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A SURVEY OF CORNEAL CHANGES CAUSED BY DAILY WEAR SILICONE HYDROGEL CONTACT LENSES

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Introduction

For a healthy cornea, oxygen is required. A cornea can be affected by the presence of a contact lens. Unfortunately, long-term contact lens usage can impair the anterior segment of the eye. This is because the environmental oxygen used by the cornea's metabolism is, to some extent, blocked by the barrier of the lens. Hypoxia appears to take place at all corneal levels.[1,2]

Oxygen passes through a contact lens by diffusion. The International Organization for Standardization (ISO) standard measure of the oxygen permeability of a lens material (at a uniform, standardized thickness) is called Dk. Dk has the unit of 10^{-11} (cm^2/s) x [ml O_2 / (ml x hPa) or (cm/sec) x (ml O_2 /ml x mmHg)]. The actual oxygen transmissibility of the lens is called Dk/t. This measurement takes into account the central thickness (t) of a -3.00 D lens (ISO standard), or the t at any other place of the lens. Dk/t has the unit of 10^{-9} (cm/s) x [ml O_2) / (ml x hPa)] or (cm/sec) x (ml O_2 /ml x mmHg).[2,3]

A transmissibility graph shows the Dk/t values across the entirety of any given lens and describes the distribution of maximum and minimum oxygen transmissibility (power, base curve).

In silicone hydrogel (SiH) contact lenses, silicone rubber is combined with conventional hydrogel monomers. The silicone component of these lens materials provides extremely high oxygen permeability. The hydrogel component facilitates flexibility, wettability and fluid transport. This aids lens movement. Their oxygen transmissibility (Dk/t) is high because silicone is a better oxygen transmitter than water. These properties may improve the comfort of wearing contact lenses. However, a disadvantage of these lenses is the higher rigidity moduli, due to the high silicone content. First generation SiH contact lenses (lotrafilcon A, balafilcon A) have

a lower water content and higher rigidity moduli, when compared with second generation SiH contact lenses (lotrafilcon B, senofilcon A, galyfilcon A, lotrafilcon B). Second generation SiH contact lenses are more comfortable, even though their oxygen permeability is lower than that of first generation SiH contact lenses. This is because they have increased water contents and reduced moduli.[4]

In this prospective non-randomized study, we investigated the effects of contact lens wear on the cornea and the corneal endothelium in subjects who were wearing second-generation silicone hydrogel lotrafilcon B (Air Optix, 33% H_2O, 8.6 mm BC, 14.2 mm diameter, CIBA Vision Corporation, Duluth, GA, USA). These subjects used soft contact lenses on a daily wear schedule.

Material and Methods

Subjects

In this study, we enrolled 55 people (110 eyes). The subjects were divided into two groups. To Group 1, we assigned 56 eyes of 28 subjects. These were habitual, non-silicone hydrogel soft contact lens-wearers (one male and 27 females with a mean age 25±7.1 years), with a mean contact lens wear time of 5.93±6.02 years (minimum: two years, maximum: 31 years). The reason for refitting these subjects with more modern contact lenses was to preserve the physiological status of the eye. In Group 2, 27 neophytes (three male and 24 females with a mean age 20±2.15 years) had never worn contact lenses before they were fitted with lotrafilcon B lenses. The subjects were examined before being fitted with the silicone hydrogel lens. They were then examined at two weeks, four weeks, three months, six months after their fitting, and six-monthly thereafter. At every visit, we recorded visual acuity by Snellen chart. This was defined by clinical measurements and biomicroscopic

examination results (lens centration and movement, morphological alterations of contact lens, anterior segment of the eye and corneal staining). Only the subjects who appeared at all of their examinations and had appraisable data were included in our study analysis. For the publication of this paper, we obtained written informed consent from all of the subjects. The protocol used in this study was in full compliance with good clinical practices, the Declaration of Helsinki (1996) and the guidelines of the Medical and Health Science Centre of the University of Debrecen.

Subjective and Objective Evaluation Methods

With the help of self-administrated questionnaires (yes or no choices), we collected the subjective experiences of the subjects. We created the response format applying several similar configurations. Inquiries included: uncomfortable sensation at the end of the day, itchy or irritating sensation, dryness, redness, inability to wear contact lenses for an entire day, blurred vision and fluctuating visual acuity with the subjects' old lenses and with their new lotrafilcon B lenses. The questionnaires were filled in before fitting the silicone hydrogel lenses and four weeks later. The endothelium cell density was measured with an EM 1100 (Tomey, Tennenlohe, Germany) contact specular microscope. The examinations were performed at scheduled intervals, with photos taken before the lotrafilcon B lenses were worn and then again at one month, six months, one, two and three years.

Before taking the photo, the cornea was anaesthetized with a drop of local anaesthetic (0.4% oxybuprocain hydrochloride). Six to seven pictures of the central region of each cornea were taken. The three best quality ones (including at least 100 cells) were analysed using EM 1200, V 1.5.1, Tomey software.

Apart from cell density, the following parameters were determined by specular microscopy: corneal thickness, average endothelium cell size, coefficient of variation of endothelial cells and the percentage of endothelial hexagonal cells. The result obtained via specular microscopy is based on reflection. Thus, it must be considered that the magnification depends on the light path length. Consequently, in thick corneas, cell density will be under-estimated and vice versa. So we corrected the determined cell density. The correction was then calculated using the equation below (given by the Tomey for use):

$Z\ (corr) = Z \times (F / 10{,}566)^2$, where:

Z (corr): corrected cell density;
Z: actual cell density;
F: focus, namely, the thickness of the cornea;
10.566: calibration data from the manufacturer

Statistical analysis

The data were analysed using SPSS 9.0 for Windows and were marked with means and standard deviations (SD). Comparisons were made using the Student's t-tests. The correlations between different parameters were assessed using Spearman's correlation coefficient (r). Repeated measures analysis of variances was used to compare each parameter at different time points. Findings with an error probability of less than 0.05 were considered to be statistically significant ($p<0.05$).

Results

In all cases, the distance corrected visual acuity was 20/20. All lenses were well centred with a 1-2 mm lens movement. The anterior segment findings were normal and staining was not more than grade I (Efron Grading Scale). Limbal hyperaemia was reduced in Group 1 but had not developed in Group 2 (Figures 1a and 1b).

Approximately 60% (16/28) of the subjects in Group 1 found their current habitual lenses to be uncomfortable. However, after the subjects were refitted with lotrafilcon B lenses, this percentage decreased to 6% (1/28). Similar results were obtained concerning the self-assessed redness of the eye. Approximately 53% (14/28) of the investigated subjects reported lens awareness and irritation with their previous, habitual lenses. This decreased to 0% after the subjects were refitted with lotrafilcon B lenses. Dryness was a problem for 60% (16/28) of the subjects but, after wearing lotrafilcon B lenses, this completely disappeared (0%). Approximately 53% (14/28) of the investigated subjects said that they could wear lotrafilcon B lenses longer than their habitual lenses. With their previous lenses, approximately 60% (16/28) of the investigated subjects complained of blurred vision. However, none reported this symptom when wearing lotrafilcon B lenses.

Approximately 44% (12/27) of the subjects in Group 2 reported lens awareness and mild irritation in the first two to four weeks but not thereafter. This feeling of discomfort is incredibly common among new lens wearers. It develops at the beginning stages of wearing lenses of all types and decreases after a period of adaptation.

Hypoxia-related complications (microcysts, Descemet's striae, corneal staining) were not discovered by slit lamp examination. However, a decrease in limbal vascularization was observed in Group 1 (Figure 1a shows more dilated limbal vessels than those three months after wearing lotrafilcon B lenses on Figure 1b).

Repeated measures analysis of variances disclosed no statistically significant difference in the measured parameters in either group during the follow up period (p=0.06 – 0.96).

The change in corneal thicknesses was not statistically significant in either group during the three-year period. (Fig. 2) The same was true for endothelial cell density. Nevertheless, we noted an interesting trend in Group 2: cell density slightly decreased in the first month, which was not observed after six months of lens use (Fig. 3.).

Cell density decreased in Group 1 by 1.62% after one year, by 0.85% after two years, and by 6.43% after three years. (p=0.25; 0.26; 0.59) This contrasts the cell density found in Group 2, which increased slightly in the first two years (0.78% after 1 year and 0.46% after two years) but decreased by 3.7% after three years. (p= 0.28; 0.06; 0.93) There was a significant difference in the ages of the two groups (the average age was 25.3 years in Group 1 and 19.89 years in Group 2; p=0.024). However, cell densities were not significantly different at baseline (2554.76 cells/mm^2 and 2629.27 cells/mm^2, respectively; p=0.17). Cell size (Fig. 4.) and cell density are interdependent variables. In a given field, cell density is higher when the cells are smaller and vice versa.

In this study, there was a correlation between the coefficient of variation and the time of lens wear. In Group 1, the coefficient of variation decreased significantly after six months compared to baseline values (the baseline coefficient of variation

was 0.47, whereas, after six months, it was 0.44; p=0.049). In Group 2, there was no significant change.

The percentage of hexagonal cells increased significantly after 1 month in Group 2 (before the lenses were worn, it was 27.78%, whereas, after 1 month, it was 28.25%; p=0.025). In Group 1, there was no significant change.

In Group 1, we observed and documented the regression of limbal hyperaemia and neovascularization in the subjects during lotrafilcon B lens wear (Figures 1a and 1b).

Age is known to be inversely proportional to cell density. This outcome was also observed in this study because cell density decreased with the progression of age (but without statistical significant level) (r=-0.43; p=0.094; Fig. 5.).

This study also found that the lens wearing time was directly proportional to the coefficient of variation (r=0.28; p=0.045; Fig. 6.).

The first correlation was examined in Group 2 using parameters that were obtained prior to the lenses being worn. This was to eliminate the influence of any previous contact lens usage on cell density. The second correlation was investigated in Group 1 using data that were obtained before the subjects were fitted with lotrafilcon B lenses.

Discussion

Our investigation found that wearing lenses with low oxygen permeability (called conventional hydrogel lenses) generated irreversible damage to the corneal endothelium (a comparison of the baseline values of the non-lens-wearing vs. lens-wearing groups). Furthermore, it showed that not even high Dk/t lotrafilcon B contact lenses were able to stop the consequential increase in cell destruction. The decrease

observed in cell density in Group 1 exceeded 0.56%, which is the mean annual decrease that has been reported.[3] The fact that neither of the examined parameters significantly decreased in Group 2 suggests that lotrafilcon B provides the cornea with enough oxygen over the three year period.

By comparing changes in cell density to age and examining the correlation between the coefficient of variation and lens-wearing time, we came to the same conclusions as Sheng et al. Their research found that age is inversely proportional to cell density and that years of contact lens wear is directly proportional to the coefficient of variation.[5] The two groups in our study is not age-matched, it is matching at the beginning age of lens wearing. This fact could be a limitation factor, and therefore further researches are needed to understand the effects of second-generation lotrafilcon B silicone hydrogel lenses on the cornea.

The coefficient of variation of the endothelial cells is a measure of the diversity in cell size. A lower coefficient of variation is considered to be better because it indicates that the cells are more similar to one another. Healthy eyes are known to possess more similar, regular shapes. The coefficient of variation is lower when, for the same or a slightly smaller mean, the standard deviation becomes smaller (which is likely to be the case for the corneal endothelium). Additionally, it is lower when, for the same or a slightly increased standard deviation, the mean becomes larger or when they both change for the better (for example, a relatively lower standard deviation and a corresponding smaller change in the mean).

The present study investigated the central region of the cornea. This is important because, according to Amann et al., the cornea has a larger endothelial cell density in the paracentral and peripheral regions, in comparison to that in the central region.[6] However, this difference cannot be seen in contact lens wearers. This

suggests that contact lens wear may cause a mild redistribution of the endothelial cells from the centre to the periphery of the cornea.[7]

Only a few published studies have examined lotrafilcon B contact lenses.[8,9] Our results support the outcomes of these papers. The daily wear of lotrafilcon B lenses improved corneal signs and health (conjunctival and limbal redness, corneal neovascularization, corneal oedema, corneal and conjunctival staining, etc.,) and subjects' symptoms (uncomfortable lens wear, redness, dryness, irritation, blurred vision, etc.). The half of the subjects in Group 2 had mild irritation in the first two to four weeks but not thereafter. This feeling of discomfort is incredibly common among new lens wearers. It develops at the beginning stages of wearinglenses of all types and decreases after a period of adaptation.[10]
Additionally, it provided excellent vision and comfort. Subjects preferred these new lenses over their habitual lenses.

Silicone hydrogel contact lenses provide enough oxygen for the cornea. Thus, they protect the cornea from the hypoxia caused changes.[11-14] Furthermore, Santos et al. have proven that silicone hydrogel contact lenses are generally less susceptible to microbial adhesion, in comparison to conventional hydrogels. This feature facilitates better lens resistance to bacteria.[15] According to a study by Lira et al. silicone hydrogel contact lenses are less susceptible to damage over time, resulting in sustained biocompatibility for longer periods of time. This contributes to the clinical success of this type of lens.[16]

The Gothenburg study has demonstrated that prolonged wearing of low Dk/t contact lenses disturbs the metabolism of the epithelium, decreases the oxygen absorption of the eye and thin the epithelium.[17] Jalbert et al. have recently shown that

this effect can be significantly reduced via the use of silicone hydrogel contact lenses.[18]

Dumbleton et al. refitted successful soft lens wearers with other high Dk/t silicone hydrogel contact lenses. They then evaluated the objective and subjective responses of subjects. Their results demonstrate that bulbar and limbal hyperaemia significantly decreased in all quadrants. This was also observed in the subjects of our study. In addition, dryness diminished and the end-of-day comfort improved.[19] Doughty et al. experienced improvement in the mean bulbar and limbal redness after six months of silicone hydrogel lens usage.[11] Consequently, high oxygen availability ensured better comfort for the wearer and in this investigation lotrafilcon B, supports the physiological metabolism and functions of the cornea by improving oxygen provision. Thus, it can be argued that contact lens wear does not provoke corneal damage.

A state of hipoxia is caused by the prolonged wearing of older hydrogel low Dk/t contact lenses.[17,20] Nearly all contact lens wearers report instances when they do not remove their contact lenses before sleeping (“closed-eye contact lens wear”). At such times, tear flow stops between the contact lens and the anterior surface of the cornea, which, in just a few minutes, induces metabolic changes in the micro-environment of the corneal epithelium.[21] After some minutes, both the stroma and the endothelial cells automatically undergo anaerobic glycolysis. The consequence of this is corneal swelling. A short-term disorder of the metabolism does not lead to irreversible deviations in the structure of the cornea. However, prolonged, frequent hypoxia results in secondary morphological changes in the epithelium, stroma, and endothelium that are only minimally reversible. Oxygen deprivation has been associated with the appearance of micro cysts in the epithelium, epithelial thinning,

slowed mitosis, the loss of hemidesmosomes, reduced epithelial oxygen consumption and an increased superficial cell size in the epithelium. Stromal changes include a chronic loss of glycosaminoglycans and thinning, and the endothelium shows signs of increased polymegethism.[22] Furthermore, conjunctival hyperaemia, corneal neovascularization, corneal oedema, corneal staining, myopic shift and a decreased resistance against microbial keratitis develop due to oxygen deprivation.[17,23,24] These effects lead to subjective symptoms, including a decreased or fluctuant visual acuity, blurred vision, seeing a rainbow circle around lights, dryness and lens awareness. Schafer et al. examined the stability of dryness symptoms after refitting subjects with high-Dk/t silicone hydrogel contact lenses. According to their results, the during-the-day and end-of-day dryness symptoms significantly improved during the first week after refitting with lotrafilcon B lenses and remained stable for three years. The presence of dryness symptoms after 1 week was associated with the discontinuation of contact lens wear.[25]

Hypoxia that affects the periphery of the cornea is an even more important problem than hypoxia of the central cornea. This is because the limbus is the only source of epithelial stem cells that ensure unlimited new epithelial cells and fast regeneration after surface damage. Any stem cell deprivation or damage consequently results in recurrent erosion, chronic keratitis or vascularization.[26]

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Figure and Table Legends

Figure 1.: Images at a higher magnification (40x magnification) of limbal hyperaemia in subjects from Group 1 before (1a) and 3 months after wearing lotrafilcon B lenses (1b).

Figure 2.: Specular microscopic analysis of endothelial cell layer performed by Tomey EM 1100 equipment.

Figure 3.: The fluctuation of cell density in Group 2. The cell density slightly decreased in the first month. However, this phenomenon did not persist after 6 months.

Figure 4.: The fluctuation of cell size in Group 2. Cell size changes are not synchronized with cell density changes because they are reversely interdependent.

Figure 5.: The correlation between age and cell density in the two groups, inverse proportion (r=-0.43; p=0.094).

Figure 6.: The correlation between the lens wearing time and the coefficient of variation in Group 1, direct proportion (r=0.28; p=0.045).

Table 1.: The results from Group 1, the parameters of the corneal physiology (corneal thickness and endothelial morphology).

Table 2.: The results from Group 2, the parameters of the corneal physiology (corneal thickness and endothelial morphology).