OVERVIEW CORNEAL SWELLING WITH HIGH AND LOW POWERED SILICONE HYDROGEL LENSES

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KEYWORDS
Corneal swelling; Silicone hydrogel lenses; Oxygen transmissibility; Optical pachometry; Corneal thickness

Abstract
Purpose: To compare central corneal swelling after eight hours of sleep in eyes wearing four different silicone hydrogel lenses with three different powers.
Methods: Twenty-nine neophyte subjects wore lotrafilcon A (Dk, 140), balafilcon A (Dk, 91), galyfilcon A (Dk, 60) and senofilcon A (Dk, 103) lenses in powers −3.00, −10.00 and +6.00 D on separate nights, in random order, and on one eye only. The contra-lateral eye (no lens) served as the control. Central corneal thickness was measured using a digital optical pachymeter before lens insertion and immediately after lens removal on waking.
Results: For the +6.00 D and −10.00 D, lotrafilcon A induced the least swelling and galyfilcon A the most. The +6.00 D power, averaged across lens materials, induced significantly greater central swelling than the −10.00 and −3.00 D (Re-ANOV A, p < 0.001), (7.7 ± 2.9% vs. 6.8 ± 2.8% and 6.5 ± 2.5% respectively) but there was no difference between −10.00 and −3.00 D. Averaged for power, lotrafilcon A induced the least (6.2 ± 2.8%) and galyfilcon A the most (7.6 ± 3.0%) swelling at the center (Re-ANOV A, p < 0.001). Central corneal swelling with +6.00 D was significantly greater than −10.00 D lens power despite similar levels of average lens transmissibility of these two lens powers.
Conclusions: The differences in corneal swelling of the lens wearing eyes are consistent with the differences in oxygen transmissibility of the silicone hydrogel lenses. In silicone hydrogel lenses central corneal swelling is mainly driven by central lens oxygen transmissibility.
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En general, el edema corneal es compuesto por diferentes componentes moleculares y celulares. El edema corneal puede ser clasificado en dos tipos principales: edema de líquido y edema celular. El edema de líquido se refiere al aumento en la cantidad de líquido intraocular, mientras que el edema celular se refiere al aumento en la cantidad de células en el área afectada.

El edema corneal puede ser causado por varios factores, incluyendo el estrés físico, la inflamación, la enfermedad sistémica y el uso de lentes de contacto. El estrés físico puede provocar un aumento en la presión intraocular, lo que puede llevar a edema corneal. La inflamación puede ser causada por diversas enfermedades, como la artritis reumatoide y la osteoartritis. La enfermedad sistémica, como la diabetes mellitus, también puede ser causa de edema corneal. El uso de lentes de contacto también puede contribuir al edema corneal, ya que los lentes pueden disminuir la transmisión de oxígeno a la córnea, lo que puede llevar a edema corneal.

El edema corneal puede ser diagnosticado mediante un examen oculista, que incluye la inspección del ojo y la medición de la presión intraocular. Si se sospecha edema corneal, se pueden realizar más pruebas para determinar la causa exacta del edema. Las pruebas que se pueden realizar incluyen la biopsia de tejido ocular, la tomografía por emisión de positrones y la resonancia magnética.

El tratamiento del edema corneal depende de la causa. En algunos casos, el tratamiento puede incluir la reducción del estrés físico, el tratamiento de la inflamación y el tratamiento de la enfermedad sistémica. En otros casos, el tratamiento puede incluir el uso de lentes de contacto especiales, la cirugía ocular o la administración de medicamentos. En algunos casos, el edema corneal puede ser irreversible y causar daño permanente a la córnea.

En resumen, el edema corneal es una condición que puede afectar a cualquier persona y puede ser causada por varios factores. El diagnóstico y el tratamiento del edema corneal deben realizarse de manera oportuna para evitar complicaciones y mejorar la calidad de vida del paciente.
be differentiated. In addition, this study aimed to investigate whether central corneal swelling is primarily driven by central or average lens transmissibility. Therefore, we compared central overnight corneal swelling induced by four different silicone hydrogel lenses with three different powers and tested the following null hypotheses:

1) There are no statistically significant differences in central corneal swelling between the lens types for each lens power.
2) There are no statistically significant differences in overall central corneal swelling between the 4 lens types.
3) There are no statistically significant differences in overall central corneal swelling between the 3 lens powers.
4) Average oxygen lens transmissibility is not the main driver of central corneal swelling in silicone hydrogel lenses.

Distribution of central corneal swelling across subjects from this study has been published showing that both the lens-wearing and control eyes followed a normal curve. This validates the use of parametric statistics for data analysis and the use of mean values to represent the central tendency of the data in this paper.

Materials and methods

Subjects

This was a non-dispensing, randomized and double-masked study. Based on the data from previous corneal swelling studies at the Center for Contact Lens Research (CCLR), 26 subjects were required to detect a 0.8 ± 1.2% difference in central corneal swelling with a power of 0.90 at α = 0.05. In this study 37 neophytes were enrolled and 29 completed the study (14 female, 15 male). Eight subjects chose to discontinue from the study for personal reasons (relocation, finding a new job, etc.) before completing all follow-up visits. Only the data from the subjects who completed all study visits were included for data analysis. The mean age of the subjects was 27.1 ± 7.9 years (median 25 years, ranging from 17 to 50 years). Every subject wore each of the 12 lenses according to a randomization table. Table 1 summarizes the refractive characteristics of the subjects enrolled in the study. Ethics approval was obtained from the Office of Human Research Ethics, University of Waterloo, and informed consent was obtained for each subject prior to enrolment in the study. All subjects were treated in accordance with the tenets of the Declaration of Helsinki.

Instrumentation and lenses

Corneal thickness of each eye was measured using a computerized digital optical pachometer mounted on a Zeiss 30 SL-M biomicroscope. To enhance precision for obtaining the corneal thickness measurement at each time point, seven consecutive measurements were taken and the highest and the lowest readings were excluded by the instrument’s custom software. The average of the remaining five measures was the recorded value of the corneal thickness provided that the standard deviation of these five measurements did not exceed 5 μm, otherwise the measurement of that time point was repeated.

Corneal swelling was derived from the percentage difference in corneal thickness compared with the baseline measurements using the following formula

\[
\text{Corneal swelling} \% = \left( \frac{\text{measured corneal thickness} - \text{baseline corneal thickness}}{\text{baseline corneal thickness}} \right) \times 100
\]

The parameters of the lenses used during the study are presented in Table 2.

Lens metrology

Central lens thickness was measured (masked for lens type and power) using a digital lens thickness gauge (Rehder Development Company, Castro Valley, CA, USA). This measurement was conducted on a random sample of the study contact lenses (i.e. 20% of lenses) worn by the subjects after lens removal. For each lens power central transmissibility was calculated using the following formula:

\[
\text{Central } Dk/t (\text{cm ml } O_2)/\text{(ml s mmHg)} = Dk (\text{cm}^2/\text{s}) (\text{ml } O_2/\text{ml mmHg})/\text{central } t (\text{cm})
\]

The measured central thickness and calculated Dk/t values are recorded in Table 3.

Computing harmonic average lens thickness and harmonic average lens transmissibility

In this study harmonic average lens thickness over a cord diameter of 6.8 mm for each lens was computed using the software by Douthwaite. Harmonic average lens transmissibility values were calculated by applying manufacturers’ quoted lens permeability values to these data using the following formula:

\[
\text{Harmonic average } Dk/t (\text{cm ml } O_2)/\text{(ml s mmHg)} = Dk (\text{cm}^2/\text{s}) \times (\text{ml } O_2/\text{ml mmHg})/\text{Harmonic average lens thickness (cm)}
\]

The computed harmonic average lens thickness and calculated harmonic average Dk/t values are recorded in Table 4.

Procedures

For each overnight period one of the study lenses was placed on one eye (according to a randomization table) in the evening, prior to sleep. Subjects were then carefully examined to ensure that the lenses were fitting properly, such that there were no debris trapped between the lens and the cornea and the lens was comfortable. The following morning subjects were woken at 7am to remove the lens. Immediately after removal, subjects were escorted to the exam room with their eyes closed. Corneal thickness of each eye was measured immediately after eye opening, after the subjects were comfortably seated at the optical pachometer. Each measurement was then repeated on both eyes every
Table 1  Subject refractive characteristics (Mean dioptres ± SD).

<table>
<thead>
<tr>
<th></th>
<th>OD</th>
<th>OS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>K-readings</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flat K</td>
<td>42.94 ± 1.42</td>
<td>42.84 ± 1.35</td>
</tr>
<tr>
<td>Steep K</td>
<td>43.44 ± 1.63</td>
<td>43.48 ± 1.52</td>
</tr>
<tr>
<td>Corneal cylinder</td>
<td>−0.69 ± 0.42</td>
<td>−0.77 ± 0.46</td>
</tr>
<tr>
<td><strong>Refractive error</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sphere</td>
<td>−0.29 ± 1.32</td>
<td>−0.14 ± 1.53</td>
</tr>
<tr>
<td>Cylinder</td>
<td>−0.38 ± 0.41</td>
<td>−0.41 ± 0.48</td>
</tr>
</tbody>
</table>

Table 2  Lens parameters.

<table>
<thead>
<tr>
<th>Lens</th>
<th>Material</th>
<th>Manufacturer</th>
<th>Dk (cm²/s)</th>
<th>Central Dk/t</th>
<th>Power (D)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>(ml O₂/ml mmHg)</td>
<td>(nominal for −3.00 D) (cm ml O₂)/(ml s mmHg)</td>
<td></td>
</tr>
<tr>
<td>Night &amp; Day®</td>
<td>lotrafilcon A</td>
<td>CIBA Vision</td>
<td>140 × 10⁻¹¹</td>
<td>175 × 10⁻⁹</td>
<td>−3.00, −10.00, +6.00</td>
</tr>
<tr>
<td>PureVision®</td>
<td>balafilcon A</td>
<td>Bausch &amp; Lomb</td>
<td>91 × 10⁻¹¹</td>
<td>101 × 10⁻⁹</td>
<td>−3.00, −10.00, +6.00</td>
</tr>
<tr>
<td>Acuvue® Advance™</td>
<td>galyfilcon A</td>
<td>Johnson &amp; Johnson Vision Care</td>
<td>60 × 10⁻¹¹</td>
<td>86 × 10⁻⁹</td>
<td>−3.00, −10.00, +6.00</td>
</tr>
<tr>
<td>Acuvue® OASYS™</td>
<td>senofilcon A</td>
<td>Johnson &amp; Johnson Vision Care</td>
<td>103 × 10⁻¹¹</td>
<td>147 × 10⁻⁹</td>
<td>−3.00, −10.00, +6.00</td>
</tr>
</tbody>
</table>

20 min over the first hour after eye opening and every hour for the subsequent two hours.

Central corneal thickness in both lens wearing and control eyes was measured using a modified optical pachometer interfaced to a PC. The anterior segment was examined with a slit lamp biomicroscope (with and without the instillation of fluorescein) for safety purposes after the last measurement.

Data analysis

Descriptive statistics were generated for all variables. The effects of lens type and lens power were examined. p-Values of less than 0.05 were considered to be statistically significant. Repeated measures analysis of variance (Re-ANOVA) was used to examine the effect of lens type (lotrafilcon A, senofilcon A, balafilcon A and galyfilcon A) and lens power (−3.00, −10.00 and +6.00 D). When appropriate the Huynh–Feldt (HF) correction was applied to adjust the p values and the HF corrected p values are reported in this paper.

For each lens power, to compare the effect of lens type, a separate Re-ANOVA was conducted. Tukey HSD Post hoc tests were used to determine the significance of all pair-wise differences.

Results

The results of the central corneal swelling for all lens types and powers are shown in Table 5.

Differences in central corneal swelling between the lens types for each lens power

Overnight central corneal swelling for each lens type with each lens power is shown in Fig. 1. For each lens power in Fig. 1, there was a statistically significant effect of lens type (Re-ANOVA, p<0.05 for all). The +6.00 D galyfilcon A lens induced greater corneal swelling than lotrafilcon A and senofilcon A (post hoc tests; p<0.05 for both), but was not different than balafilcon A (post hoc test; p>0.05). The

Table 3  Central thickness (mean ± SD) and transmissibility by lens and power.

<table>
<thead>
<tr>
<th>Lens</th>
<th>Lens center thickness (microns)</th>
<th>Lens central Dk/t (cm ml O₂)/(ml s mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>−10.00 D</td>
<td>−3.00 D</td>
</tr>
<tr>
<td>lotrafilcon A</td>
<td>66 ± 4.7</td>
<td>67 ± 4.5</td>
</tr>
<tr>
<td>senofilcon A</td>
<td>66 ± 2.5</td>
<td>64 ± 5.5</td>
</tr>
<tr>
<td>balafilcon A</td>
<td>86 ± 3.8</td>
<td>89 ± 2.5</td>
</tr>
<tr>
<td>galyfilcon A</td>
<td>62 ± 1.4</td>
<td>66 ± 2.5</td>
</tr>
<tr>
<td>Mean</td>
<td>70</td>
<td>72</td>
</tr>
</tbody>
</table>
-10.00 D lens also induced greater swelling with the galyfilcon A than lotrafilcon A (post hoc test; p < 0.05), but not than the other two lenses (post hoc tests; p > 0.05 for both). With -3.00 D lens, swelling induced by balafilcon A was greater than lotrafilcon A (post hoc test; p < 0.05), but was not different than the other two lenses (post hoc tests; p > 0.05 for both).

**Effect of lens type on central corneal swelling**

Averaged for power, there was a significant effect of lens type (Re-ANOVA; P_HF < 0.001) lotrafilcon A induced the least (6.2 ± 2.8%) and galyfilcon A the most central corneal swelling (7.6 ± 3.0%) (post hoc tests; p < 0.05). There was no

**Table 4** Computed harmonic average thickness and average lens transmissibility by lens and power for 6.8 mm cord diameter.

<table>
<thead>
<tr>
<th>Lens</th>
<th>Average lens thickness (microns)</th>
<th>Lens average Dk/t (1/cm ml O2/ml s mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>-10.00 D</td>
<td>-3.00 D</td>
</tr>
<tr>
<td>lotrafilcon A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>senofilcon A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>balafilcon A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>galyfilcon A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Figure 1** Overnight central corneal swelling for each lens power (vertical bars denote 0.95 confidence intervals, the significantly different pairs are indicated by brackets and asterisks).

**Figure 2** Overnight central corneal swelling (lens vs. control) (vertical bars denote 0.95 confidence intervals).

There was a significant effect of lens power on central corneal swelling (Re-ANOVA; P_HF < 0.001) as illustrated in Fig. 3. The +6.00 D power, averaged across lens materials, induced significantly greater central swelling than the −10.00 and −3.00 D (post hoc tests; p < 0.05 for both), (7.7 ± 2.9 vs. 6.8 ± 2.8 and 6.5 ± 2.5% respectively) but there was no difference between −10.00 and −3.00 D (post hoc test; p > 0.05) (Fig. 3).

**Table 5** Mean (± SD) overnight central corneal swelling.

<table>
<thead>
<tr>
<th>Eye</th>
<th>Lens wearing (swelling %)</th>
<th>No lens (swelling %)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>−10.00 D</td>
<td>−3.00 D</td>
</tr>
<tr>
<td>lotrafilcon A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>senofilcon A</td>
<td></td>
<td></td>
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<tr>
<td>balafilcon A</td>
<td></td>
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<tr>
<td>galyfilcon A</td>
<td></td>
<td></td>
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<tr>
<td>Mean</td>
<td></td>
<td></td>
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</tbody>
</table>
Computed central and harmonic average lens transmissibility

The central lens thickness measurements and respective calculated central oxygen transmissibility values (from the permeability values provided by the lens manufacturers) of each lens type and computed values of harmonic average lens thickness and average lens transmissibility over 6.8 mm cord diameter are shown in Tables 3 and 4 respectively. For each lens type as expected and can be seen from these tables the central lens transmissibility of high and low minus powered lenses were similar and both were markedly different than the central Dk/t in plus lens power (Table 3). In contrast, harmonic average lens transmissibility values in high powered plus and minus lenses were similar and notably different than harmonic average Dk/t in –3.00 D lens (Table 4). Discussion

In this study we used 12 different silicone hydrogel lenses with central oxygen transmissibility values ranging from 31 to $10^{-9}$ (cm ml O$_2$)/(ml s mmHg). Central corneal swelling differences between the lens types were particularly pronounced in high powered lenses and are clearly seen in both –6.00 D and –10.00 D lens powers in Fig. 1, suggesting that the corneal swelling response especially in the higher lens powers may be minimized by using silicone hydrogel lenses in the higher transmission end. These results are consistent with the difference in the calculated central oxygen transmission values between the silicone hydrogel lenses shown in Table 3 and show that at high levels of Dk/t, central corneal swelling with silicone hydrogel lenses can still be differentiated based on the lens oxygen transmissibility. The exception to this statement was galyfilcon A which did not induce the most swelling among lenses in –3.00 D power (Fig. 1) as would be predicted from the other lens power results in this study and other published work (Moezzi AM, Fonn D, Simpson TL. Comparison of overnight corneal swelling induced by prototype lotrafilcon A toric versus balafilcon A toric. American Academy of Optometry Meeting Abstract. 2006;060095). This can be attributed to sampling or perhaps other possible uncontrolled lens specific or ocular surface related factors which may have influenced the corneal swelling response in addition to lens Dk/t warranting further investigation in future studies. The small but significant differences in central corneal swelling between the study lenses in each high powered group (i.e., –10.00 or +6.00) (Fig. 1) are probably not clinically relevant. However, some subjects exhibited high levels of corneal swelling as we reported previously and for those it would seem sensible to use the lenses that cause the least amount of swelling.

Fig. 2 demonstrates an inverse relationship between oxygen transmissibility and mean overnight central corneal swelling induced by the silicone hydrogel study lenses. Also, this figure illustrates that with all study lenses, the lens wearing eye showed significantly more swelling than in the contralateral non-lens wearing eye as shown previously (Fonn D, Moezzi A, Simpson T, Situ P. Confirmation of a yoked corneal swelling response between the test and contralateral control eye. Optom Vis Sci. 2004;81(125):30) suggesting that even lenses that exceed the Holden and Mertz $10^{-9}$ (cm ml O$_2$)/(ml s mmHg) will not avoid overnight lens induced edema (Table 5). The additional swelling produced by the lens compared to the same closed eye condition without the lens has been partially attributed to lens-related corneal swelling factors other than hypoxia.

Despite differences in thickness of the central and peripheral cornea there are similar oxygen demands across the cornea, independent of corneal location. Even after blinking, the effect of tear mixing to equilibrate the oxygen tension under a soft lens is insignificant. To maintain normal corneal physiology and health, it is important that high powered soft contact lenses provide sufficient local oxygen transmissibility through the thickest part of the lens. Bruce compared local Dk/t measurements of spherical lotrafilcon A and balafilcon A lenses of various powers and found that lotrafilcon A exceeded the Holden and Mertz criterion of $10^{-9}$ (cm ml O$_2$)/(ml s mmHg) at all lens locations in the range of 3.00 to –6.00 powers, however only balafilcon A of +1.00 D power met this criterion across the lens. In our study none of the plus powered lenses met the minimum Dk/t of $10^{-9}$ (cm ml O$_2$)/(ml s mmHg) at the center as the highest central Dk/t was $10^{-9}$ (cm ml O$_2$)/(ml s mmHg) with +6.00 D lotrafilcon A (Table 3) All minus powered lenses in this study meet or exceed the Holden and Mertz criterion for extended wear at the center (Table 3).

Previous studies with conventional hydrogel lenses under closed eye conditions showed greater central corneal swelling with higher minus lens power but the same center thickness as the lower power lenses, and similar levels of central corneal swelling with minus compared to plus hydrogel lenses. This was despite greater central thickness and therefore lower central Dk/t of plus lens powers. These findings were explained by assuming that average of the central area of the lens instead of local central lens transmissibility was responsible. However, findings from these previous studies with hydrogel lenses are at odds.
with results from our study with silicone hydrogel lenses (Fig. 3).

For the ease of illustration, the mean values of central and average lens transmissibility for each lens power are shown in the right side of the last rows in Tables 3 and 4 respectively. Central corneal swelling with +6.00 D was significantly greater than −10.00 D lens power (Fig. 3) despite similar levels of average lens transmissibility of these two lens powers (Table 4, last row). However, central oxygen transmissibility in +6.00 D was significantly lower than −10.00 D lens power as shown in Table 3 and this is in line with the higher central corneal swelling induced by +6.00 D lenses in this study. Therefore, the greater central swelling induced by +6.00 D compared to the −10.00 D and −3.00 D in Fig. 3 can be explained by the lower central oxygen transmission of the plus lens power. Also central corneal swelling induced by −10.00 and −3.00 D lens powers in Fig. 3 were not significantly different despite obvious differences in average lens transmissibility between high and low minus lens powers (Table 4, last row). In contrast, the similar level of central corneal swelling induced by −10.00 D and −3.00 D lens powers (Fig. 3) can be easily predicted from the similarity in central lens transmissibility between these two lens powers as shown in Table 3 (last row). A correlation analysis (that was not statistically significant as only three pairs of data were compared) showed a very strong linear association between central corneal swelling and central lens $Dk/t$ ($r^2 = 0.94$) and a weaker association between the central corneal swelling and average lens transmissibility ($r^2 = 0.68$). Therefore, these findings from our study suggest that in silicone hydrogel lenses central corneal swelling is mainly driven by central lens oxygen transmissibility. Average oxygen transmissibility is less likely to primarily affect the outcome here and a likely reason was that these lenses were in the high transmissibility range. These results are in agreement with a suggestion from at least one previous study which predicted a more prominent role for the effect of local oxygen transmissibility, rather than the averaging effect in higher transmissible hydrogel lenses.14

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Conflicts of interest

Professor Desmond Fonn is a consultant for Alcon Laboratories and CooperVision Inc. None of the other authors of this manuscript have any potential financial interest in a product reported in the manuscript.

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References


