Effect of Controlled Adverse Chamber Environment Exposure on Tear Functions in Silicon Hydrogel and Hydrogel Soft Contact Lens Wearers

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PURPOSE. To prospectively evaluate the effect of controlled adverse chamber environment (CACE) exposure on tear function, including tear osmolarity, in subjects wearing narafilcon A versus those wearing etafilcon A soft contact lenses (SCL).

METHODS. Thirty-one healthy subjects with no history of contact lens wear (13 women, 18 men; average age, 30.5 ± 6.5 years) were randomly divided into age- and sex-matched groups (15 subjects wearing narafilcon A SCL; 16 subjects wearing etafilcon A SCL) and entered a CACE for 20 minutes. All subjects underwent tear osmolarity, tear evaporation rate, strip meniscometry, tear film breakup time, fluorescein vital staining, and functional visual acuity measurement before and after exposure to the controlled adverse chamber.

RESULTS. The mean blink rate increased with significant deterioration in the mean symptom VAS scores, mean tear osmolarity, tear evaporation rate, strip meniscometry score, and tear stability with CACE exposure along with a decrease in visual maintenance ratio in functional visual acuity testing in etafilcon A wearers. The mean symptom VAS scores, mean tear evaporation rate, tear stability, blink rates, and visual maintenance ratios did not change significantly in narafilcon A wearers after CACE exposure.

CONCLUSIONS. This study suggested marked tear instability, higher tear osmolarity, and increased tear evaporation with marked dry eye and visual symptomatology in nonadapted hydrogel SCL wearers, suggesting that silicone hydrogel SCLs may be suitable for persons who live and work in cool, low-humidity, and windy environments.

Recent estimates suggest that approximately 34 million Americans wear contact lenses.1 Even healthy subjects with normal tear function who wear contact lenses may experience discomfort or dryness associated with contact lens wear.2 Riley et al.2 reported that 25% of 1092 current contact lens wearers experience symptoms of dryness. Other studies suggested that at least half of contact lens wearers had dryness-related symptoms.3 An epidemiologic study in Japan on 3549 office workers showed that 39.2% were contact lens users, 20.9% of whom had clinically diagnosed dry eye and 50% of whom had severe symptoms of dry eye disease.4 Contact lens wear was also found to be a significant risk factor for dry eye disease in a study including 3433 high school students in Japan; 17.4% of boys and 20.9% of girls wearing contact lenses had clinically diagnosed dry eye disease with a higher risk ratio for soft contact lens (SCL) wear, and 37% of either boys or girls among contact lens wearers had severe dry eye symptoms.5

Many mechanisms can account for the dry eye symptomatology in contact lens wearers, among which environmental factors have been reported to considerably impact dryness symptoms during contact lens wear.6–8 Environmental factors such as humidity, wind, and temperature may be difficult to avoid or control in the daily environment.9–11 The variability of signs and symptoms during contact lens wear can complicate evaluation of the ocular surface effects of contact lens wear. The environmental and behavioral differences among subjects are indeed a challenging issue in establishing a reliable baseline and accurate evaluation of different contact lens materials.

When evaluating the effects of new contact lens materials on tear functions, sources of such variation must be reduced by regulation of the environmental factors and the subject’s activities. Controlled adverse chamber environments (CACE) provide a useful tool for investigating the tear function and ocular surface alterations associated with new contact lens materials.12

In this study, we evaluated the effect of CACE exposure on tear functions, including tear osmolarity, in subjects wearing a new silicone hydrogel SCL, narafilcon A, and compared the results with those of subjects wearing a hydrogel SCL, etafilcon A.

SUBJECTS AND METHODS

Subjects

Thirty-one healthy subjects with no history of contact lens wear (13 women, 18 men; average age, 30.5 ± 6.5 years) were randomly divided into age- and sex-matched SCL wear groups (15 subjects, narafilcon A [True Eye, base curve 8.5-mm diameter, 14.2 mm]; Johnson & Johnson Vision Care, Jacksonville, FL; 16 subjects, etafilcon A [1-Day Acuvue, base curve 8.5-mm diameter, 14.2 mm]; Johnson & Johnson Vision Care, Jacksonville, FL).
Care) and were then asked to enter a CACE for 20 minutes. Subjects with a history of previous contact lens use, ocular diseases, systemic diseases with known associations to ocular surface diseases, and positive smoking history were excluded from the study. Subjects with diagnoses of dry eyes according to the diagnostic criteria of the Dry Eye Research Group in Japan and subjects with meibomian gland disease were also excluded from the study.13

All subjects initially underwent automated refractometry and visual acuity measurements to determine the SCL powers before the experiments and wore their prescription lenses 1 week before adverse chamber experiments which provided some period of adaptation to the SCLs worn. SCLs used in this study were purchased from Ginza Optical Store (Tokyo, Japan). On the day of the tear film and ocular surface examinations, subjects initially underwent tear film breakup time test and fluorescein vital stainings. The ocular surface was washed with unpreserved artificial tears. After 60 minutes of waiting, subjects wore their contact lenses and were asked to wait for another hour. All subjects then underwent tear osmolarity, tear evaporation rate, and strip meniscometry measurements, followed by functional visual acuity measurements, while wearing their SCLs. The subjects were allowed to enter the CACE in groups of two and stayed in the room for 20 minutes (Supplementary Fig. S1, http://www.iovs.org/lookup/suppl/doi:10.1167/iovs.106841/-/DCSupplemental). Tear sample collections for osmolarity testing were collected at the end of 20 minutes, just before the subjects left the room, and were immediately tested with the tear laboratory device outside the CACE room. All subjects again underwent tear evaporation rate, strip meniscometry, and functional visual acuity testing. After removal of the SCLs, all subjects waited another 60 minutes and then underwent tear film breakup time measurement and fluorescein vital staining one more time. Symptoms of dryness, foreign body sensation, and satisfaction with vision quality during functional visual acuity testing were quantified before and after exposure to the CACE using visual analog scale (VAS) scores. Informed consent was obtained from all subjects. This study was approved by the local ethics board and adhered to the tenets of the Declaration of Helsinki.

Controlled Adverse Chamber Environment Settings

Subjects were placed in a CACE located in Keio University School of Medicine. The controlled chamber was an isolated room 2.38 m wide, 2.95 m long, and 2.44 m high. The room was equipped with a closed air circulation system consisting of a circular duct with propellant and return vents (Daikin, Osaka, Japan). Temperature and relative humidity (RH) could be precisely controlled between 0°C and 50°C and RH between 0% and 100%, with 10% tolerance. The control of RH was achieved with a 110-W and a 1.0-kg/h humidifier (WM-BNB; Daikin, Osaka, Japan). Control of the adverse chamber room conditions was achieved with a 110-W and a 1.0-kg/h humidifier (WM-BNB; Daikin, Osaka, Japan). Temperature and RH were carefully supervised during the entire duration of the experiments, with adjustment switches set outside the chamber that were used to measure temperature and humidity. For this study, the temperature was set at 18°C, and the RH was 18%. The temperature and RH were recorded at the beginning and at the end of each experiment, and the mean values (±SEM) were 18.0°C ± 1.0°C and 18.5% ± 1.0%, respectively. The wind flow was controlled by eight electric fans (Yamazen, Shanghai, China). All subjects were asked to stand 1 m away from the fans, facing the fans for 20 minutes. The wind velocity in the room 1 m away from the fans was 1.2 m/s, which was constant throughout the experiments and was measured by a wind velocity meter (Tesco, Yokohama, Japan). We chose an environmental setting that we thought would resemble the effect of a dry, windy, cool day on the ocular surface and tear functions of SCL wearers.

Evaluation of Ocular Fatigue Symptoms

Symptoms of dryness, foreign body sensation, and vision quality change were evaluated with VAS scores. Participants checked on the VAS sheets before and after exposure to the adverse chamber environment. Lower scores on the VAS referred to less severe degree of symptomatology whereas higher VAS scores indicated severe symptoms in this study (minimum, 0 point; maximum, 100 points).

Tear Evaporation Rate Measurements

We measured the tear evaporation rate (TEROS) with a quartz crystal humidity sensor (Kao Analytical Research Center, Tochigi, Japan).14,15 The temperature and humidity of the outer examination room were within 23°C to 25°C and from 30% to 40%, respectively.

Tear Osmolarity Measurements

The TearLab osmolarity test uses a temperature-corrected impedance measurement to provide an indirect assessment of osmolarity (range, 275–400 mOsm/L). The equipment consists of single-use test cards containing microchannels to collect 50 mL tear fluid, held by a pen designed to facilitate tear collection, and a portable reader unit that elaborates and displays the osmolarity results. Tear samples were collected from the outer lower tear meniscus, slightly sliding the pen over the lid margin, taking care not to touch the conjunctival surface and collecting the tears in one brief attempt. Tear osmolarity was measured in both eyes in accordance with the manufacturer’s instructions. Subjects had been requested not to wear makeup on their eyelids and not to use any eyedrops 2 hours before testing. Accordingly, a time frame of at least 120 minutes was set between the ocular surface wash and osmolarity measurements in this study. The more severe of the bilateral measurements was used in analysis because of the asymmetric effects of transient compensatory mechanisms attempting to drive down tear osmolarity in response to environmental stress.16

Strip Meniscometry Testings

The tip of the meniscometry strip was briefly inserted for 5 seconds into the lateral lower tear meniscus without touching the ocular surface. The duration of the test was measured strictly by a stopwatch chronometer at each testing. The length of the stained tear column in the central membrane ditch was regarded as the SM value in that eye in millimeters. The SM testing has been reported to be useful in the evaluation of tear meniscus volume, as reported previously.17

Functional Visual Acuity Measurements

Functional visual acuity measurements (FVA Measurement System; Nidek, Gamagori, Japan) were used to examine the time change in the continuous visual acuity. The device consists of three parts: a hard disc, a monitor, and a joystick. The Landolt optotypes are presented on the monitor, and their sizes change, depending on the correctness of the responses. In brief, the optotypes are displayed automatically, starting with the smaller ones. Display time of an optotype was set at 2 seconds. Patients delineated the orientation of the automatically presented Landolt rings by handling the joystick. When the response is correct, smaller optotypes are presented. If the responses are incorrect, larger optotypes are presented automatically. Visual acuity (VA) is continuously measured from the baseline best-corrected Landolt VA, which is the best-corrected Landolt VA. FVA measurement can measure VA from 20/10 to 20/200, depending on the choice of examination distance (5, 2.5, or 1 m). The monitor was placed at 5 m from the subjects in the present study. When there was no response within the set display times, the answer was assumed to be an error, and the optotype was automatically enlarged. Visual maintenance ratio (VMR), which is defined as the ratio of FVA divided by the value of baseline VA, a parameter delineating the ability of a subject to maintain his or her baseline acuity over the testing time, was chosen as the end point in FVA testing. FVA testing was performed during a 60-second normal blink period. Blink frequency was also measured during the 60-second testing.18

Tear Function Tests

The standard tear breakup time (TBUT) measurement was performed after instillation of a 2-μL volume of a 1% fluorescein dye in the
conjunctival sac with a micropipette. Patients were then instructed to blink several times for a few seconds to ensure adequate mixing of the dye. The interval between the last complete blink and the appearance of the first corneal black spot in the stained tear film was measured three times, and the mean value of the measurements was calculated. A cobalt blue filter was used to measure the TBUT.19

**Vital Staining**

Fluorescein stain scoring of the ocular surface was performed. The fluorescein staining scores of the ocular surface ranged between 0 and 9 points.13 In fluorescein staining, the cornea was divided into three equal upper, middle, and lower zones. Each zone had a staining score ranging between 0 and 3 points, with the minimum and maximum total staining scores ranging between 0 and 9 points.19

**Statistical Analysis**

For statistical analyses, the paired t-test was used for comparison of tear functions and ocular surface tests before and after exposure to CACE. P < 0.01 was considered statistically significant. Data were processed using statistical software (Instat 3.0; GraphPad, San Diego, CA).

**RESULTS**

**Foreign Body Sensation VAS Scores**

The mean foreign body sensation (FBS) VAS score showed an insignificant increase from 15.2 ± 6.02 points to 23.6 ± 19 points in the narafilcon A group (P = 0.02) but a significant increase from 15.8 ± 13.8 points to 40 ± 25 points in the etafilcon A group on exposure to the CACE, as shown in Figure 1A (P = 0.002).

**Dryness VAS Scores**

The mean dryness VAS score showed an insignificant increase from 22.3 ± 21 points to 32.6 ± 13 points in the narafilcon A group (P = 0.02) but a significant increase from 12.1 ± 13.3 points to 40.2 ± 26 points in the etafilcon A group on exposure to the CACE, as shown in Figure 1B (P = 0.0004).

**Self-Reported Quality of Vision VAS Scores**

The mean vision quality VAS scores before and after CACE exposure were 29.1 ± 31.8 points and 27.7 ± 21.4 points in the narafilcon A group (P = 0.38). The mean vision quality VAS score showed a significant increase from 23.2 ± 20 points to 49.2 ± 30 points in the etafilcon A group on exposure to the CACE, as shown in Figure 1C (P = 0.005).

**Tear Evaporation Rate Changes**

The mean TEROS showed a statistically significant increase from 5.0 ± 2.8 × 10⁻⁷ g/cm²/s to 9.1 ± 3.1 × 10⁻⁷ g/cm²/s after CACE exposure in the etafilcon A group (P < 0.0001). The mean TEROS showed an insignificant increase from 4.5 ± 3 × 10⁻⁷ g/cm²/s to 5.9 ± 3.3 × 10⁻⁷ g/cm²/s with CACE exposure in the narafilcon A group, as shown in Figure 2 (P = 0.06).

**Tear Osmolarity Changes**

The mean tear osmolarity showed an insignificant increase from 304.6 ± 12.1 mOsm/L to 306 ± 14.8 mOsm/L after CACE exposure in the narafilcon A group (P = 0.35). It also showed a significant increase from 290 ± 15.3 mOsm/L to 313.5 ± 13 mOsm/L with CACE exposure in the etafilcon A group, as shown in Figure 3 (P < 0.0001). Three eyes (20%) in the narafilcon A group had a tear osmolarity value greater than 312 mOsm/L before CACE exposure, whereas the tear osmolarity exceeded 312 mOsm/L in nine eyes (56%) after CACE exposure.

None of the eyes (0%) in the etafilcon A group had a tear osmolarity value greater than 312 mOsm/L before CACE exposure, whereas the tear osmolarity exceeded 312 mOsm/L in nine eyes (56%) after CACE exposure.

**Strip Meniscometry Score Changes**

The mean strip meniscometry (SM) score showed an insignificant decrease from 2.38 ± 1.55 mm to 1.82 ± 1.13 mm after CACE exposure in the narafilcon A group (P = 0.25). The mean SM score showed a significant decrease from 3.28 ± 1.89 mm to 2.69 ± 1.33 mm after CACE exposure in the etafilcon A group (P = 0.0004).
to 1.96 ± 1.44 mm with CACE exposure in the etafilcon A group, as shown in Figure 4 (*P < 0.006).

**Tear Breakup Time Changes**

The mean TBUT showed a statistically significant decrease from 9.96 ± 4.7 seconds to 6.04 ± 2.8 seconds after CACE exposure in the etafilcon A group (*P < 0.0002), whereas no statistically significant changes were observed before (7.86 ± 3.91 seconds) and after (7.18 ± 3.29 seconds) CACE exposure in the narafilcon A group, as shown in Figure 5 (*P < 0.22).

**Fluorescein Staining Score Changes**

The mean fluorescein staining scores did not show significant changes with CACE exposure in the narafilcon A or the etafilcon A group, as shown in Figure 6.

**Blink Rate Changes**

The mean blink rate showed a significant increase from 14 ± 8 blinks/min to 20 ± 8 blinks/min with CACE exposure in the etafilcon A group (*P < 0.004). The mean blink rates did not show significant changes with CACE exposure in the narafilcon A or the etafilcon A group (*P < 0.38), as shown in Figure 7.

**Functional Visual Acuity Changes**

The mean functional visual acuity (FVA) did not show any statistically significant changes with CACE exposure in the narafilcon A group (*P < 0.16), but it decreased significantly from 0.97 ± 0.28 to 0.80 ± 0.15 in the etafilcon A group with CACE exposure, as shown in Figure 8 (*P < 0.009).

**Visual Maintenance Ratio Changes**

The mean VMR did not show any statistically significant changes with CACE exposure in the narafilcon A group (*P < 0.14), but it decreased significantly from 0.97 ± 0.02 to 0.94 ± 0.02 in the etafilcon A group with CACE exposure, as shown in Figure 9 (*P < 0.0007).

**DISCUSSION**

Previous research suggested the propensity of contact lens wear to instigate symptoms of ocular dryness. This has been attributed to disruption of the normal tear film with thinning of the tear film and lipid layer over the lens surface and increased tear evaporation. The ability of environmental conditions to contribute to and exacerbate contact lens–related dryness has also been reported. Environmental chambers that create controlled environments in relation to humidity, temperature, or air flow have been suggested to be very useful for understanding how the environment affects the ocular surface and provokes signs and symptoms of dry eye. They have also been used to improve the design of clinical trials and to evaluate the effect of contact lens wear on the ocular surface.

In this report, we evaluated the tear and ocular surface effects of 20-minute CACE exposure in healthy subjects with normal tear functions who were assigned to the silicon hydro-
gel SCL (narafilcon A) or a hydrogel SCL (etafilcon A) wear group. CACE settings were adjusted to resemble a cool and windy day with low humidity.

All SCL wearers in our study reported increased foreign body sensation and dryness VAS scores and alterations in tear function, suggesting that the CACE exposure elicited the intended effects as expected.

Although the mean tear evaporation rates increased in both groups in this study, the increase was markedly significant in the etafilcon A group. Along with increases in tear evaporation rates, we observed a significant increase in the hydrogel SCL wear group. Simultaneous increases in tear evaporation rates and tear osmolarity values can also explain the increased symptomatology in both contact lens wear groups. Indeed, increased tear osmolarity has been reported to be associated with increased dry eye symptomatology. Increased tear osmolarity has been reported to be associated with increased dry eye symptomatology. In this study, significantly higher symptom scores were noted in the hydrogel SCL group than in the silicon hydrogel group. Silicon hydrogel SCLs have been reported to perform better than hydrogels in dry environments. Our study found that hydrogel contact lens wearers had significantly more symptoms, which may relate to the lens water content. Oursler et al.12 reported that CACE exposure increased discomfort scores in subjects wearing senofilcon A or other habitual contact lenses with better mean discomfort scores while wearing senofilcon A SCLs. No statistically significant trends were found for conjunctival redness scores, TBUT, or vital staining scores between senofilcon A and habitual lenses with CACE exposure in that study. It should, however, be noted that no direct comparisons can be made between the Ousler et al.12 study and ours because the type of habitual lenses was not clarified and Ousler et al.12 included the presence of wind parameter.

Apart from increased symptomatology, significant destabilization of the tear film was observed in the hydrogel SCL wear group without any significant change in the silicon hydrogel wearers. Indeed, a short TBUT has been linked to reports of subjective discomfort. Maruyama et al. previously reported that the tear film on hydrogel SCLs became thinner, the noninvasive TBUT became shorter, and symptoms of dryness increased when room temperature and relative humidity decreased in controlled adverse environments. Our study investigated the tear film breakup over the ocular surface instead of the contact lens surface. Maruyama et al. also found that dryness was significantly worse in SCLs with higher water content although the water content was not found to have a significant effect on noninvasive TBUT, and they concluded that temperature and humidity did not seem to have an apparent effect on ocular surface tear volume.

Interestingly, our study noted that etafilcon A wearers experienced a significant decrease in strip meniscometry values,
which have been reported to reflect the tear meniscus volume. The decrease in the tear meniscus volume in etafilcon A wearers might have resulted from increased tear evaporation from the ocular surface. These differences from the Maruyama et al. study, we believe, can be attributed to the presence of a windy setting in our adverse chamber environment.

We believe that the increased tear evaporation rate resulted in reduced tear meniscus volume and increased tear osmolarity value, which destabilized the tear films and caused dry eye or foreign body sensation, or both, in the etafilcon A lens wear group.

The extent of dryness symptoms, tear instability, and alterations of other tear functions were significantly higher in the hydrogel SCL wearers. Of interest was the significant increase in the blink rates of the etafilcon A SCL wear group compared with the narafilcon A SCL wear group. We think the relatively higher blink frequency in etafilcon A wearers was a compensation mechanism to alleviate the relatively higher dryness over the lens surface. We also noted with interest that FVA scores and visual maintenance ratios in functional visual acuity testing were significantly lower in hydrogel SCL wearers, who also reported worsening of vision quality symptom scores on exposure to the CACE. This might have been due to the higher blink rates in hydrogel SCL wearers, which might have interfered with the continuous visual acuity testing process. Our study reported the tear osmolarity changes in hydrogel and silicon hydrogel SCL wearers exposed to CACE and for the narafilcon A SCL in a cool, low-humidity, windy setting for the first time. Although mean tear osmolarity slightly increased with adverse chamber exposure in etafilcon A wearers, the increase was significant in etafilcon A wearers in our study. Mean tear osmolarity values both before and after exposure were within the normal range in our study. Stahl et al. previously reported that although no association between tear film osmolarity and ocular comfort was observed with 6 hours of SCL wear in nonhabitual or occasional SCL wearers, SCL osmolarity was observed to be more associated with wear comfort.

Differences in ocular symptomatology with adverse environment exposure observed in this study might have been due to differences in contact lens osmolarity. Indeed, tear film hyperosmolality during contact lens wear has been shown to be a function of evaporation, contact lens osmolarity, or both. Karkkainen also showed an increase in contact lens osmolarity during contact lens wear and postulated that elevated contact lens osmolarity could contribute to tear film osmolarity by producing an osmotic gradient and could be a cause of ocular discomfort. It has been reported, similar to our findings, that the effect of contact lens wear in normal eyes is a small elevation in osmolarity that is not outside the normal range. The effects of contact lens wear in subjects with dry eye is different, with much larger increases in tear osmolarity, because ocular surfaces with dry eye disease may be unable to maintain tear homeostasis in response to environmental or contact lens stress. The cutoff value for tear osmolarity in differentiating mild-moderate dry eye disease from the normal condition was reported to be 312 mOsm/L (73% sensitivity, 92% specificity) in a recent study. There was a 20% increase in the number of eyes exceeding that previously reported cutoff value after CACE exposure in the narafilcon A group, whereas there was a 56% increase in the number of eyes exceeding the 312 mOsm/L cutoff value after CACE exposure in the etafilcon A group. Our results provide further evidence of the extent of tear osmolarity stress imposed by different SCL materials on the ocular surface when exposed to a desiccating environment.

One of the shortcomings of the present study was that first-time contact lens users were recruited instead of long-time adapted contact lens wearers. A brief period of 1 week of SCL wear, however, was allowed before the adverse chamber experiments began. This should have provided some adaptation, but we think it also prevented us from looking into immediate effects of SCL wear on tear functions on exposure to the adverse chamber environment. Although recruitment of first-time SCL wearers allowed control of many variables associated with long-time adapted SCL wear, such as differences in wear protocols, wear times, cleaning solutions, and medication use, future studies looking into the effects of adverse environments in long-time adapted SCL users should be carried out and would add immensely to the literature. Such studies on both symptomatic and asymptomatic adapted lens wearers would also add invaluable information to our current knowledge.

In summary, this study found marked tear instability, higher tear osmolarity, and increased tear evaporation with marked dry eye and visual symptomatology in nonadapted hydrogel SCL wearers, suggesting that silicone hydrogel SCLs may be suitable for persons who live and work in cool, low-humidity, windy environments, as tested in this study.

References


