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Title

Mechanical complications induced by silicone hydrogel contact lenses.

Permalink

<https://escholarship.org/uc/item/3gc209bt>

Journal

Eye & contact lens, 39(1)

ISSN

1542-2321

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Publication Date

2013

DOI

10.1097/icl.0b013e31827c77fd

Peer reviewed

Mechanical Complications Induced by Silicone Hydrogel Contact Lenses

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Abstract: With the introduction of silicone hydrogel (SiHy) lenses over a decade ago, clinicians have seen both improvements and challenges in contact lens (CL) wear. Regardless of lens design or material, the presence of a CL on the ocular surface induces mechanical complications. Although some of these complications have diminished in frequency and severity with newer generations of SiHy lenses, others persist at previously reported levels. The aim of this review is to provide up-to-date information on mucin balls, superior epithelial arcuate lesions, corneal erosions, CL-induced papillary conjunctivitis, conjunctival epithelial flaps, lid wiper epitheliopathy, and meibomian gland dropout. The conclusions in this review should provide a sound basis for identifying the future areas of research to help minimize mechanically driven adverse events during CL wear with SiHy lenses.

Key Words: Silicone hydrogel—Contact lenses—Mechanical complications—Mechanical adverse events—Mucin balls—Superior epithelial arcuate lesions—SEAL—Corneal erosions—Contact lens-induced papillary conjunctivitis—Conjunctival epithelial flaps—Lid wiper epitheliopathy—Meibomian gland dropout.

(*Eye & Contact Lens* 2013;39: 115–124)

Since the advent of silicone hydrogel (SiHy) contact lenses (CLs), many undesirable clinical complications resulting from CL-induced hypoxia have been eliminated. However, a CL on an eye inevitably disrupts the ocular surface by mechanical interactions—the posterior lens surface is in close contact with the entire cornea, limbus, and surrounding bulbar conjunctiva, whereas the anterior surface interacts with the palpebral conjunctiva and upper/lower lid margins. Therefore, it is not surprising that mechanically driven events continually and inevitably occur with SiHy CLs, because these lenses cannot truly mimic the ocular surface.

Mucin balls, superior epithelial arcuate lesions, corneal erosions, and papillary conjunctivitis are some examples of mechanically driven complications associated with CL wear. Since the initial launch of SiHy CLs, these adverse events have been extensively discussed in published review articles. This article provides updates on these topics from the past decade and discussions related to newer

findings on complications such as conjunctival epithelial flaps, lid wiper epitheliopathy (LWE), and meibomian gland dropout. This article also aims to identify the areas of research that warrant further investigations that may help minimize the occurrence of these mechanically induced complications during SiHy lens wear.

MUCIN BALLS

Mucin balls (Fig. 1) are spherical and translucent or opalescent bodies sandwiched between a CL and the cornea that can be observed within minutes after lens insertion. They are composed primarily of mucin,¹ and their sizes have been reported to range between 20 and 200 μm in diameter.^{2–7} Because they can be significantly larger than the thickness of the postlens tear film^{8–11} or the corneal epithelium, it is not surprising that some mucin balls can become deeply embedded into the cornea. They can be blinked away or leave depressions on the corneal epithelium on lens removal.^{7,12} These depressions are best observed with fluorescein instilled in the eye as the dye pools in the imprinted areas (Fig. 2) and are usually resolved within 24 hrs. Mucin balls and mucin ball-induced depressions are not associated with decreased lens-wearing comfort or compromised vision, and patients are usually asymptomatic.^{2,3}

Mucin balls were first described as a mechanical adverse event with SiHy CLs when worn for 30 consecutive days, otherwise known as continuous wear (CW),^{2,3} but they can also be observed with conventional hydrogel lenses.^{4,6} The frequency of mucin balls is similar between the two lens types, but the severity (i.e., number of mucin balls) is greater with SiHy CLs (e.g., lotrafilcon A) compared with conventional lenses (e.g., etafilcon A).⁴ According to a recent 12-month CW study with SiHy lenses, 54.2% of the subjects presented with mucin balls for at least 1 visit, and 32.8% of the subjects had recurrent episodes.¹³ Several studies have shown that the occurrence of mucin balls peaked after 1 month of CW and extended wear (EW), in which lenses are worn for 7 consecutive days and removed on the seventh night each week.^{4,13,14} Steeper corneal curvature, better front-surface lens wettability, and fewer back-surface deposits have been reported in association with increased presence of mucin balls, whereas plasma surface treatment (compared with plasma surface coating) has been associated with the decreased presence of mucin balls.^{4,14} Furthermore, Asian race has been found to be associated with a lower probability of recurrence, whereas blepharitis has been associated with a higher probability.¹³ It is unclear how the use of rewetting drops is related to the presence of mucin balls, because conflicting results have been reported.^{4,13} The exact mechanisms for each factor are not well understood. In general, mucin balls are believed to be mechanical in origin—formed by the mechanical interaction of a lens with

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M. Lin received an honorarium from CLAO for presenting the paper at the SiHy symposium (Silicone Hydrogel Lenses - Ten Years Later) and preparation of the manuscript for this special issue of *Eye & Contact Lens*.

The authors have no other conflicts of interest to disclose.

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Accepted November 4, 2012.

DOI: 10.1097/ICL.0b013e31827c77fd

FIG. 1. Translucent mucin balls located posterior to the contact lens seen with retroillumination (image courtesy of UC Berkeley Clinical Research Center).

the mucin layer of the tear film combined with shear force exerted on the ocular surface by the upper eyelid during blinking. Management strategies such as changing lens material (i.e., switching over from SiHy to traditional hydrogel lenses) and avoiding flat fitting lenses have been suggested.^{4,14}

The clinical significance of the presence of these entities is unclear. One study observed that stromal cells immediately beneath the depressions were stimulated to proliferate with an increase in localized cell density.¹² A recent study reported that the presence of mucin balls is significantly associated with a decreased incidence of corneal infiltrative events during CW with SiHy CLs.¹³ These authors postulated that the presence of mucin balls represents a more concentrated or viscous mucus layer, which prevents the upregulation of the immune response against bacterial ligands. Undoubtedly, mucin balls result from the mechanical interactions between the lens surface and the postlens tear film; however, its clinical significance remains unclear. Some may argue that the mucin balls are not an adverse event. In any case, future investigations are needed to provide evidence for its clinical insignificance to classify them as lens-induced changes instead of an adverse event.

FIG. 2. Mucin ball indentions seen with sodium fluorescein (image courtesy of UC Berkeley Clinical Research Center).

SUPERIOR EPITHELIAL ARCUATE LESION

Superior epithelial arcuate lesions (SEALs) were first described in the 1970s as a complication of conventional soft CL wear (Fig. 3).^{15–17} The SEALs can be full-thickness lesions located 1 to 3 mm from the superior limbus between the 10- and 2-o'clock meridians on the cornea. Depending on the distance from the limbus, they have been described as limbal or paralimbal SEALs.¹⁸

Patients with paralimbal SEALs are more symptomatic and may complain of foreign body sensation or irritation, whereas those with limbal SEALs may be asymptomatic.¹⁸ Most cases are unilateral. On slitlamp examination, the lesion, which is usually 0.1 to 0.3 mm wide and 1 to 5 mm in length, often appears with raised and irregular edges, separated from the limbus by a clear region. The lesion stains intensely with sodium fluorescein but may not be apparent after resolution. The lesion may also be accompanied by subepithelial infiltrates either immediately beneath or surrounding the lesion. Paralimbal SEALs are more likely to provoke an infiltrative response and are found to be associated with back-surface deposition.¹⁸ Patients diagnosed with a SEAL should be instructed to discontinue lens wear until staining and infiltration are resolved (between 1 and 7 days).^{19,20} To prevent recurrence, patients may be refitted into a different lens type (i.e., material or design) or instructed to change wearing modality (e.g., from EW to daily wear [DW]) and monitored closely.^{19–21} One study showed a 63% rate of recurrence of SEALs, where 50% did not suffer a third episode after being refitted into another lens type or lens care system and 13% continued to have recurrence regardless of any changes made.¹⁹ Refitting into a rigid gas permeable lens should be considered if the recurrence persists (generally three times).^{19,20}

The reported incidence of SEALs has varied greatly over the years, occurring in a variety of study cohorts and study designs (e.g., frequency of follow-up visits), and lens materials and lens-wearing modalities. The incidence of SEALs has been approximately the same between EW with conventional hydrogel lenses (0.9%–4.0%)^{19,21,22} and CW with first-generation SiHy CLs (0.2%–4.5%).^{20,23} A recent study found that first-generation SiHy CLs demonstrated a greater incidence of SEALs than the second-generation

FIG. 3. Superior epithelial arcuate lesion (image courtesy of UC Berkeley Clinical Research Center).

lenses when worn on a DW basis.²⁴ Although there is anecdotal evidence to suggest that SEALs occur more frequently with EW compared with DW, a study that directly compared the two wearing modalities did not verify this, perhaps because of a small sample size.²⁵ When comparing results from different studies, the reported incidence of SEALs seems higher with EW than with DW. Of interest, a report derived from database analysis of a primarily Indian population demonstrated the highest reported incidence rate of 18.7% of eyes per year for those in an EW regimen.²⁶ It is unclear whether ethnicity or other factors may have played a role.

Several theories have been proposed regarding the cause of SEALs, three of the most popular being mechanical disturbance, hypoxia, and desiccation.²¹ Because these events are still prevalent today with SiHy CLs, hypoxia has been eliminated as a possible cause, and the mechanical theory has become more widely accepted. This theory states that when there is a misalignment between the CL and the superior ocular surface, shear force induced by the upper eyelid results in chaffing of the limbal area. Because of the stiffness of the CL, it is unable to flex and conform to the shape of the eye in this region. Instead, the lens vaults the limbus in the open-eye state, but on eye closure is forced into a compromised “S” shape that does not perfectly align with the eye. The result is greater pressure applied in the location of greatest misalignment, thereby causing mechanical irritation.²⁷ Several risk factors have been proposed: (1) CL wearer characteristics (e.g., steep corneas, tight upper eyelid, male gender, and presbyopia), and (2) lens design characteristics (e.g., lathe-cut hydrogel lenses, rigid or thick materials, moncurve design, and plus lenses).^{21,27–29} Two main hypotheses regarding the cause of SEALs point to a combination of lens design (back surface and edge), lens material, lens surface, and corneal topography as the primary factors that lead to the development of SEALs.¹⁹ However, one study found no significant difference in the central corneal curvature between the SEAL and non-SEAL groups, but that poorer wettability and tighter fitting lenses established at baseline in the SEAL group lead to greater shear forces in the superior cornea during EW compared with the non-SEAL group.³⁰ Further studies examining the peripheral corneal topography and corneal scleral junction may help to minimize the incidence of SEAL by potentially improving the CL fit in the periphery and providing a better understanding of how these factors vary among different individuals and relate to lens fitting characteristics.

CONTACT LENS-INDUCED CORNEAL EPITHELIAL EROSION

Corneal epithelial erosions (Fig. 4) related to CL wear are epithelial defects with a wide range of clinical presentations.^{26,31} In general, they can be characterized as localized, well-circumscribed lesions that can be as small as 0.1 mm in diameter or encompass a much larger area of the cornea.³¹ They can present anywhere on the cornea, but 87.5% have been found inferiorly and, more commonly, near the vertical midline just below the pupil.^{32,33} The lesions can be superficial, affecting only the first one to three layers of the epithelium or deep into the basement membrane, and stain with sodium fluorescein with no underlying infiltrates.^{26,31,34} Alternatively, the epithelium may become detached centrally but remain adherent at the border, representing an early stage of development.³¹ There is no mucopurulent discharge, and there may be localized limbal and bulbar conjunctival injection.³¹ Patients may be asymptomatic or experience

FIG. 4. Corneal epithelial erosion induced by a silicone hydrogel (SiHy) lens (image courtesy of UC Berkeley Clinical Research Center).

foreign body sensation, especially on awakening if lenses are worn overnight, or sharp pain exists on lens removal.³¹ Although the aim of management is to reduce pain, prevent infection, and promote reepithelialization, there is no consensus on how best to do so.³⁵ In general, lens wear discontinuation, ocular lubricants in the form of drops, gels, or ointments, and prophylactic antibiotics are all believed to help with the healing process.^{20,35} Bandage CLs are avoided in cases of CL-induced erosion to reduce the risk of infection.³¹

Because of its quick resolution time and symptom-based diagnosis, CL-induced corneal erosion incidence rates have not been widely published, but they have been reported with gas-permeable (GP), conventional hydrogel, and SiHy lenses.^{20,24,31,36–38} A retrospective study published in 2010 serves as the most comprehensive report of incidence rates for various combinations of lens materials and wearing modalities.³⁷ The incidence of corneal erosion is greater with EW (0.60%–2.60% of visits) than with DW (0.01%–0.05% of visits) and greater with first-generation SiHy CLs (0.95%–1.68% of visits) than with conventional hydrogel lenses (0.05%–0.35% of visits). Interestingly, no corneal erosions were experienced by the daily disposable (DD) lens group.

The underlying mechanism leading to CL-related corneal erosion has yet to be understood, but several hypotheses regarding lens characteristics and corneal physiology have been proposed to support a mechanical cause. It is believed that the cause can be purely mechanical and occur abruptly on removal of a tight or bound CL,³⁹ or it can be a combination of mechanical and physiologic events that result in the gradual weakening of adhesion complexes that causes the corneal epithelium to detach on CL removal.³¹

Some lens characteristics have been reported to be the causative factors in corneal erosion. Specifically, a tight-fitting lens can result in lens adhesion, and when nudged loose on blinking or on lens removal, the lens can force the epithelium to be pulled away from the corneal surface.³⁹ Thin high-water CLs can induce dehydration in the central or central inferior cornea that can exacerbate thinning of the postlens tear film, resulting in mechanical erosion.^{38,40,41} Also, low-Dk CLs can cause a reduction of hemidesmosomes in the corneal epithelium, and thus, there is more risk for erosion in cases of long-term hypoxia.^{42,43}

The CL-induced corneal erosion may be exacerbated by certain physiologic factors that otherwise occur normally. For example, it has been suggested that matrix metalloproteinases (MMPs) may facilitate CL-induced erosion, especially after overnight CL wear.³¹ The MMPs are a family of enzymes that maintain and remodel

tissue architecture and, when present in controlled amounts, are important in maintaining homeostasis in the cornea. Matrix metalloproteinase-9 (MMP-9) is the primary matrix-degrading enzyme produced by the basal epithelial cells and is known to be active against major components of the basement membrane, including the fibrils that anchor the basement membrane to the stroma.⁴⁴⁻⁴⁸ If present in uncontrolled amounts, these enzymes can have collagen-degrading effects and may increase the risk of epithelial erosion formation.⁴⁹ It has been reported that a substantial upregulation of MMP-9 occurs before awakening compared with the open-eye state, which implies that the removal of a CL after overnight wear can cause mechanical harm to a system that is already susceptible to erosion.^{50,51} A recent study that explored changes in tear film MMP-9 after CW of SiHy lens found a marginal, but not statistically significant, higher MMP-9 concentration in the SiHy lens group than the non-lens wearing control group after 12 months of intervention. However, it is unclear if the collection time of the tear samples was controlled between study groups and if the sample size of the study was adequate to detect a statistical significance.⁵² In addition to MMPs, bacterial proteases (e.g., *Pseudomonas aeruginosa*, *Vibrio cholerae*) also seem to have the ability to degrade epithelial adhesion complexes,⁵³ contribute to matrix degradation,⁵⁴ and cleave corneal collagen.⁵³

It has been speculated that decreased tear exchange under the lens during CL wear may increase the concentration of bacterial proteases, pathogens, inflammatory cells, and other unwanted substances trapped underneath the lens and,⁵⁵⁻⁵⁹ as a result, increase the risk for corneal erosion and perhaps other lens-induced adverse events.³¹ A large sample size study taking demographic and ocular characteristics into account may be helpful in identifying additional risk factors and understanding how these risk factors relate to postlens tear mixing and MMP-9 concentrations.

CONTACT LENS-INDUCED PAPILLARY CONJUNCTIVITIS

Contact lens-induced papillary conjunctivitis (CLPC) is an inflammation of the upper palpebral conjunctiva and is one of the main reasons for CL discontinuation. It is characterized by enlarged papillae (>0.3 mm), hyperemia, and mucus strands. Two presentations of CLPC have been described: local and general. When the upper tarsal conjunctiva is divided into 5 discrete zones, local CLPC (Fig. 5) is described as being confined to 1 or 2 zones and general CLPC (Fig. 6) is described as being scattered

FIG. 6. General contact lens-induced papillary conjunctivitis (image courtesy of Cheryl McKinnon, O.D., Ph.D.).

across 3 or more zones.⁶⁰ Patients who have CLPC can be asymptomatic or experience acute ocular discomfort with complaints of itching, mucus or ropy discharge, lens awareness, and blurred vision, which are the results of increased front-surface lens deposits and excessive lens movement.^{61,62} The CLPC is managed by frequent cleaning and replacement of lenses, reducing wearing time, changing in lens-wearing modality to DD wear, and refitting into a different lens type or material.⁶³⁻⁶⁵ On discontinuation of the lens, there is usually a rapid relief in symptoms, with ocular signs dissipating over the course of several days, sometimes longer.

Contact lens-induced papillary conjunctivitis was first reported in 1974 with conventional soft CLs.⁶⁶ Since then, CLPC has been reported with polymethylmethacrylate, GP, and, most commonly, soft CLs.^{22,67} The reported incidence has varied widely (0.4%–47.5%),^{24,61} depending on lens type, lens materials, wearing schedule, and lens care solutions used in each study. Incidence rates of CLPC have been 13.0% to 47.5% with EW of conventional hydrogel lenses,^{61,68} 2.0% to 16.0% with EW planned-replacement hydrogel lenses,^{69,70} and 0.4% to 12.3% with EW and CW of SiHy lenses.^{24,25} A study comparing the effects of EW planned-replacement lenses and CW of SiHy lenses showed no difference in overall incidence of CLPC between lens materials, but did find that the incidence of general CLPC was greater with EW of planned-replacement CLs and local CLPC was greater with CW of SiHy CLs.⁷¹ The CLPC with first-generation SiHy CLs (balafilcon A, lotrafilcon A, and lotrafilcon B) occurs more frequently than with some later generations of SiHy CLs.^{24,72,73} For example, clinical studies have shown that CLPC scores have been significantly lower with galyfilcon A lenses compared with lotrafilcon A.^{72,73} There have been no published reports of CLPC with third-generation SiHy CLs. Studies comparing different lens-wearing modalities have failed to show any significant difference in the incidence among DW, EW, and CW^{25,74,75}; however, one prospective case-controlled study reported that the risk of developing CLPC in patients wearing DD lenses was half that of patients wearing planned-replacement lenses.⁷⁶ Studies comparing various lens care solutions have found no significant differences,^{36,74} but one study that compared various combinations of SiHy CLs and lens care solutions found a significant difference in the incidence of CLPC between solutions but not between lens materials.²⁴ This study found the greatest incidence of CLPC with peroxide- and POLY-QUAD-based lens care solutions compared with polyhexamethylene biguanide-based solutions; however, the number of cases of CLPC was too low to make definitive conclusions. Further investigation is

FIG. 5. Local contact lens-induced papillary conjunctivitis (image courtesy of Cheryl McKinnon, O.D., Ph.D.).

warranted to better understand the impact that lens care solutions have on CLPC with different lens materials, because the degree of mechanical or immunologic stimuli may differ with different combinations of care systems and lens materials.

The cause of CLPC is still not well understood, but several factors have been suggested as possible causes. It was first believed that CLPC was an immunologic response to denatured tear film proteins that deposit on the front surface of CLs.^{77,78} Mechanical trauma, types I and IV hypersensitivity, and meibomian gland dysfunction (MGD) were considered as other possibilities.^{77,79} Since the advent of SiHy CLs and the report of two clinical presentations of CLPC, the paradigm has shifted to suggest that perhaps local CLPC is caused by mechanical trauma and general CLPC is a hypersensitivity reaction, caused by lens surface deposits, lens coatings, or solutions.^{79–81} One study found local CLPC to be slightly, but not significantly, higher with SiHy CLs and general CLPC to be significantly greater with low-Dk disposable hydrogel lenses, supporting the theory of mechanical trauma caused by the higher modulus soft CLs.⁷¹ However, another study investigated the level of IgE from patients who experienced CLPC and found that, although the levels were heightened in CLPC patients compared with that in non-CLPC patients, there was no significant difference in IgE levels between local and general cases, implying that local and general CLPC may be induced by the same pathway.⁸²

Contact lens–induced papillary conjunctivitis has been associated with delayed tear clearance, which might increase the protein and inflammatory mediator concentrations in the tear film and contribute to the pathogenesis or aggravate the severity of CLPC.⁸³ Of interest, MGD is common for patients with CLPC,⁸⁴ but no association was found between MGD and delayed tear clearance.⁸³ It has been proposed that a tear clearance test be incorporated in the eye examination for CL wearers with CLPC, as the treatment modality can be adjusted accordingly.⁸³ In cases of decreased tear clearance, nonpreserved steroids may be indicated. If tear clearance is normal, then changing the lens material may be recommended first, because mechanical trauma may be a more significant contributor compared with inflammation.

CONJUNCTIVAL EPITHELIAL FLAPS

Conjunctival epithelial flaps (CEFs) were first reported with SiHy CLs in CW in 2005.⁸⁵ Conjunctival epithelial flaps are bulbar conjunctival lesions that are best observed with fluorescein dye under cobalt blue light with a yellow filter. In 65% of cases, they occur bilaterally and are most often located in the superior quadrant of the bulbar conjunctiva, followed by the inferior and temporal quadrants.⁸⁶ The size of CEFs vary based on the lens-wearing modality with SiHy CLs, ranging from 0.1 to 0.5 mm during DW (Fig. 7) to approximately 9.0 mm during CW (Fig. 8).⁸⁶ The CEFs have been reported with DW and CW of SiHy and with CW of GP CLs.^{85,86} A recent study reported that the probability of developing a CEF is significantly greater in CW than in DW, especially after a minimum of a week of CW with SiHy CLs and 3 weeks with GP lenses.⁸⁶ The CEFs with SiHy CLs occur at approximately 3% with DW and approximately 8% to 37% with CW,^{86–89} in contrast to 26% with GP CW.⁸⁶ This condition has no age, gender, or ethnicity predilection.⁸⁶

The cause of CEFs is mechanical in origin and possibly associated with lens characteristics, whereby higher modulus lens

FIG. 7. Conjunctival epithelial flap with daily wear of SiHy CLs (image courtesy of UC Berkeley Clinical Research Center).

materials along with a non–rounded edge design can increase the risk of developing CEFs. The CEFs occur after the bulbar conjunctival epithelium delaminates from its underlying tissue as a result of mechanical interactions between a lens edge and the bulbar conjunctiva. The jagged tissue associated with CEFs usually marks the limit of vertical movement of a CL. The recovery time after lens cessation depends on the extent of the flap; a small lesion takes a minimum of 24 hrs to resolve, whereas larger flaps can take several weeks.⁸⁶ Although the long-term consequences of CEFs are not known, patients with CEFs should discontinue lens wear until the conjunctiva is recovered.⁸⁶ Management of CEFs may involve modifying the wearing modality (e.g., CW to DW) and changing to a lower-modulus or rounded-edge lens.⁹⁰

Various studies have examined the cellular composition of CEFs observed in CW. One study conducted impression cytology after 1 week of CW and showed that CEFs were composed primarily of

FIG. 8. Conjunctival epithelial flap with continuous wear of SiHy CLs (image courtesy of UC Berkeley Clinical Research Center).

vital epithelial and goblet cells.⁹¹ Another study examined conjunctival cells collected by biopsy from two cases of CEFs using histopathology, which allowed the examination of the entire thickness of the flaps, and found minimal abnormality.⁹² However, it is not clear what the elapsed time was from the initial occurrence of the CEFs to when the biopsy samples were collected. In contrast, clinical observation using Rose Bengal found that CEFs observed after 1 week of CW did not stain with the vital dye, but after 30-day CW in the same subjects, the flap edges, localized delaminated area, and the surrounding region stained brightly with Rose Bengal.⁸⁶ This may suggest that the cells of the CEFs and those affected immediately beneath the flaps become devitalized over time, or it may be that there is an insufficient protective layer of mucin covering the flap. Clearly, the long-term effect of this condition on ocular health during lens wear requires further elucidation.

LID WIPER EPITHELIOPATHY

The lid wiper is a localized portion of the marginal conjunctiva of the upper eyelid that has a rubbing effect on the ocular surface during blinking.^{93,94} This wiping effect is believed to be essential for spreading the tear film over the ocular surface or the surface of a CL. It is postulated that when the tear film is thinned or becomes unstable or a lens surface does not provide a stable and wettable surface, there might be a more mechanical/frictional effect on the lid wiper as the lid travels across the ocular or lens surface during blinking.⁹⁴ As a result of insufficient boundary lubrication, the lid wiper is traumatized and develops into LWE that can be viewed clinically when the epithelium of the marginal conjunctiva is stained with commonly used ophthalmic dyes (Fig. 9).^{84,95,96}

To diagnose LWE, Korb et al. recommend 1 application of sodium fluorescein or lissamine green dye and waiting for 60 sec before observing the everted eyelid. Alternatively, 30 to 60 sec after 1 application of Rose Bengal dye will also facilitate the examination of LWE. However, a preferred method is to use 2 applications of sodium fluorescein or lissamine green dye, applied 5 min apart for best viewing. When sequential staining is conducted, it is important to evert the eyelid 1 min after the second application of the dye to avoid iatrogenic staining because of desiccation of the lid wiper.

It is important not to confuse LWE with the Marx line (Fig. 10) that is on the mucocutaneous junction of the lid margin near meibomian gland orifices rather than on the margin of the palpebral

FIG. 10. Marx line (image courtesy of UC Berkeley Clinical Research Center).

conjunctiva. The normal width of the Marx line is approximately 0.1 mm and can be stained and visualized along the entire upper and lower lids,⁹⁷ whereas a normal lid wiper width is 0.4 to 0.6 mm and is increased and stained with ophthalmic dyes when epitheliopathy develops because of microtrauma. Additionally, the Marx line of the upper lid is visible in upgaze without lid eversion, whereas lid wiper requires lid eversion.⁹⁸ This is because the Marx line is not the contact area for wiping of the ocular surfaces by the upper lid, because it is not possible for the contact area to be visible and also be in contact with the ocular surface during blinking.⁹⁹ The functions of the Marx line and lid wiper continue to be controversial; however, the nature of the controversy is beyond the scope of this review article.^{97,100–103}

It has been widely reported that CL-induced dryness symptoms often do not correlate with clinical signs. However, Korb et al.⁹⁴ observed LWE in 80% of symptomatic patients but in only 13% of asymptomatic patients. Another group of investigators reported similar findings.¹⁰⁴ It is possible that LWE may be a missing link in CL-induced dry-eye diagnosis and treatment.

It has been suggested that LWE has a mechanical cause with secondary inflammation.⁹⁴ Some clinicians speculate that LWE occurs more often with lenses of high coefficient of friction (e.g., GP, some SiHy CLs).¹⁰⁵ Theoretically, the coefficient of friction is not strongly dependent on the lens material surface properties as long as the lens surface is well lubricated.¹⁰⁶ However, more surface roughness might have undesirable implications compared with a smooth lens surface. It is possible that this anecdotal evidence is influenced by the assumption that the differences in CL surface chemistry might lead to dissimilar interactions with the prelens tear film, which in turn give rise to changes in frictional forces between a lens and the eyelid. If this hypothesis is correct, the incidence of LWE might be divergent among SiHy CLs, as each brand has either specific surface treatment or no surface treatment/coating and might uniquely interact with the surrounding tears. Surface-active components of lens care or packaging solutions may also facilitate a different interaction between the eyelid and a lens surface. The surface-active agents, which presumably improve lens surface wettability, are nowadays introduced in all lens-packaging

FIG. 9. Lid wiper epitheliopathy (image courtesy of UC Berkeley Clinical Research Center).

solutions.¹⁰⁷ Further investigation is needed to indubitably specify and discern the impact of SiHy lens materials from that of lens care or packing solutions on lid wiper health, especially as the popularity of SiHy increases.

In the case of CL wearers, CL surface is a major external cause of tear film instability. Therefore, the preventive treatments of LWE should augment hydrodynamic lubrication, reduce or eliminate excess trauma, and counteract possible associated inflammation—all ultimately assisting in shear stress reduction and prevention of “dry” contact between the eyelid wiper and the CL surface. Artificial tears (e.g., lipid emulsion), steroids, punctal plugs, ointment at night after lens removal, and meibomian gland management, and lens wear cessation or a change in lens type (e.g., a low modulus CL) are possible treatment plans. Additionally, because incomplete blinking can be associated with LWE, patient education on complete or efficient blinking during lens wear may increase the therapeutic benefit to LWE.¹⁰⁸

MEIBOMIAN GLAND DROPOUT

Meibomian gland dropout (MGDo) refers to the partial or total loss of acinar tissue detected by meiboscopy, meibography, or confocal microscopy.¹⁰⁹ To date, it is uncertain whether MGDo can result in deficiency in meibomian gland expressibility or alteration in lipid secretions that are frequently associated with lid margin inflammation commonly seen in MGD.^{110,111} Although alterations to meibomian gland morphology may be suggestive of MGD, such changes are difficult to ascertain in a routine eye examination. Researchers have designed imaging systems to facilitate meibomian gland examination and diagnosis, including a combined system of infrared photography and transillumination biomicroscopy.¹¹² More recently, noncontact, patient-friendly meibographic techniques using infrared illumination systems have been introduced, which allow for quick and thorough examinations of morphologic changes in meibomian glands.^{113,114} Using the new technology, the authors reported that CL wear accelerates age-related changes in the meibomian glands.¹¹⁵ They also found that CL wearers with an average age of 32 years demonstrated an average meiboscore similar to that observed in a 60- to 90-year-old age group from the normal population.¹¹⁵ Additionally, loss of meibomian glands depends on the duration of CL wear, but not on the CL materials (e.g., GP vs. conventional CLs).¹¹⁵ It is unclear whether MGDo can be recovered after CL cessation.

Evidence for these meibomian gland morphologic changes was further provided by a recent *in vivo* histopathologic study using a laser scanning confocal microscope (LSCM).¹¹⁶ This LSCM study of meibomian glands showed significantly decreased basal epithelial cell density, lower acinar unit diameters, higher glandular orifice diameters, and greater inhomogeneity of the periglandular interstices in CL wearers compared with that in controls. These authors interpret such morphologic changes as signs of MGDo, duct obstruction, and glandular inflammation. More investigation is warranted to better understand the relationship between morphologic changes of meibomian glands and MGDo.

The mechanism for CL-induced MGDo is unclear. One recent study reported shortening of the meibomian glands in CL wearers (Fig. 11), particularly at the distal end, producing significantly greater effects in the upper than in the lower eyelid, supporting a mechanical theory.¹¹⁵ However, other authors reported no association between

FIG. 11. Meibomian gland dropout seen with noncontact infrared meibography (image courtesy of Reiko Arita, M.D., Ph.D.).

MGDo in the lower eyelid and CL wear.¹¹⁷ The disagreement in study results is possibly because of the authors from the latter study not examining or imaging the full extent of both upper and lower eyelids, but rather only the central portion of the lower eyelid.

Chronic blockage of meibomian glands may eventually lead to anatomical changes in meibomian glands. One proposed theory speculates that flexing of ultrathin hydrogel lenses results in trauma to the meibomian orifices and deposition of keratic materials into the gland, impeding secretion of these glands.¹¹⁸ In more recent literature, others also postulated that mechanical trauma from CLs causes hyperkeratization of meibomian glands, leading to duct blockage.¹¹⁹

Much remains unknown about the effect of CLs on meibomian glands. If flexing of ultrathin hydrogel lenses is to be blamed, we may assume that GP lenses should induce a different rate of MGDo, and yet one study did not find statistically significant differences in MGDo between GP and conventional CLs.¹¹⁵ Further investigation with modern technology is needed to elucidate the mechanisms responsible for meibomian gland morphologic changes because of CL wear, to examine whether these changes differ between conventional and SiHy CLs or between different wearing modalities, and to determine how these anatomical changes affect the function (e.g., gland expressibility, lipid compositions) of meibomian glands and lens-wearing comfort.

CONCLUSIONS

Since the United States Food and Drug Administration approved the first SiHy CLs in 1999, the CL industry has made significant strides to improve SiHy CL performance. A review of the last decade of mechanically induced adverse events associated with SiHy CL wear has yielded interesting trends related to lens materials, wearing modalities, and duration of wear. Although first-generation SiHy lenses eliminated many undesirable CL-induced hypoxia complications, it fell short in some other categories. Compared with conventional hydrogel lenses, first-generation SiHy CLs are associated with greater severity of mucin balls and higher incidence of corneal erosion.^{4,37} However, the lower-modulus second-generation SiHy lenses are associated with decreased occurrence of SEALs, CLPC, and CEFs.^{24,72,73,87} The incidences of SEALs, corneal erosion, and CEFs are greater with EW/CW than with DW, but wearing modality does not seem to influence the incidences of mucin balls and CLPC.^{26,37,71,86} Finally, the frequency of mucin balls, CLPC,

CEFs, and meibomian gland dropout increases with duration of lens wear.^{4,14,79,86,119} Despite the wealth of published information related to SiHy CLs, much more needs to be elucidated about their effects on lid wiper and meibomian gland anatomical and physiologic changes. Additionally, future studies using newer-generation SiHy CLs are needed to accurately assess how incidence rates of mechanically induced complications correlate with the evolution of lens materials.

In general, many mechanically induced complications seen with SiHy CLs are the result of less-than-ideal alignment between a CL and ocular surface curvatures. This mismatch may be exacerbated in certain CL wearers if their lids produce higher degrees of shear force exerted on the ocular surface during blinking. Studies have suggested that, in addition to lens characteristics, patient ocular characteristics are also critical to good alignment between the CL and ocular surface.²⁶ Additionally, ethnicity/race can affect how ocular surface responds to CL wear.^{8,26,59,120,121} Further studies are needed to understand how race/ethnicity and age play a role in the successful lens wear, especially because SiHy CLs are gaining interest worldwide, particularly in Asia where myopia control with soft CLs is of great interest for the prevention and treatment of myopia in young children.

The interaction between SiHy lens materials and lens care systems has gained much attention in the CL research community during the past decade. The degree of mechanical or immunologic stimuli may differ with various combinations of lens materials and care systems.²⁴ Therefore, future studies assessing the incidence of some mechanically driven complications should not ignore the possible confounding factors introduced by different lens care solutions. The possible effects of surface-active components present in the lens-packaging solutions should also be taken into consideration, especially for DD SiHy lenses.

The relationships between CLs and MGD, and between CLPC and MGD, remain unclear. Whether CLPC is a sequela of MGD, or vice versa, is not well understood. Studies have shown that LWE and meibomian glands can be adversely affected by CL wear.¹¹⁵ The extent of this effect by SiHy CLs is not known. Therefore, a CL-screening examination should not be considered complete without assessing the lid wiper and meibomian glands. In other words, lid eversion is essential for a complete ocular surface examination in CL wearers.

Furthermore, some of these mechanically induced adverse events are not associated with compromised vision or significant discomfort that would raise concerns in patients or clinicians. Therefore, early signs may be considered innocuous or too readily dismissed for the lack of understanding about their potential long-term effects, which need to be more fully investigated. It is conceivable that to increase the longevity of successful CL wear, we must pay more attention to changes in the ocular surface as a chronic irritation that can potentially trigger immunologic responses.

Additional areas of research that can potentially minimize mechanical complications during SiHy CL wear include tear mixing and the topography of peripheral cornea and corneal scleral junction, and lubricity of the CL surface. To minimize these mechanical adverse events, the industry should aim to develop CLs that minimally disrupt the ocular surface (cornea, conjunctiva, and lids). This is a great challenge, because not only should the lenses be biocompatible with ocular tissues but the lenses must also be compatible with various lens care solutions to make the entire system (i.e., lens + care system) truly biocompatible. It is the hope

of researchers and clinicians that with continual technological advances and multidisciplinary research approaches, many mechanisms responsible for these mechanically induced complications may be elucidated, and consequently minimized, if not eradicated.

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