Humidity Effects on Corneal Hydration

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Overall corneal hydration control expressed as the percent recovery per hour (PRPH) can be assessed with an exponential model that uses data derived from two kinds of corneal thickness measurements; one from monitoring recovery after inducing corneal swelling, and the other from measurements made after the eye has been open long enough to reach its open-eye steady-state (OESS) corneal thickness. Up to now these thickness measurements have been made without controlling the ambient humidity. It is possible that changes in relative humidity may effect tear film osmolarity sufficiently to change the state of corneal hydration. To evaluate the effects of humidity on hydration control, the OESS and PRPH were determined under several humidity levels. For both the OESS and the PRPH, two substudies were conducted. For the OESS, substudy 1 consisted of measuring corneal thickness when humidity was changed from 30% (ambient) to 52 or 97% controlled humidity. This resulted in mean ± standard deviation (SD) changes in OESS thickness amounting to −0.33 ± 3.5 μm and 2.6 ± 3.4 μm, respectively, with a differential change of 2.94 ± 3.04 μm (95% confidence interval [CI] from 0.77 to 5.11 μm). Corresponding results for substudy 2 connected with changes from 43% (ambient) to 12 or 97% controlled humidity were −2.4 ± 2.7 μm and −0.3 ± 1.9 μm, respectively, with a differential change of 2.1 ± 1.8 μm (95% CI from 0.9 to 3.4 μm). For the PRPH evaluations, ten subjects provided ten right–left eye comparisons at controlled humidities of 52% vs 97%, and substudy 2 with ten additional subjects yielded ten right–left comparisons at controlled humidities of 12 vs 97%. The difference between PRPH under the two controlled humidities in substudy 1 was 2.6 ± 6.6%/hr (95% CI from 2.1 to 7.3%/hr), and the corresponding difference in substudy 2 was 1.85 ± 6.5%/hr (95% CI from 2.8 to 6.5%/hr). Based on the results of this study, it seems unlikely that precorneal humidity would have any substantial effect on OESS corneal thickness or the corneal deswelling response.


Accurate measurements of corneal function would provide a method for determining the effects that disease or surgery and other clinical interventions have on corneal health. Recently, we reported on a method for evaluating corneal function using a procedure that gives an assessment of overall corneal hydration control.1 This assessment is made by using an exponential model to analyze data that is derived from two kinds of corneal thickness measurements—one from monitoring recovery after inducing corneal swelling and the other from measurements made after the eye has been open long enough to reach its open-eye steady-state (OESS) corneal thickness. The combined analysis of these two data sets provides an estimate of the percent corneal thickness recovery per hour (PRPH), which characterizes the approximately exponential recovery of corneal thickness after induced swelling and thereby serves as a measure of corneal hydration control. Until now, these thickness measurements have been made without controlling the ambient humidity to which the eye is exposed. However, it is possible that ambient humidity may have sufficient effect on tear film osmolarity to substantially influence the assessment of corneal hydration control obtained by this procedure.

There is some evidence to suggest that ambient humidity does influence corneal hydration control. For example, Mishima and Maurice found that in the in vitro rabbit, evaporation resulted in 28 μm/hr of corneal thinning. However, when humidity was increased to eliminate evaporative forces, the cornea maintained a constant thickness.2 In another set of experiments, Sherrard removed the corneal endothelium in rabbit eyes and demonstrated that evaporation alone could dehydrate an edematous cornea.3 Also, O’Neal and Poise measured human corneal thinning rates under open and closed eye conditions and found that the deswelling rate was substantially slower when the eyes were closed than when they

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were open. This also suggests that increased humidity levels associated with the closed-eye condition may affect corneal dehydration.4,5

In contrast to these findings, Klyce and Maurice showed that evaporative forces would have very little effect on corneal hydration by demonstrating that when an isolated cornea was bathed on both surfaces by identical media there was almost no increase in corneal thickness.8 Also, experiments such as those described above which have used eye closure to increase humidity and eliminate evaporation may be in error, since it has been shown recently that eye closure can cause substantial amounts of corneal swelling that cannot be explained by changes in tear tonicity alone.7 The mechanism involved in this phenomenon may also influence the deswelling rate when the eyes are closed. Consequently, differences in deswelling in closed, compared to open-eye, conditions cannot necessarily be attributed to evaporative and tear osmolarity mechanisms.

Currently, there is insufficient information to evaluate the effects of humidity per se on human corneal hydration control. However, if assessments of corneal hydration control are to be generally useful as a clinical test of corneal function, it is critical to know the impact of ambient humidity. Consequently, we have evaluated humidity effects on corneal hydration control by using a controlled humidity environment in order to measure OESS thickness and open-eye corneal deswelling under several controlled-humidity conditions.

Materials and Methods

Subjects

Twenty subjects, who had no previous history of contact lens wear, were recruited from the campus community at the University of California, Berkeley. The study group consisted of 11 men and 9 women aged 18 to 36 yr (mean 24.2 ± 6.5 yr). The procedures of the study were explained fully to all subjects and then informed consent was obtained. (The University of California, Berkeley Committee for the Protection of Human Subjects had granted approval for the research project and for the Informed Consent Form and Medical Subject's Bill of Rights given to all participants.) All subjects passed a complete eye examination that indicated normal ocular health. Also, each subject was given a detailed slit-lamp examination to ensure again that the cornea was free of disease. Additional examination of the corneal endothelium was done by specular photomicroscopy, and each photomicrograph was digitized and analyzed for cell count, cell size, and cell size variation (ie, polymegathism). The morphometric analysis indicated that all three endothelial characteristics were within the normal ranges.8-10

Instrumentation

Corneal thickness: Corneal thickness was measured using a modified Haag-Streit pachometer affixed to a Topcon slit-lamp biomicroscope that had small light-emitting diode (LED) lights attached to assist in fixation and alignment. The pachometer was connected to a microcomputer to provide a digital printout of time and corneal thickness. Details of this instrument are described elsewhere.11

Open-eye humidity control: Relative humidity (RH) was controlled by fitting each subject with swim goggles modified with an inlet hole at the bottom of the goggle for the entry of humidified air. Humidity was maintained by passing air through one or more gas wash bottles that were set in a heated bath to maintain a temperature of 23 ± 0.5°C at the eye. The humidified air that passed across the eyes then was exhausted around the periphery of the goggles. The goggle chambers were detached from one another, and each was held on the subject's head by its own elastic strap so that one goggle could be kept on when the other was removed to make pachometry measurements. Humidity and temperature were monitored with a probe (Fisherbrand; Fisher, Springfield, NJ) that was inserted directly into the top of each goggle chamber through an aperture that was opened as needed to make measurements.

Procedures

The basic strategy in this study was to use the two eyes of each subject to make paired comparisons of corneal measurements under two different humidity conditions. The overall study consisted of two substudies that differed according to the pair of humidity levels that were applied to the subjects' right and left eyes. In the first substudy, with ten subjects, one randomly chosen eye was tested at a target humidity of 50% while the contralateral eye was tested at 100%. In the second substudy, with ten additional subjects, the humidity range was extended; the target humidities were 20 and 100%.

Each subject was studied on two separate test days. On the first test day OESS thickness was measured, first at laboratory humidity without goggles and then under controlled-humidity conditions, after the eye had adapted to an applied goggle/humidity environment. On the second test day corneal recovery after inducing swelling was studied simultaneously in the two eyes under the same target humidity conditions that were used in the second phase of the previous...
OESS test. Some more details of the OESS and corneal recovery tests are as follows.

The OESS test was started after the subject had been awake for at least 6 hr and it could safely be assumed that OESS corneal thickness had been reached. The corneal thickness was measured every 10 min for 1 hr, and then the goggles and appropriate target humidities were applied to the two eyes. In preliminary studies, 30 min was found to be sufficient time for corneal thickness to adapt to the goggle/humidity environment. Therefore, after 30 min, a sequence of four groups of corneal thickness measurements, at 30-min intervals, was obtained for estimating the adapted OESS thickness. Each group consisted to two sets of ten quick replicate pachometry measurements with repositioning of the subject between each set. The goggle was removed only when the eye it covered was being measured. These data provided assessments of OESS thickness under goggle/humidity conditions and also contributed to paired comparisons for assessing the change in corneal thickness associated with the change from ambient to one of the target humidities provided by the goggle environment.

During the first part of the OESS test the ambient humidity was measured three times at 30-min intervals. After adaptation to the goggle environment, the goggle humidity was measured four times at 30-min intervals. These values were averaged to give a summary level for the individual subject, and the mean and standard deviation of these values were calculated to establish the actual humidity levels applied to the eyes.

In substudy 1, during the OESS test the mean and SD of ambient humidity from subject to subject was 30 ± 7%. The goggle target humidities were 50 and 100%, but the actual mean humidity levels achieved and the corresponding standard deviations were 52% ± 2 and 97% ± 1, respectively. In substudy 2, which was conducted after substudy 1 had been completed, the mean and SD of ambient humidities was 43 ± 11%. Corresponding to the target humidities of 20 and 100%, the actual achieved humidities were 12% ± 3 and 97% ± 1, respectively.

On another day, ranging from 7 days earlier to 13 days later, each subject was given a second test designed to provide information about each eye's corneal recovery under the same target humidity condition—20, 50, or 100%—which the eye received during the last part of the OESS test, when it was exposed to the goggle/humidity environment. First, the subjects were fitted with 400-μm thick, 40% water content hydrogel lenses which they wore for 2 hr with the eyes closed to produce approximately 60 μm of corneal swelling. The measured transmissibility (Dk/L) of these lenses was $4.5 \times 10^{-9}$ (cm × ml × O2)/(sec × ml × mmHg), which reduced the oxygen tension at the corneal surface to near 0 mmHg when worn with the eyes closed. After the 2-hr stress period, the eyes were opened, lenses were removed, corneal thickness was measured, and a goggle was placed on each eye to control humidity during recovery. To monitor recovery, goggles were removed, one at a time for approximately 2 min as needed, to make two sets of ten replicate corneal thickness readings at 20–30-min intervals over a 3-hr period. Temperature and humidity in the goggle environment were monitored at 20–40-min intervals.

For each eye, data from the “stress” test and data from the last part of the OESS test, which were obtained under the same target humidity conditions, were analyzed by means of a composite exponential model to obtain an estimate of the PRPH, which serves as a measure of overall corneal hydration control. This analytic approach using the data from both the OESS and stress tests yields estimates with substantially more precision than can be achieved with analysis of only the deswelling data from a stress test. In previous reports using this technique, corneal thickness measurements made shortly after removal of the “stress lens” were used along with subsequent measurements to estimate PRPH. Recent work currently being prepared for publication suggests that there is an initial phase of corneal recovery lasting 20–30 min which proceeds at a slower rate than subsequent recovery. Possibly this early slower recovery is an aftereffect of the hypoxic stress used to induce corneal swelling. To avoid any such influences in the estimation of PRPH, only deswelling data obtained after a 20–30-min delay after removal of the stress lens were used in this study for the estimation of PRPH. This method of analyzing data to estimate PRPH gave a mean PRPH of 59.1%/hr, which was 5.9%/hr higher than the mean PRPH of 53.2%/hr that was obtained using the earlier method.

Results

Changes in OESS Thickness

The changes in OESS thickness associated with the transition from ambient humidity without goggles to the humidified goggle environment are shown in Figure 1. The results for the ten subjects in substudy 1, in which the mean ambient humidity was 30% and the target humidities were 50 and 100%, are shown on the left side of the figure. The corresponding results for the ten subjects in substudy 2, with mean ambient humidity of 43% and the more extreme target humidities of 20 and 100%, are shown on the right. A connecting line is used to indicate pairing in the data.
that resulted from using each subject’s two eyes to compare the effects of applying the two different goggle environments.

With the OESS data there are three different paired comparisons that can be examined in each substudy. The first two concern the mean change in OESS thickness in ten eyes associated with the shift from ambient to one of the goggle/humidity conditions. These mean changes presumably reflect the effects of applying goggles, changing humidity, or both. The third paired comparison concerns the mean difference between the changes in corneal thickness in the ten subjects that occurred in the left vs the right eye when each eye was shifted from ambient humidity to its particular target humidity. Both sides of this comparison are balanced with respect to the effect of goggles in order to assess more directly the effect of different humidities, per se.

For the ten eyes that experienced a shift from ambient to 50% target humidity in substudy 1, the mean and SD of changes in corneal thickness were —0.33 ± 3.5 μm. The 95% CI for the true mean change corresponding to this small shift is —2.83 to 2.17 μm. These results are derived from the corneal thickness measurements with mean and SD equal to 533.13 ± 26.12 μm at ambient humidity compared to 532.81 ± 27.44 μm after the eyes stabilized in a mean humidity of 52% in the goggle environment.

For the ten eyes that experienced a shift from ambient to 100% target humidity the corresponding changes in corneal thickness were 2.6 ± 3.4 μm with a 95% CI from 0.17 to 5.03 μm. The mean and SD of corneal thickness were 534.14 ± 24.05 μm at ambient humidity vs 536.76 ± 25.31 μm after stabilization at 97% humidity in the goggle environment.

The differential shift in corneal thickness associated with humidity changes from ambient to 100 vs 50% target humidity obtained from comparisons between eyes using the ten pairs of eyes in substudy 1 was 2.94 ± 3.04 μm with a 95% CI from 0.77 to 5.11. Apparently there is a real but small difference in the effects of these two target humidities.

In substudy 2, the ten eyes that experienced a shift from ambient to 20% target humidity had corneal thickness changes whose mean and SD were —2.4 ± 2.7 μm with a 95% CI for the mean change from —4.3 to —0.5. At ambient humidity the mean and SD were 535.5 ± 36.7 μm, and after stabilization at the achieved 12% humidity, the corresponding results were 533.1 ± 36.7 μm. Following the same reporting conventions, the results for the contralateral eyes exposed to 97% humidity in the goggle environment were —0.3 ± 1.9 μm with a 95% CI from —1.6 to 1.1 μm for changes, 535.1 ± 36.3 μm for levels and 95% CI from 0.9 to 3.4 μm. Again, as in substudy 1, there was a small but apparently real difference between the effects of the more extreme target humidities used in this substudy.
Changes in PRPH

For the portion of the study concerning PRPH, the only paired comparison available is the one between the subject’s two eyes, which received the different target environments. In Figure 2 the paired measurements of PRPH for the ten subjects in substudy 1 with target humidities of 50 and 100% are shown on the left side, and the ten subjects in substudy 2 with target humidities of 20 and 100% are shown on the right.

In substudy 1 the mean and SD for PRPH for ten eyes at 52% goggle humidity were 60.2 ± 9.6%/hr. The corresponding results for ten eyes at 97% goggle humidity were 57.6 ± 11.1%/hr. The differences for ten subjects (PRPH at 52–97%) have estimated means and SDs of 2.6 ± 6.6%/hr with a 95% CI for the true mean difference given by the interval from 2.1 to 7.3%/hr. The observed mean difference, which gives the best available estimate of the effect of the humidity differential, indicates faster recovery at lower humidity, as would be expected on theoretic grounds, and the 95% CI indicates that the true humidity effect is not likely to be very large.

Discussion

This study shows that the OESS corneal thickness is relatively stable when the cornea is exposed to large changes in humidity. We did measure some changes in corneal thickness that corresponded to the predicted directions (e.g., the transition from lower to higher humidity resulted in an increased corneal thickness). However, the changes were too small to have any substantial effect on the state of corneal hydration and probably would not influence the measurement of corneal hydration in the clinical setting.

Moreover, our results indicate that the corneal recovery rates measured under varying humidity levels are about the same. Even when humidity conditions were varied as much as 90%, the differences in PRPH values were only on the order of 2–3%/hr.

These findings differ from those of O’Neal and Polse⁴,⁵ who found that corneal deswelling under high-humidity conditions tended to substantially reduce corneal recovery. However, in their experiments high-humidity environments were maintained by having the subjects close their eyes. More recent information suggests that this procedure most likely resulted in corneal hypoxia. Closed-eye hypoxia was first suggested by Schoessler and Orsborn, who observed an increase in endothelial polymegethism in
the superior cornea of a patient with unilateral ptosis, which presumably resulted from hypoxia to the super-
ior cornea covered by the upper lid. More recently, 
Koch and colleagues demonstrated in rabbit studies 
that eye closure can cause substantial amounts of 
corneal swelling that cannot be explained on a simply 
smotic basis. It therefore seems that the effect of 
humidity on corneal deswelling rates cannot be de-
termined accurately when the humidity level is in-
creased by eye closure.

Based on the results of the current study, it seems 
unlikely that normal humidity changes in the clinical 
or laboratory environment would have any substan-
tial effect on the corneal deswelling response. For ex-
ample, we monitored our laboratory ambient humid-
ity over 8 months and found that the RH varied from 
about 35 to 70%. This range is considerably smaller 
than the humidity range used in the controlled hu-
midity experiments. The resulting changes in PRPH 
from typical laboratory humidity shifts therefore 
would be expected to be minimal.

Key words: corneal function, relative humidity, hypoxia, 
corneal edema, endothelial function

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