Critical Oxygen Levels to Avoid Corneal Edema for Daily and Extended Wear Contact Lenses

Brien A. Holden and George W. Mertz

The relationship between corneal edema and hydrogel lens oxygen transmissibility was examined for both daily and extended contact lens wear by measuring the corneal swelling response induced by a variety of contact lenses over a 36-hr wearing period. The relationships derived enable average edema levels that occur with daily and extended wear in a population of normal young adults to be predicted to within ±1.0%. The critical lens oxygen transmissibilities required to avoid edema, for the group as a whole, for daily and extended contact lens wear were obtained from the derived curves. It was found under daily wear conditions that lenses having an oxygen transmissibility of at least $24.1 \pm 2.7 \times 10^{-9}$ $(cm \times ml \ O_2)/(sec \times ml \times mmHg)$, an Equivalent Oxygen Percentage (EOP) of 9.9%, did not induce corneal edema. This level of oxygen transmissibility can be achieved (1) in standard, low water content, poly-HEMA lenses by using an average lens thickness of $33 \ \mu m$ or less, or (2) in a higher water content material, such as Duragel 75, by using an average thickness of $166 \ \mu m$ or less. The critical hydrogel lens oxygen transmissibility needed to limit overnight corneal edema to 4% (the level experienced without a contact lens in place) was found to be $87.0 \pm 3.3 \times 10^{-9}$ $(cm \times ml \ O_2)/(sec \times ml \times mmHg)$—an EOP of 17.9%. This ideal level of oxygen transmissibility cannot, at present, be provided with hydrogel materials. We suggest a compromise criterion for acceptability of hydrogel lenses for extended wear: zero residual swelling, ie, the level of oxygen transmissibility required to allow the cornea to return to normal thickness soon after eye opening following sleep with lenses. To meet this criterion, the oxygen transmissibility needs to be $34.3 \pm 5.2 \times 10^{-9}$ $(cm \times ml \ O_2)/(sec \times ml \times mmHg)$—an EOP of 12.1%. The authors suggest this as the minimum desirable oxygen transmissibility for extended wear as it limits the overnight swelling to approximately 8%, allowing the cornea to recover normal thickness soon after eye opening. Invest Ophthalmol Vis Sci 25:1161-1167, 1984

When a hydrogel contact lens is worn, the maintenance of normal corneal function depends primarily on sufficient oxygen diffusing through the lens material. The oxygen transmissibility of such a lens $(Dk/L)$ is directly proportional to the oxygen permeability $(Dk)$ of the material polymer (a function of water content in hydrogel materials) and inversely proportional to the thickness of the lens $(L)$. While the minimum oxygen level necessary to avoid corneal swelling has been investigated, the critical lens oxygen transmissibilities to support both daily and extended wear have not yet been established.

Recently, Holden, Mertz, and McNally reported on corneal thickness changes in ten subjects during 7 days continuous wear of three types of hydrogel contact lenses of different back vertex powers. The two main findings from this study were (1) that current extended wear lenses cause 10-15% overnight corneal edema and 2-6% swelling during the day and (2) that when the lenses were left in place, the cornea showed an ability to consistently deswell approximately 8% once the eyes were opened following sleep.

Although the long-term effects of the levels of edema occurring with current extended wear lenses are not yet known, the development of contact lenses that do not produce corneal swelling is intuitively desirable. We, therefore, set out to determine (1) the relationship between the amount of contact lens-induced edema and lens oxygen transmissibility, so that the mean level of edema could be predicted for any lens of known oxygen transmissibility, and (2) the critical lens oxygen transmissibility necessary to avoid corneal edema for both daily and extended contact lens wear. These aims were achieved by measuring the corneal edema response over a 36-hr period including a normal wake/sleep cycle with a variety of lenses having a wide range of oxygen transmissibilities.

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Table 1. Ocular parameters summary

<table>
<thead>
<tr>
<th>Subject</th>
<th>Mean</th>
<th>Standard deviation</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>20.4</td>
<td>1.7</td>
<td>18 to 24</td>
</tr>
<tr>
<td>Sph. refr. error (D)</td>
<td>−1.22</td>
<td>1.83</td>
<td>+1.00 to −5.00</td>
</tr>
<tr>
<td>Cyl. refr. error (D)</td>
<td>−0.35</td>
<td>0.25</td>
<td>0 to −0.75</td>
</tr>
<tr>
<td>Horiz. K-reading (D)</td>
<td>42.67</td>
<td>1.42</td>
<td>40.75 to 45.50</td>
</tr>
<tr>
<td>Corneal toricity (D)</td>
<td>0.61</td>
<td>0.41</td>
<td>0.37 against rule to 1.25 with rule</td>
</tr>
</tbody>
</table>

Materials and Methods

Subjects

Ten subjects (7 men, 3 women) from whom informed consent had been obtained, participated in the study. Ocular parameters for the group fell within normal limits and are summarized in Table 1. All subjects were unadapted to contact lens wear and free of ocular disease.

Lenses

Lens oxygen transmissibility: The specifications of the lenses used in this and the previous study are provided in Table 2. Central and peripheral lens thickness measurements were made for all lenses to an accuracy of ±1 μm with a device described elsewhere.

These data were used to calculate average lens thickness for the central 6 mm of each lens type in a manner similar to that proposed by Fatt. Using published polymer oxygen permeability data, and manufacturers specifications (for Hydrocurve II, Weicon 38 and Weicon 60), lens oxygen transmissibilities were calculated for each lens. The data for the oxygen permeability (Dk), measured center thickness (Lc) and calculated average thickness (Lavg), with corresponding oxygen transmissibilities (Dk/Lc and Dk/Lavg respectively), are included in Table 2.

Equivalent oxygen percentage: The level of corneal oxygenation for each lens was also calculated in terms of the “Equivalent Oxygen Percentage” (EOP)—an expression used by Hill to describe the oxygen level at the anterior corneal surface expressed as a percentage concentration of oxygen in the atmosphere. For example, a contact lens that transmits all the oxygen available in the atmosphere would have an EOP of 20.9%.

Table 2. Lens data

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Lens name</th>
<th>Water content</th>
<th>Diameter</th>
<th>Nominal center thickness</th>
<th>Oxygen permeability (Dk/×10^9)</th>
<th>Nominal back vertex power</th>
<th>Measured center thickness (Lc)</th>
<th>Calulated avg lens thickness</th>
<th>Oxygen transmissibility (Dk/Lc)</th>
<th>Central Dk/Lc (×10^9)</th>
<th>Average Dk/Lc (×10^9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>B &amp; L, Inc. (Rochester, NY)</td>
<td>Soflens 04</td>
<td>38.6%</td>
<td>14.5 mm</td>
<td>35 μm</td>
<td>8.0 × 10</td>
<td>−1.25 D</td>
<td>32 ± 4 μm</td>
<td>36 μm</td>
<td>25.0</td>
<td>22.2</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>−6.00 D</td>
<td>39 ± 4 μm</td>
<td>60 μm</td>
<td>20.5</td>
<td>13.3</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>−9.00 D</td>
<td>38 ± 5 μm</td>
<td>78 μm</td>
<td>21.1</td>
<td>10.3</td>
<td></td>
</tr>
<tr>
<td>Cooper Labs, Inc. (Palo Alto, CA)</td>
<td>Permalens</td>
<td>71%</td>
<td>13.5 mm</td>
<td>Approx. 200 μm (var. with power)</td>
<td>34.3</td>
<td>−1.25 D</td>
<td>215 ± 11 μm</td>
<td>221 μm</td>
<td>16.0</td>
<td>15.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>−6.00 D</td>
<td>153 ± 22 μm</td>
<td>186 μm</td>
<td>22.4</td>
<td>18.4</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>−3.00 D</td>
<td>103 ± 7 μm</td>
<td>126 μm</td>
<td>38.1</td>
<td>31.7</td>
<td></td>
</tr>
<tr>
<td>Dow Corning Corp. (Midland, MI)</td>
<td>Silsoft Silicone Elastomer</td>
<td>0%</td>
<td>12.5 mm</td>
<td>110 μm</td>
<td>182§</td>
<td>−2.50 D</td>
<td>129 ± 21 μm</td>
<td>137 μm</td>
<td>133</td>
<td>133</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Special order nonmarketed lenses.
† Values quoted at room temperature. Units: (cm^3 × ml O2)/(sec × ml X mmHg).
‡ Oxygen transmissibility. Units: (cm × ml O2)/(sec × ml × mmHg).
§ Oxygen permeability of silicone is reported to increase with lens thickness. The Dk reported here is representative of the average thickness of the lenses in the study (137 μm).
||±1 SD.
It is assumed with this technique that a lens that produces a corneal oxygen uptake rate identical to that of a gas of known oxygen concentration (balance nitrogen), must be delivering the same level of oxygen to the cornea. Although this may not be strictly true, because the goggle situation does not incorporate the other environmental changes induced by contact lenses such as raised temperature and decreased tear tonicity, the Hill method provides an extremely useful relative index.

Figure 1 shows EOP as a function of Dk/L for some of the lenses studied by Hill. The regression analysis of this data shows that there is strong correlation between EOP and lens oxygen transmissibility, the empirical relationship derived from the data in Figure 1 is:

\[
\text{EOP} \, (\%) = 6.195 \times \ln (\text{Dk/L} \times 10^9) - 9.778; \\
\rho = 0.995, \quad S_{\text{est}} = 0.74\%.
\]

Procedures

Five of the subjects who had previously participated in the Holden, Mertz, and McNally study \(^9\) wore a silicone lens (Dow Corning Silsoft silicone elastomer) on one eye and an extremely thin, low water content hydrogel lens (Hydron special order, 20-\(\mu\)m thick, parallel front and back surface) on the opposite eye for 35 hr. After a month of no lens wear, the same five subjects wore Titmus Eurocon Weicon 38 lenses on one eye and Titmus Eurocon Weicon 60 lenses on the opposite eye for 36 hr. After an additional month of no lens wear, the same five subjects wore a CooperVision Duragel 75 lens on one eye for 36 hr and no lens on the opposite eye.

Corneal swelling response to the lenses was determined by measuring corneal thickness with an electronic digital pachometer as previously described. \(^9,19,21\) Baseline pachometry measurements were taken before and immediately after lens insertion on the morning of the first day of wear. Subsequent measurements with lenses in place were taken after 1, 2, 4, 6, 8, and 12 hr of lens wear. Measurements were taken at the moment of eye opening following 8 hr of overnight eye closure (sleep) and at 1, 5, and 12 hr after eye opening. Corneal swelling was calculated as the percentage difference in corneal thickness compared with the measurements taken immediately after lens insertion.

The corneal swelling responses of the other five subjects were recorded after 2, 4, and 6 hr wear of medium (0.11 mm) and thick (0.31 mm) Hydron lenses. It was considered inadvisable to allow these subjects to sleep with these lenses considering the magnitude of their day 1 swelling responses. These data are included in this paper, however, to give a greater range with which

to derive the relationship between the level of oxygen transmissibility and maximum corneal swelling with daily wear.

Published Data

Data from Holden, Mertz, and McNally \(^9\) that were collected in an identical manner over the first 36 hr of lens wear to that reported for the lenses studied in this paper (Tables 2, 3), are included in the analysis (Table 4) to provide information from a wider range of lenses.

Results

The mean corneal swelling results for 36 hr wear of Dow Corning Silsoft silicone elastomer and Hydron 20 \(\mu\)m parallel surface lenses are shown in Figure 2. Similarly, the degree of swelling during 36 hr wear of Weicon 38 and Weicon 60 lenses is shown in Figure 3 and that for CooperVision Duragel 75 lenses and the no lens condition in Figure 4. The mean swelling results during 6 hr wear of thicker Hydron lenses are shown in Figure 5.

Table 3 summarizes the corneal swelling results obtained in both this and the Holden, Mertz, and McNally study \(^9\) for the maximum swelling measured on day 1, the overnight swelling measured at eye opening, and the day 2 residual swelling measured 12 hr after eye opening. These data were submitted to a regression analysis to derive empirical relationships for corneal swelling as a function of \(\ln \text{Dk/L} \), \(\ln \text{Dk/L}_{\text{avg}}\). The results of this analysis are summarized in Table 4. The highest correlations were achieved using the lens average oxygen transmissibility. Plots of day 1 maximum swelling, overnight swelling, and day 2 residual swelling as a function of \(\text{Dk/L}_{\text{avg}}\) are shown in Figures 6–8, respectively.
Table 3. Mean corneal swelling results

<table>
<thead>
<tr>
<th>Lens type</th>
<th>Power (D)</th>
<th>Dk/L* (×10⁻⁹)</th>
<th>Day 1 maximum swelling</th>
<th>First overnight swelling</th>
<th>Day 2 residual swelling (36 hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soflens 04†</td>
<td>−1.25</td>
<td>22.2</td>
<td>−0.1%</td>
<td>10.3%</td>
<td>0.5%</td>
</tr>
<tr>
<td></td>
<td>−6.00</td>
<td>13.3</td>
<td>2.4%</td>
<td>12.0%</td>
<td>2.4%</td>
</tr>
<tr>
<td></td>
<td>−9.00</td>
<td>10.3</td>
<td>3.6%</td>
<td>14.9%</td>
<td>5.8%</td>
</tr>
<tr>
<td>Permalens†</td>
<td>−1.25</td>
<td>15.5</td>
<td>2.1%</td>
<td>11.5%</td>
<td>3.0%</td>
</tr>
<tr>
<td></td>
<td>−6.00</td>
<td>18.4</td>
<td>1.6%</td>
<td>9.8%</td>
<td>3.0%</td>
</tr>
<tr>
<td>Hydron 20 μm</td>
<td>−1.25</td>
<td>16.2</td>
<td>2.1%</td>
<td>12.1%</td>
<td>5.1%</td>
</tr>
<tr>
<td></td>
<td>−9.00</td>
<td>10.5</td>
<td>2.4%</td>
<td>12.6%</td>
<td>5.5%</td>
</tr>
<tr>
<td>Weicon 38</td>
<td>−3.00</td>
<td>14.3</td>
<td>0.6%</td>
<td>11.8%</td>
<td>2.1%</td>
</tr>
<tr>
<td>Weicon 60</td>
<td>−3.00</td>
<td>16.8</td>
<td>1.6%</td>
<td>11.3%</td>
<td>2.6%</td>
</tr>
<tr>
<td>Duragel 75</td>
<td>−3.00</td>
<td>31.7</td>
<td>0.5%</td>
<td>9.5%</td>
<td>1.6%</td>
</tr>
<tr>
<td>Hydron 120 μm</td>
<td>−3.00</td>
<td>7.2</td>
<td>6.8%</td>
<td>7.2%</td>
<td>−0.8%</td>
</tr>
<tr>
<td>Hydron 300 μm</td>
<td>−1.25</td>
<td>2.6</td>
<td>8.5%</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Silsoft</td>
<td>−3.00</td>
<td>133</td>
<td>1.5%</td>
<td>2.6%</td>
<td>−0.5%</td>
</tr>
<tr>
<td>No lens</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

* Units: (cm × ml O₂)/(sec × ml × mm Hg).
† See reference 9.

Discussion

The first objective of this study was to examine the relationship between lens oxygen transmissibility and the amount of corneal edema occurring during both daily and extended wear, so that it would be possible to predict the amount of corneal edema induced by any hydrogel lens of known oxygen transmissibility. The second objective was to derive the critical oxygen levels that must be transmitted by a contact lens to avoid corneal edema under daily and extended wear conditions. These objectives are important both (1) in evaluating the efficacy of current contact lens designs and materials and (2) in developing guidelines for the development of contact lenses that provide less physiologic challenge to the eye. The main deficiencies of previous attempts to define the oxygen transmissibilities needed to avoid edema in daily and extended contact lens wear are that either: (1) center thickness was used to define Dk/L and/or (2) the studies were not carried out during a normal wake/sleep cycle.

Average versus central oxygen transmissibility: As Wilson has pointed out, using center thickness (L) of the lens to define oxygen transmissibility falsely implies that all lenses of a given polymer with the same center thickness will provide the same amount of oxygen. Indeed, we have shown that higher minus-powered, hydrogel lenses cause greater central corneal swelling than lower minus-powered lenses of the same polymer and central thickness (due to the greater lens peripheral thickness). It also is clear from the present study that oxygen transmissibility based on the average thickness of the lenses studied is a better predictor of corneal swelling for day 1 maximum swelling, overnight swelling, and day 2 residual swelling. As can be seen from Table 4, in all cases the standard error of the estimate (Sₑₑₑ) for predicting corneal swelling using lens average thickness is approximately one-half that of the standard error of the estimate using lens central thickness.

Normal wake/sleep cycle: Several investigators have studied corneal swelling caused by various types of

Table 4. Regression analysis—corneal swelling vs lens oxygen transmissibility

<table>
<thead>
<tr>
<th>Swelling response</th>
<th>Central oxygen transmissibility</th>
<th>Average oxygen transmissibility</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Correlation coefficient</td>
<td>Standard error of the estimate (Sₑₑₑ)</td>
</tr>
<tr>
<td>Day 1 maximum</td>
<td>−0.89 ± 1.1%</td>
<td>−0.96 ± 0.6%</td>
</tr>
<tr>
<td>First overnight</td>
<td>−0.57 ± 1.7%</td>
<td>−0.92 ± 0.8%</td>
</tr>
<tr>
<td>Day 2 residual</td>
<td>−0.41 ± 2.0%</td>
<td>−0.82 ± 1.2%</td>
</tr>
</tbody>
</table>
The Derivation of Critical Oxygen Transmissibility

In the model we present here for determining the critical oxygen requirements for daily and extended wear contact lenses, we assume that corneal swelling response ranges from some finite maximum level for lenses with zero oxygen transmissibility, to a base level beyond which an increase in oxygen transmissibility does not reduce the swelling response. It has been shown experimentally, for example, that overnight swelling ranges from approximately 25% for presurgical cataract patients wearing very thick aphakic hydrogel lenses \((Dk/L_{avg} = 3 \times 10^{-9} \text{ (cm X ml O}_2)/[\text{sec X ml X mmHg}])^{28}\) to about 4% for corneas not wearing any lenses \((\text{infinite Dk/L}_{avg})^{9,29,30}\) The regression curves shown on Figures 6–8 and detailed in Table 4 were used to derive the critical oxygen transmissions necessary to avoid contact lens-induced edema under both daily (day 1 maximum swelling) and extended wear conditions (overnight and day 2 residual swelling). Table 5 summarizes the critical lens Dk/L_{avg} values necessary for no edema on day 1, overnight corneal swelling to be limited to 4%—the level experienced when no lens is worn—and the day 2 residual corneal swelling to fall to zero soon after eye opening (zero residual wear situation).
swelling). These critical Dk/Lavg values were converted to Hill's EOP values using the empirical relationship described previously. Also recorded in Table 5 are the critical average lens thicknesses for poly-HEMA and Duragel 75 materials that would be necessary to meet the three criteria.

The Critical Oxygen Transmissibility Needed to Avoid Edema with Daily Wear

Critical lens oxygen transmissibilities for open and closed eye wear, based on previous estimates of the oxygen levels needed to avoid edema,\(^7\) have been suggested as \(5 \times 10^{-9}\) (cm × ml O₂)/(sec × ml × mmHg) for open eye lens wear and \(15 \times 10^{-9}\) (cm × ml O₂)/(sec × ml × mmHg) for closed eye lens wear.\(^8\) As can be seen from Tables 2 and 3, a number of lenses meeting these criteria caused significant corneal swelling both during day and overnight wear. Our results indicate that the oxygen level needed to avoid edema is somewhat higher than previously proposed, and are closer to the levels determined by Holden, Sweeney, and Sanderson.\(^9\)

The Critical Oxygen Transmissibility Needed to Avoid Edema with Extended Wear

In considering the critical oxygen requirements for extended wear lenses, the alternatives we have suggested are: (1) the lens oxygen transmissibility needed to limit overnight edema to 4% (the level occurring without a lens) and (2) the lens oxygen transmissibility needed to allow the daytime level of edema to fall to zero soon after eye opening (zero residual swelling).

The Dk/Lavg which limits overnight swelling to 4% is predicted to be \(87.0 \pm 3.3 \times 10^{-9}\) (cm × ml O₂)/(sec × ml × mmHg)—an EOP of 17.9%. To satisfy this criterion with hydrogel lenses, the average lens thickness would have to be reduced well below manufacturing feasibility (See Table 5). The results of this study suggest that this ideal 4% overnight swelling criteria can only be met at present with silicone lenses. However, the persistent problem of the adherence of these lenses to the cornea\(^3\) questions their suitability for extended wear at the present time.

The zero residual swelling criterion for extended wear allows overnight swelling levels of greater than 4%, as long as the cornea can eliminate the edema
soon after eye opening. From the relationship derived between lens Dk/Lavg and residual swelling shown in Figure 8 and Table 4, the critical lens Dk/Lavg to meet this zero residual swelling criterion is 34.3 ± 5.2 x 10^{-9} (cm x ml O2)/(sec x ml x mmHg)—an EOP of 12.1%. The lens thickness necessary to achieve this appears feasible from a manufacturing point of view, at least in higher water content hydrogel materials. We would, therefore, suggest that this oxygen transmissibility should be considered the desirable minimum value for extended wear contact lenses. 

Key words: contact lens, oxygen transmissibility, corneal edema, daily wear, extended wear

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References