipid film is thicker on the inferior cornea than on the superior cornea. This uneven distribution in the vertical meridian correlates with the asymmetry in comalike aberration.

We note that the aberrations measured in the present study are nominally those associated with the anterior surface of the tear film. It is possible that the assumptions made by the software used regarding the refractive index of the tear film may not be correct, since the effective tear index may change modestly with time after a blink. For any given linear thickness, the optical path through the tears and hence the overall aberration introduced by the tear film may also be subject to changes due to changing refractive index caused by time-dependent variations in the composition of the film. However, the small differences in tear film refractive index that are observed in practice14 suggest that these effects are unlikely to affect our conclusions substantially regarding the temporal changes in aberration.

Perhaps a more important limitation to our data is the fact that our measurements refer only to the aberration associated with the anterior surface of the tear film. The aberrations of the whole eye and hence the optical quality of the actual retinal image, however, depends on the whole optical path into the eye and includes the effects of the posterior cornea, crystalline lens, and other elements of the eye. It is known that, in most eyes, the aberrations of the crystalline lens tend to be opposite in sign to those of the tear lens–cornea system and hence that the total aberration of the eye tends to be lower than that of its isolated components.15–17 It may be, then, that the time at which the minimum aberration is found for the anterior surface of the tear film does not necessarily correspond to the time at which it is found for the whole eye. In an earlier study2 with poorer time resolution (10 seconds) in which both corneal and total aberration were measured, it appeared that minimal aberration occurred at about the same time in both cases, but this study should be repeated with improved time resolution.

The typical interblink interval in normal patients is approximately 4 to 5 seconds and in those with dry eyes is approximately 1 to 2 seconds in normal conditions.16 Patients with dry eye evaluated in this study showed an interblink interval of 2.2 ± 0.6 seconds, which agrees well with previous literature. It is interesting to note that both normal subjects and patients with dry eye blinked about 1 second before wavefront aberration started to increase, suggesting that the interblink interval may depend on the tear stabilization time. This would imply that there ought to be individual correlation between the time at which the minimum RMS value occurs and the interblink interval.

We note that clinical TBUT measurements tend to have poor reliability, because of the many factors that may influence the outcome of the TBUT examination, such as the dose of fluorescein applied, the expertise of examiner, the interval between instillation and examination, and slit lamp quality. Figure 4 suggests that dynamic wavefront aberrometry could be useful as a noninvasive, objective alternative method for the evaluation of tear film quality.

To summarize, the changes with time in the wavefront aberration associated with the anterior cornea in patients with dry eye are qualitatively similar but occur faster than in normal subjects. In both patient groups, total RMS wavefront aberration passes through a minimum (at 2.9 ± 0.4 seconds after a blink in dry eyes in comparison with 6.1 ± 0.5 seconds in normal eyes). Corneal wavefront aberrometry should be helpful in the study of tear film characteristics in normal eyes and different types of dry eye disorder.

References