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Evaluated conjunctival blood flow velocity in daily contact lens wearers

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Abstract

Objective—This study examined conjunctival microvasculature development in long-term habitual contact lens wearers following a night of sleep.

Methods—Twenty habitual contact lens wearers (15 females and 5 males, age 28.6 ± 6.9 years, mean age $\pm$ standard deviation) who had worn contact lenses on a daily basis for at least 3 years and forty non-contact lens wearers (23 females and 17 males, age 36.5 ± 6.6 years, mean age $\pm$ standard deviation) participated in the study. A functional slit lamp biomicroscopy (FSLB) imaging system was used to image the temporal bulbar conjunctiva. Imaging was performed in the morning while the contact lens wearers were not wearing their lenses after a night of sleep. The conjunctival vessel diameters, blood flow velocities and flow rates were measured. In addition, fractal analyses were performed to obtain the vessel network density (D_{box}) and complexity (D_0).

Results—The average blood flow velocity in habitual contact lens wearers after a night of sleep was 0.59 ± 0.19 mm/s, which was significantly higher than that in non-contact lens wearers (0.48 ± 0.17 mm/s, $P < 0.05$). The microvessel network density and complexity levels ($D_{box} = 1.64 \pm 0.05$ and $D_0 = 1.71 \pm 0.05$, respectively) in the habitual contact lens wearers were significantly higher than those in non-contact lens wearers ($D_{box} = 1.61 \pm 0.05$ and $D_0 = 1.69 \pm 0.04$, both $P < 0.05$). The blood flow velocity was positively correlated with the duration of contact lens wear ($r = 0.46$, $P < 0.05$) and with the daily number of lens-wearing hours ($r = 0.49$, $P < 0.05$) in habitual contact lens wearers.

Conclusions—This study identified microvascular alterations in the conjunctiva in response to daily contact lens wear after a night of sleep in long-term daily contact lens wearers. The unrecovered changes may indicate that para-inflammation occurs on ocular surfaces due to contact lens wear and that overnight sleeping with no lenses may not sufficiently restore the ocular surface to an intact state.

Keywords

bulbar conjunctiva; blood flow velocity; microvascular network; functional slit-lamp biomicroscopy (FSLB); hemodynamics

Wearing contact lenses through a daily wear regime is regarded as a safe way to correct refractive errors, although complications still occur.^{1–4} Studies have reported that the risks of contact lens-related complications are much lower among daily contact lens wearers than among extended contact lens wearers.⁴ With the introduction of new silicone hydrogel contact lens materials, the oxygen transmission of lenses has improved, and hypoxia under daily wear regimes has been apparently eliminated.^{5–8}

More attention has been dedicated to contact lens-related ocular discomfort (CLD)^{9–12} and non-infection complications, such as corneal infiltration and sterile corneal ulcers.^{6,13–16} Ocular hyperemia is regarded as the vascular response to contact lens wear,^{17–21} and acute red eye (ARE) is recognized as an adverse event that occurs when wearing traditional contact lenses composed of low oxygen transmission materials (i.e., hydrogel).^{20,22,23} A precise, quantitative detection of subtle vascular changes in contact lens wearers may help elucidate the mechanisms underlying contact lens-related adverse events. However, ocular vascular responses to contact lens wear have not been widely studied due to technical difficulties associated with quantifying microvascular circulation and networks along the ocular surface (mainly the conjunctiva).

The functional slit lamp biomicroscopy (FSLB) imaging system was designed to quantitatively analyze bulbar conjunctival microvessel circulation and microvascular networks.^{24–27} Our previous study showed that bulbar conjunctival microcirculation and vessel networks become stronger after a short period of lens wear.²⁵ The microcirculation levels found in habitual contact lens wearers were also elevated when lenses were worn relative to the levels found in non-contact lens wearers (Hu L, et al. IOVS 2016;57: ARVO E-Abstract 4735).

However, whether vascular responses can recover after a night of sleep without lenses remains untested. Addressing this crucial question may help elucidate how eyes respond to daily contact lens wear and whether alterations can be used as an image marker of ocular surface sub-clinical chronic inflammation, which occurs over long periods of contact lens wear. In addition, this study was performed to address whether one night is sufficient for the bulbar conjunctiva to return from previously demonstrated elevated microcirculation levels to normal levels.

The goal of the present study was to determine ocular microvasculature and microcirculation levels after a night of sleep with no lenses in long-term habitual contact lens wearers.

Methods and Materials

This study was approved by the institutional review board for human research at the University of Miami. Informed consent was obtained from each subject, and all subjects

were treated in accordance with tenets of the Declaration of Helsinki. The FSLB imaging system was used to image the bulbar conjunctiva. This imaging system was thoroughly explored and described in details in our previous studies.^{25–28} Via high-speed video capture, the blood flow in conjunctival microvessels can be recorded. Using a series of image-processing procedures, vessel diameters, blood flow velocities and flow rates can be measured from the captured videos.^{6–8} In addition, microvessel networks of the bulbar conjunctiva on the temporal side were photographed, and fractal analysis was performed to determine fractal dimensions. The box-counting analysis method was used to obtain D_{box} (representing vessel density), and the fractal dimension from multi-fractal analysis yielded D_0 (presenting vessel complexity).^{25–28}

Two groups of subjects were recruited. The long-term habitual contact lens (HCL) wearers included contact lens wearers who had worn soft contact lenses on a daily basis for at least 3 years, and the control group (non-contact lens wearers, NCL) was defined as self-reported healthy subjects with no history of contact lens use. Exclusion criteria applied to both groups included the following: a history of eye surgery; a history of trauma; a history of systemic disease, such as hypertension, diabetes, sickle cell anemia, cerebral small vessel disease, stroke and other cardiovascular, cerebrovascular or vascular diseases; a history of tobacco or alcohol use; and current medication use.

The average age of the 20 HCL wearers (15 females and 5 males) was 28.6 ± 6.9 years (range 20 – 47 years). The average age of the 40 NCL wearers (23 females and 17 males) was 36.5 ± 6.6 years (range 25 – 54 years). The average power of the soft contact lenses used by the HCL group was -4.66 ± 1.97 diopters. The average duration of contact lens wear was 11.0 ± 6.0 years (range 3 – 30 years) and 13.0 ± 2.0 hours (range 8 – 15 hours) daily. Of 20 HCL wearers, 10 (50%) subjects wore biweekly disposable contact lenses, 5 (25%) subjects wore daily disposable soft contact lenses, 4 (20%) wore monthly disposable contact lenses, and 1 (5%) wore yearly replacement soft contact lens.

An imaging session was performed in the morning for HCL wearers while they were not wearing their contact lenses. A previous study found no difference in bulbar conjunctival blood flow velocities during office hours in NCL wearers. An imaging session was performed during office hours from 9 AM to 5 PM for the control group. All data management and statistical analyses were carried out in Excel (ver. 2010, Microsoft, Redmond, WA). All parameters were compared between HCL wearers and NCL wearers through unpaired t-tests. Pearson's correlation coefficient was used to determine the relation between blood flow velocity and vessel diameter. A P-value of less than 0.05 ($P < 0.05$) was considered statistically significant.

Results

The average diameter of bulbar conjunctiva venules in the HCL group was 16.9 ± 1.3 μm , which did not differ from the value of 17.3 ± 1.6 μm for the NCL group ($P > 0.05$, Figure 1). The average blood flow velocity of conjunctiva venules in the HCL group was 0.59 ± 0.19 mm/s, which was significantly higher than that in the normal group (0.48 ± 0.17 mm/s, $P < 0.05$, Figure 1). The average blood flow rate in the HCL group was 119 ± 38 pl/s, which was

significantly higher than that obtained for NCL wearing eyes (92 ± 39 pl/s, $P < 0.05$, Figure 1). The density and complexity ($D_{\text{box}} = 1.64 \pm 0.05$ and $D_0 = 1.71 \pm 0.05$) of microvascular networks in the HCL group were significantly higher than those in the control group ($D_{\text{box}} = 1.61 \pm 0.05$ and $D_0 = 1.69 \pm 0.04$, both $P < 0.05$, Figure 1). Blood flow velocities increased as a function of vessel diameter. Compared to the control group, the HCL group showed increased blood flow velocities across the entire range of vessel diameters ($P < 0.05$, Figure 2).

In the HCL group, the blood flow velocity had positive correlations with the duration of contact lens wear ($r = 0.46$, $P < 0.05$, Figure 3) and the duration of daily contact lens wear ($r = 0.49$, $P < 0.05$, Figure 3). However, the blood flow velocity showed no correlation with the subject's age ($r = 0.34$, $P > 0.05$, Figure 3) or with contact lens power ($r = 0.16$, $P > 0.05$, Figure 3). The microvascular network density and complexity of the bulbar conjunctiva in the HCL group showed no significant correlations with the duration of contact lens wear ($r_{D_{\text{box}}} = 0.18$, $P > 0.05$; $r_{D_0} = 0.04$, $P > 0.05$, Figure 4), the duration of daily contact lens wear ($r_{D_{\text{box}}} = 0.27$, $P > 0.05$; $r_{D_0} = 0.03$, $P > 0.05$, Figure 4), age ($r_{D_{\text{box}}} = 0.27$, $P > 0.05$; $r_{D_0} = 0.03$, $P > 0.05$, Figure 4) or contact lens power ($r_{D_{\text{box}}} = 0.07$, $P > 0.05$; $r_{D_0} = 0.13$, $P > 0.05$, Figure 4).

Discussion

This study documented whether a night of sleep without wearing contact lenses facilitates the recovery of ocular vascular responses in the microcirculation and microvessel networks of daily contact lens wearers. The results show that vascular alterations, such as increased blood flow velocities and microvessel networks, do not recover after a night of sleep without wearing lenses. This phenomenon can be explained by the occurrence of para-inflammation during daily lens wear which echoes the recent suggestion about the role of para-inflammation in uncomplicated contact lens wear.²⁹

Para-inflammation is considered as the status between homeostasis and inflammation.³⁰ It may serve in a protective function in contact lens wearers, which is supported by the Manchester Keratitis study.^{16,31,32} The Manchester study showed contact lens wearers had lower risk of developing a corneal infiltrative event if the ocular healthy is compromised. The protective mechanism has been suggested to be mediated by recruitment of macrophages and Langerhans cells.^{33,34} Alzahrani et al. employed confocal microscopy to examine Langerhans cells in lid-wiper of the contact lens wearers and found an increased volume of Langerhans cells, indicating the occurrence of inflammation processes in the lid wiper region. Shen et al. used ultra-high resolution optical coherence tomography to study the contact lens edge and found conjunctival indentation in the majority of lens edges with a round-edged configuration.³⁵ Cheung et al. studied ocular surface vasculature using computer-assisted intravital microscopy (CAIM) and found vasculopathies on the ocular surface that exhibited vessel compression and tortuosity in long-term contact lens wearers.³⁶

Responses to contact lens, for various reasons, show that vascular alterations in the ocular surface occurred during contact lens wear and that the changes did not fully recover after an overnight rest of non-lens wear; this finding may indicate that the ocular surface in these

habitual lens wearers may not be fully comparable to the ocular surface in subjects who never wear contact lenses. The evaluated microcirculation and increased vessel density levels may be used as image markers of para-inflammation along the ocular surface.

The present study and previous studies (Hu L, et al. IOVS 2016;57: ARVO E-Abstract 4735) help further understanding of microvascular responses to contact lens wear and may also help identifying optimal lens materials and designs. Ideally, a lens on the eye should not induce any or should induce very minimal vascular responses over the long term and should cause no chronic inflammation along the ocular surface. If this ideal situation is achieved, adverse events associated with contact lens wear may be reduced or eliminated. However, this ambitious goal may not be achievable and the ideal situation may never happen. A better deal may be in place during contact lens wear. Efron has recently argued that the chronic, low grade, sub-clinical inflammatory status of the ocular surface during contact lens wear, may have a positive and protective phenomenon. The vascular response as the up-regulation of the immune system, in a non-damaging way, may maintain the eye in a state of “heightened alert,” ready to ward off any extrinsic noxious challenge. A small amount of sub-clinical inflammation during the long term of lens wear may well be a positive attribute, and therefore this state of inflammation needs to be modulated rather than eliminated. This notion of the protective effect may explain the success of long term habitual lens wearers, who never experienced severe contact lens associated complications.

Successful lens wearers may present very few symptoms in eye examinations based on traditional approaches such as slit lamp microscopy. Quantitatively evaluating conjunctival hyperemia using traditional grading scales of bulbar redness may not be feasible if the changes are subtle. In typical contact lens clinics, conjunctival blood flow is not evaluated due to technique difficulties. When FSLB or similar approaches, such as CAIM developed by Cheung et al.,³⁶ are used, sub-clinical changes in vascular responses can be evaluated, and this information may reveal new opportunities for the quantitative analysis of ocular vascular responses that may effectively represent the ocular inflammation induced by contact lens wear. Surprisingly, conjunctival microcirculation was found to remain elevated after a night of sleep. The changes were almost the same as the acute response to 6 hours of lens wear in neophytes.²⁵ This finding may indicate that quantifications of blood flow velocities and vessel networks are sensitive to sub-clinical changes in the ocular surface.

This study addressed whether recovery of microvascular responses to long-term contact lens wear can occur after a night of sleep. We previously reported that microcirculation increases during contact lens wearing (i.e., lens wearing) in habitual lens wearers (Hu L, et al. IOVS 2016; 57: ARVO E-Abstract 4735). This previous report clearly showed that changes in microcirculation occur when lenses are worn. In the present study, we did not perform a comparison with measurements taken after habitual lens wearers put in their contact lenses. A broader conclusion can be reached when our previous studies are considered, as illustrated in Figure 5. Indeed, the HCL group included some subjects who had been recruited in the previous study reported by Hu et al. (Hu L, et al. IOVS 2016; 57: ARVO E-Abstract 4735). We did the unpaired t-test to examine the significant difference between HCL wearing contact lens (0.66 mm/s) in Study 2 (Hu L, et al. IOVS 2016; 57: ARVO E-Abstract 4735) and HCL not wearing contact lens (0.59 mm/s) in the present study. There was no significant

difference between the two groups, indicating the recovery was marginal (did not reach a significant level). The statistical analysis between the two groups supports the hypothesis that the altered vascular changes remain unrecovered after one night of sleep. Future studies are needed to validate the viewpoint by using self-controlled subjects (habitual wearers assessed at the end of a day). This study also showed that the blood flow velocity of the bulbar conjunctiva in HCL wearers shows a positive correlation with years of contact lens wear and with the hours of daily contact lens wear. These two major factors may indicate the presence of a cumulative effect that maintains chronic inflammation.

In the present study, we did not ask contact lens wearers to stop wearing their lenses and it may not be speculated how long the altered vascular changes last based on currently available data, which warrants further study. Due to the limited sample size used, we did not stratify the contact lens subjects into subgroups to examine specific changes or recovery levels for the different types of contact lenses used. Further studies may address whether the contact lens materials and designs play a role in the microvasculature changes of the ocular surface.

In summary, this study identified microvascular alterations in the conjunctiva in response to daily contact lens wear after a night of sleep in long-term daily contact lens wearers. The unrecovered changes may indicate the para-inflammation status on the ocular surface as a result of contact lens wear and that a night of sleep without wearing lenses may not fully restore the ocular surface. These findings can inspire the execution of future studies on improved lens materials and designs that may minimize or modulated ocular vascular responses.

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Figure 1.

Conjunctival vascular measurements in habitual lens wearers (HCL) and non-lens wearers (NCL). Although no significant difference in vessel diameter (A) was found, the blood flow velocity (B), blood flow rate (C) and fractal dimensions representing vessel density and complexity (D) were significantly higher in habitual lens wearers (HCL) than that in non-lens wearers (NCL). Bars = standard deviation.

Figure 2.

Blood flow velocity as a function of vessel diameter. The blood flow velocity distribution showed a positive correlation between blood flow velocities and vessel diameters in habitual lens wearers ($N = 20$) and the control group ($N = 40$). However, the blood flow velocities in habitual lens wearers (HCL) were higher across all vessel diameter ranges compared to those in the control group (NCL) ($P < 0.05$).

Figure 3.

Correlations between blood flow velocity and years of contact lens wear, hours of daily contact lens wear, age and main power of contact lens in 20 habitual contact lens wearers (HCL). Although we found that blood flow velocities were positively correlated with years of contact lens wear (A) and with hours of daily contact lens wear (B), the blood flow velocities showed no correlation with age (C) and main power of contact lenses (D).

Figure 4.

Correlation between microvascular network density and complexity and years of contact lens wear, hours of daily contact lens wear, age and main power of contact lens in 20 habitual contact lens wearers (HCL). The microvascular network density and complexity showed no correlation with years of contact lens wear (A), hours of daily contact lens wear (B), age (C) and main power of contact lenses (D).

Figure 5.

Comparison of studies based on the same imaging protocol. The present study and two previously published studies based on the same imaging protocols investigated conjunctival blood flow velocities in contact lens wearers and non-contact lens wearers (NCL). Study 1 examined changes after 6 hours of lens wear in neophytes (N = 22) and found a significant increase in conjunctival blood flow velocity after 6 hours of lens wear.²⁵ Study 2 examined conjunctival blood flow velocities in habitual contact lens wearers (HCL, N = 22) when they wore their lenses (Hu L, et al. IOVS 2016; 57: ARVO E-Abstract 4735). A significant increase in velocity was found relative to that in the non-lens wearers (NCL, N = 20). In the present study, the blood flow velocities found in non-lens wearers (NCL, N = 40) were similar to those of non-lens wearers found in the two previous studies. However, these habitual lens wearers (HCL, N = 20) showed a significant increase in blood flow velocities when they were not wearing their lenses after a night of sleep. There was no significant difference between HCL wearing contact lens (0.66 mm/s) in Study 2 and HCL not wearing contact lens (0.59 mm/s) in the present study. Bars = standard error.