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Accounting for Ethnicity-Related Differences in Ocular Surface Integrity as a Step Toward Understanding Contact Lens Discomfort

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Abstract: Contact lens discomfort is a common problem that can lead to unsuccessful or limited contact lens wear. Although many factors may contribute to contact lens discomfort, limited research has explored the influence of ethnicity-related differences in the anatomy and physiology of the ocular surface. Therefore, we performed a search of the literature in PubMed using key words related to "ocular surface" paired with the terms "race" and "ethnicity." The goal of this review was to determine potential areas of research regarding ethnicity differences, particularly between Asian and non-Asian eyes, in ocular surface integrity to advance our understanding of contact lens discomfort.

Key Words: Contact lens discomfort—Race—Ethnicity—Contact lenses—Ocular surface—Tear film—Eyelid—Cornea—Dry eye—Symptoms—Palpebral aperture size—Epithelial barrier function—Tear mixing—Adverse event.

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Given the high prevalence of contact lens discomfort,[1,2] it is crucial to understand how comfort with lens wear is linked to variations in the anatomy and physiology of the ocular surface and how ophthalmic devices impact ocular surface integrity. Like dry eye disease, contact lens discomfort has multifaceted etiologies (Fig. 1). For example, contact lens wear history (e.g., duration of wear,[3] use of lens care solutions,[4] wearing modality[3]), environmental factors, and demographics (e.g., age,[5] gender,[6,7] ethnicity[5–7]) can all contribute to the progression of discomfort. Ethnicity-related variations in the anatomy of the eye are widely documented in the literature. However, to gain a better understanding of the less well-known ethnicity-related variations involving contact lens discomfort, particularly between Asian and non-Asian eyes, these potentially contributing factors must be taken into consideration.

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ADVERSE EVENTS DURING CONTACT LENS WEAR

Adverse reactions to contact lens wear have been well documented in the literature, although little has been reported on variations in ethnic groups. These reactions may be incited by various contact lens-related factors, such as changes to tear chemistry, mechanical stress to the ocular surface, poor oxygen delivery, or buildup of toxic debris. Corneal staining is a commonly used clinical measure to assess the safety of contact lens wear.[5] Asians have consistently demonstrated more bulbar hyperemia and corneal staining, and to a greater degree of severity than non-Asian subjects with contact lens wear.[5,6] In a 1-year longitudinal study, subjects wore 30-day continuous wear silicone hydrogel contact lenses. Asian subjects had a significantly greater number of adverse events than did non-Asians, with approximately 47% of Asian subjects having at least one adverse event, compared with approximately 16% of non-Asians.[8] Specifically, the risk of inflammatory adverse events was significantly higher in Asians (29%) than in non-Asians (4%).

Additionally, the interactions between tear lipid, tear aqueous components, and certain ingredients of ophthalmic medications and lens care solutions can influence tear film stability, which can affect successful contact lens wear.[7,9,10] Specifically, some components of lens care solutions significantly alter dynamic interfacial properties and rheological behavior of human tear lipid films.[11–13] Clinical results suggest that both Asian and non-Asian groups exhibited increased corneal staining in response to biguanide-preserved solutions, although Asian subjects demonstrated greater sensitivity to the solutions than did non-Asian subjects.[4] However, the severity of ocular signs does not always correlate with overall lens wear comfort in Asian subjects, and thus may not be an impediment to overall satisfaction.[4,6] Another study investigated the impact of daily irrigation with sterile saline with a continuous wear modality in mitigating the onset of adverse events by enhancing post-lens tear mixing. The results showed that Asians were at a higher risk of contact lens–induced problems without irrigation, whereas non-Asians demonstrated more complications with daily irrigation.[8] This evidence further supports the findings that ethnicity-related differences in tear chemistry (more discussion in Tear Film section) may influence ocular response to ophthalmic topical solutions and contact lens wear. Further studies are needed to better explore the ethnicity-related biological and physiological responses to a wider variety of contact lens care solutions and preservatives, to gain a more thorough understanding of which solutions are most suitable for certain populations.

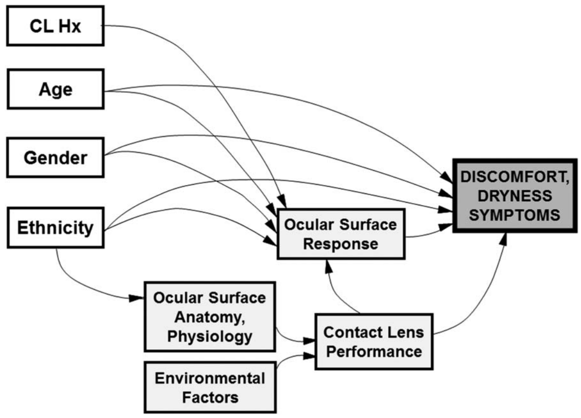

FIG. 1. Directed acyclic graph depicting some of the many complex interrelationships among factors that can directly or indirectly affect ocular symptomatology.

Additionally, a contact lens compartmentalizes the tear film into prelens and postlens layers.[14,15] It has been shown that increased corneal epithelial permeability (or more compromised corneal epithelial barrier function), even without the presence of corneal staining, is significantly associated with adverse events during 30-day continuous silicone hydrogel lens wear.[16] This indicates that a chronic irritation of the corneal epithelial surface at the postlens tear film interface can adversely disrupt ocular surface homeostasis. Therefore, it has been hypothesized that a reduction in a stagnant postlens tear film (i.e., a continual replenishment of healthy tear film in the postlens tear film) is a necessary requirement to achieve safe contact lens wear, especially during sleep.[8] A poor postlens tear exchange, especially with soft contact lenses, leads to the buildup of inflammatory cells, metabolic byproducts, and debris in the postlens tear film that may cause adverse ocular responses.[9,10,14] Supporting this theory is the fact that gas-permeable lenses demonstrate high levels of tear mixing similar to physiologic tear turnover[17] as well as fewer serious ocular complications commonly seen with soft lens extended wear.[2] The apparent difference between rigid and soft lenses, linked to variations in size and material properties, lies in their dissimilar capabilities to mix and replenish the postlens tear film.

Despite advances in lens materials and designs, the rate of adverse effects with traditional HEMA-based soft contact lenses is the same with highly oxygen transmissible silicone–hydrogel lens materials, further suggesting that contact lens–induced hypoxia is not a unique pathway to complications during contact lens wear. It is possible to manipulate a soft contact lens fitting to minimize fluid flow resistance and preserve the integrity of corneal epithelial barrier function, which can be used as an adequate proxy for tear mixing evaluation.[8] We can use this measure because studies[16,18,19] suggest that the stagnant tear film with "presumed" altered biochemical and biophysical properties can compromise corneal epithelial barrier function. For example, fluid flow may be increased by fitting soft lenses with steeper base curve radii (BCR) or rigid lenses flatter to enhance postlens tear mixing and thus minimize microtrauma of the corneal epithelium during closed-eye wear.[20] By improving postlens tear mixing, the incidence of adverse effects may be reduced, particularly in ethnic groups more inclined to an adverse ocular response because of poor tear mixing. However, a prospective randomized clinical trial is warranted to confirm this hypothesis.

According to dispersive mixing models, a thicker postlens tear film enhances tear flushing underneath a soft contact lens.[21] In particular, Asian eyes were found to have thinner postlens tear films than non-Asians eyes,[14] which can contribute to a higher incidence of adverse events with contact lens wear. Studies have proposed design innovations to increase postlens tear thickness (e.g., altering BCR, adding fenestrations, or back-surface channels/grooves). However, a low-modulus soft lens with a steeper base curve radius only proved successful in enhancing postlens tear thickness in non-Asian eyes. It provided no benefit in Asians because of the anatomy and eyelid tension of the Asian eye as the low-modulus lens material was incapable of providing a significant difference in sagittal depth despite changes in BCR.[14] With other lens designs using higher modulus soft lens materials and back-surface grooves, Asian subjects experienced marginal benefits in postlens tear mixing compared with non-Asians. This divergence was explained by the increased upper eyelid tension of large Asian eyes that enhanced transverse motion of the high-modulus lens material and therefore also improved tear mixing.[9] These results suggest the importance of understanding eyelid–lens interactions with different lens materials, as it may have clinically significant impact on postlens tear mixing.

INHERENT ETHNICITY-RELATED DIFFERENCES IN OCULAR SURFACE ANATOMY AND PHYSIOLOGY AND HOW THESE DIFFERENCES AFFECT CONTACT LENS WEAR

Although little has been reported on ethnicity differences concerning contact lens wear, many studies have looked into differences in anatomy and physiology across ethnic groups. Given these differences, we can hypothesize that differences in successful contact lens wear can be attributable to inherent anatomic or physiologic variations between different races.

Eyelid

Many defining and principally different features between Asian and non-Asian ocular anatomy lie within the eyelid structure, which is widely discussed in the literature. These include obliqueness of eye shape,[22,23] smaller palpebral fissure and aperture,[24,25] a thicker brow fat pad,[26] and the presence of epicanthal folds[27] typical for Asians compared with non-Asians. The combination of a smaller palpebral fissure and thicker brow fat pad not only affects surgical techniques implemented on an Asian eyelid,[25] but also impacts contact lens performance.[5,6] Eyelid tension is another factor that can have clinical implications for successful contact lens wear. Although a direct measurement of eyelid tension has not shown ethnicity-related differences (perhaps because of poor instrumental accuracy, poor repeatability, and a small sample size),[28] clinicians presume that for Asians, eyelid tension is higher than in non-Asians based on clinical anecdotal evidence. Several studies have shown associations between "presumed" eyelid pressure and changes in corneal topography, particularly induced astigmatism.[29–34]

There are conflicting results regarding whether Asian palpebral aperture size (PAS) is smaller than that of non-Asians.[5] The reasons responsible for these discrepancies include different sampling

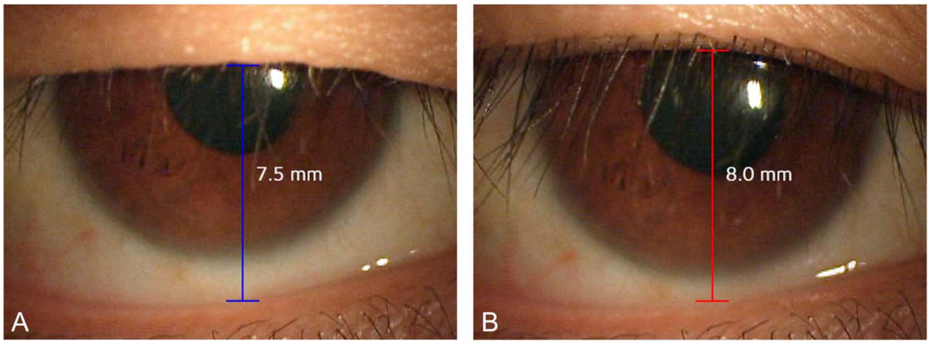

FIG. 2. An example underestimation of an Asian palpebral aperture size: (A) eyelid skin obscures the truce location of upper eyelid margin; (B) location of upper eyelid margin appears after lifting the eyelid. full color online

of study cohorts, definitions of ethnic groups, and measurement techniques. Another reason for conflicting results is that some eyelids present with overhanging skin that obscures the upper eyelid margin position, resulting in an underestimation of PAS (Fig. 2). Additionally, not all Asians have a small PAS. Of particular interest is the distinction between single-fold and double-fold eyelids in Asian eye anatomy. In a double-fold eyelid, there is the ability to raise the skin below the crease line because of increased stiffness, resulting in increased opening or bigger PAS in a double eyelid.[27,35] Therefore, PAS should not be used as a proxy variable for ethnicity.

PAS can be measured behind the slitlamp with low magnification and low illumination with a diffuser, while using a reticule in the eyepiece to measure the distance in millimeters from the lower to the upper eyelid margin. An analysis of data using this measurement technique, from a database provided by the University of California, Berkeley Clinical Research Center, found that a larger PAS was significantly associated with a more stable tear film ($P<0.0001$; Fig. 3). In this cohort of 219 subjects (546 records), ranging in age from 18 to 92 years with a mean (SD) of 33.0 (17.8) years, noninvasive tear breakup time (NITBUT) was measured three times per eye, with a minimum of 30 sec between measurements, using a Placido disk-based corneal topographer (Medmont E300; Medmont Pty Ltd, Victoria, Australia). Mixed-effects models were used to account for potential within-subject correlations because of measuring both eyes of each subject across multiple visits. When data were stratified by ethnic group, NITBUT was found to be significantly longer with larger PAS for both Asians ($P=0.0001$) and non-Asians ($P<0.0001$). Together these analyses suggest that PAS itself can have a clinically significant effect on tear film dynamics. We hypothesize that in an eye with a small PAS, the tear lipid layer is not able to efficiently perform its usual expansion and compression during a normal blink in a confined area, resulting in a less stable tear film, which can disrupt homeostasis of the cornea. Further investigation is warranted to examine the interplay between PAS and prelens tear film dynamics.

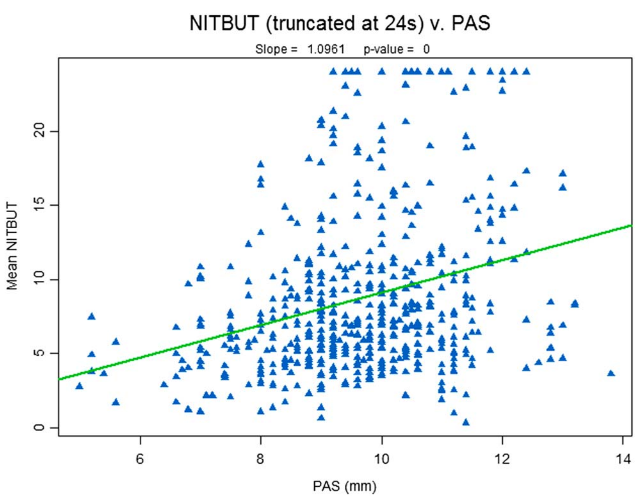

FIG. 3. Noninvasive tear breakup time is linearly associated with palpebral aperture size. full color online

Not only is a larger PAS associated with a more stable tear film, but there is also evidence suggesting an association with higher corneal epithelial barrier function in overnight contact lens wear.[16,18] It is conceivable that PAS affects the degree of eyelid–lens interaction that can impact the efficiency of post-lens tear mixing, which in turn affects corneal epithelial permeability.

Cornea

Horizontal visible iris diameter (HVID) and corneal curvature are other important anatomic differences to consider between different ethnic groups because of their impact on successful contact lens fitting. Several studies have found that HVID values were significantly smaller for the Asian cohort than the white group.[5,24,36,37] A smaller HVID may indicate a faster rate of corneal flattening in Asians. This was confirmed with topographical measurements that demonstrated significantly flatter horizontal keratometry values in Asian subjects.[24] However, existing data on corneal topography in the literature are inconsistent, as some report steeper corneas in Asian populations,[38] whereas others have published the opposite findings.[4,9,14,16,18,24] In general, studies that included only eyes without prior contact lens wear history provide repeatable and reproducible results showing that Asian corneas are flatter than non-Asian corneas. However, if the study cohorts included a mixture of eyes with and without contact lens wear, then the results tend to be inconsistent, suggesting that lenses (i.e., old and new generations of contact lenses) have differing effects on corneal curvatures in ethnic groups. Provided that there are differences in corneal curvature, contact lens practitioners would be prudent to choose lens designs with appropriate base curves that are matched with varying ethnic backgrounds to gain a more optimal fit.

The transitional region from the cornea to the sclera, also known as the corneoscleral junction (CSJ), also exerts potential influence on the fit and comfort of large diameter contact lenses (e.g., soft lenses, scleral lenses). Limited data are available about the anatomy of the CSJ because of difficulties of measuring the subtle directional change that takes place between the cornea and sclera. Thus far, the CSJ has been quantified in two ways: angle measurement and fitness of a linear regression to the CSJ profile. The former method has its limitations, specifically poor repeatability and reproducibility.[23] Using the latter method with optical coherence tomography imaging, Tan et al.[39] were able to show an accurate description of the CSJ with repeatable measurements. With their technique, the CSJ was reported to be significantly steeper or rougher, especially at the nasal quadrant. The CSJ was reported to be steepest in white subjects followed by Latino and Asian subjects, respectively.[39] Further investigation is warranted to understand how CSJ differences affect the physical fit of soft contact lenses and especially scleral lenses.

The biomechanical properties of the cornea, namely corneal hysteresis (CH) and corneal resistance factor (CRF), are indicators of corneal health, such that several studies have shown a significant decrease in these properties in postoperative and diseased eyes.[40–42] A study by Yeh et al.[43] found that Asians exhibited lower mean CH and CRF when compared with their non-Asian counterparts at baseline before orthokeratology treatment. This difference has been hypothesized as a factor in explaining why Asian corneas are more difficult to deform from their baseline state and are likely to rebound to baseline much quicker than non-Asian corneas during overnight orthokeratology treatment. The differences in biomechanical properties may also have implications for orthokeratology treatment and refractive surgery outcomes in different ethnic groups.

Corneal thickness has become an increasingly important measurement in refractive surgery and the management of corneal conditions, ocular hypertension, and glaucoma. In general, central corneal thickness (CCT) is greatest at initial eye opening and reduces as the cornea deswells throughout the day. The CCT is influenced by a diurnal fluctuation of tear osmolarity, but this osmolarity effect may not be clinically relevant in normal eyes. Evidence indicates that there is no ethnicity-related difference in the relationship between osmolarity and corneal thickness.[44] However, there is a clinically significant difference in CCT among different ethnic groups. For example, on average, African Americans have a thinner CCT when compared with whites.[45–47] Other studies have demonstrated that Asians have a thicker CCT than African Americans, but little-to-no difference when compared with a Hispanic or white populations.[44,48,49] Given these inherent ethnicity-related differences in CCT, it is imperative to determine the individual magnitude of change in CCT before and after an intervention (e.g., contact lens wear) to determine its safety and efficacy. In studies where corneal edema is used as a "safety" index (e.g., development of prototype contact lenses or assessment of contact lens oxygen-transmissibility effects on corneal thickness), simply comparing group means can be misleading because within-subject variability and the range of magnitudes of individual changes in CCT from preintervention to postintervention are not taken into account.

The corneal endothelium, which is responsible for maintaining proper corneal hydration, has also exhibited differences among various ethnic groups. A properly functioning endothelium becomes important in the success of corneal surgeries and the response to hypoxic stress, such as with contact lens wear. Several studies have demonstrated that Asians have a higher corneal endothelial cell density than non-Asians.[50–52] Interestingly, anatomic differences may not always be in agreement with functional differences. Asian corneas have shown an increase in endothelial bleb formation, corneal swelling before contact lens wear, and corneal swelling in response to contact lens wear despite their greater endothelial cell density.[53]

Corneal epithelial response to stress, such as contact lens wear, has also been found to vary between Asian and non-Asian groups. The corneal epithelium serves as a mechanical barrier to foreign microorganisms and plays a key role in the innate defense mechanism of the ocular surface. Therefore, variations in the permeability of this tissue can have significant impacts on the safety of contact lens wear[20] and the efficacy of topical medication delivery.[23] Previous studies have shown that Asians who have no history of contact lens wear and no apparent corneal staining with fluorescein dye have higher corneal epithelial permeability when compared with non-Asian subjects.[20,23] According to one study, the inherent ethnicity-related difference, on average, is 27.7%.[23] Anatomic and physiological differences in eyelid structure have been the most accepted explanations of this inherent difference. Asian eyelids have a higher volume of orbital fat, smaller PAS, thinner postlens tear film, and tighter positioning of the lids, which may lead to increased shearing force across the ocular surface during blinking, resulting in increased permeability of the corneal epithelium. The mechanical insult to the cornea has been shown to be responsible for epithelial cell apoptosis, desquamation, and disruption of tight junctions.[54–58] These changes have been implicated as contributing factors to inflammatory responses associated with dry eye and are likely responsible for increased corneal epithelial permeability, which can significantly impact comfortable contact lens wear in certain ethnic groups more than others.

Contact lens wear, particularly extended or continuous wear, creates an increasingly stressful environment for the cornea when compared with no lens wear or lens wear on a daily basis. Previous studies have found that corneal epithelial permeability is significantly affected by contact lens wear.[18,19,59] Although corneal epithelial permeability increases linearly with lens-induced hypoxic dose,[18] sleeping while wearing contact lenses can significantly compromise corneal epithelial barrier function despite the level of oxygen transmissibility of a contact lens.[16] It is of interest to note that the degradation in corneal epithelial barrier function after overnight contact lens wear observed with soft lenses exceeds that observed with rigid gas–permeable lenses.[16,18,19] The greater shear force on the ocular surface by Asian lids may result in increased lens–cornea interactions that lead to greater corneal epithelial trauma during contact lens wear.[14,18,24,27,46,60] This apparent difference between Asian and non-Asian corneas in their response to contact lens wear agrees with other reports that lens-induced epithelial trauma, evidenced by the presence of superficial punctate keratitis, is more common in Asian than non-Asian eyes.[6,61]

Tear Film

The tear film is the first line of defense protecting human eyes from environmental effects. It also provides nutrients and enzymes to maintain ocular surface health. Little is known about the naturally occurring variabilities of tear film stability, composition, and biophysical properties. The tear lipid film is the outermost layer of the tear film and provides timely and adequate responses to environmental challenges. Therefore, a disruption or malfunction of the tear lipid film can lead to a serious failure in tear film stability.[62,63]

Studies have shown that Asians have less stable tear films compared with non-Asians.[64,65] Despite similar lipid film thicknesses, healthy Asian subjects have a 11% to 24% shorter tear film breakup time than non-Asians.[64,66,67] Although no single component can be attributed to contact lens discomfort, a rapid tear breakup time was found to be the most consistent finding.[7] This suggests that even healthy Asian subjects may experience more discomfort with contact lens wear than non-Asians. There is indirect evidence that the compositions of human tear lipids diverge between people of different ethnicities.[62,68] In a study conducted by a research group in Australia,[68] it was found that human tear lipids contain 12%±7% polar lipids, such as phospholipids and sphingolipids, and 4.4%±0.6% of hydroxyl fatty acids. These components were not found in meibum collected from the same individuals. Lam et al.[69] found that tear lipids collected using Schirmer strips were composed of 6 to 8 molar percent polar phospholipids. The fact that most of this study cohort was Chinese might be the reason why there is 5 molar percent less polar lipids identified in this study when compared with the results reported by the Australian researchers.[68]

The biophysical properties of tear lipids, such as dynamic interfacial behavior, elasticity, and viscosity, are crucial factors controlling tear film stability.[54,62,70,71] These properties are likely to be closely linked and strongly dependent on tear lipid composition. Evidence for dissimilarities in the biophysical properties between Asian and white tear lipid film emerged during investigations of the dynamic properties of the human tear lipid film.[62] Figure 4 shows an example of dynamic surface pressure as a function of tear lipid film thickness for 2 samples: one from an Asian subject and another from a white subject. These curves are similar at low surface pressures, but at pressures above 30 mN/m, the curves diverge drastically. Caucasian tear lipid films exhibit steeper slopes in both compression (upper) and expansion (lower) branches. When compressed, the tear lipid film reaches maximum surface pressure of 50 mN/m, corresponding to a maximum film stability at thicknesses of approximately 50 nm. Asian tear lipid film has to be compressed to a greater thickness (i.e., ~70 nm in this case) to reach the same maximum surface pressure and film-stability region. These differences were explained by the interfacial rheology of these tear lipid films. It was found that, on average, Asian lipids have significantly lower elasticity modulus, higher interfacial viscosity, and longer relaxation time compared with white tear lipid films.[62] Further investigation is warranted to understand how or if these differences in biophysical and biochemical properties of the tear film relate to the variations in adverse events during contact lens wear, as mentioned in the previous section.

Our unpublished data[72] have demonstrated that, with the exception of interleukin 8 (IL-8) and IL-13, Asians exhibited lower concentrations of tear cytokines compared with non-Asians. Significant ethnicity-related differences were found for interferon γ, IL-1α, IL-6, IL-10, IL-12p(70), and IL-17 in Asian tears compared with those of non-Asians.[72] The impact of these differences must be considered in ethnically diverse studies that use tear cytokine levels as a quantitative measure of inflammation during disease. Further studies are warranted to understand how these inherent ethnicity-related differences in baseline tears can contribute to balancing cytokines toward an anti-inflammatory role in inflammatory situations (e.g., contact lens wear).

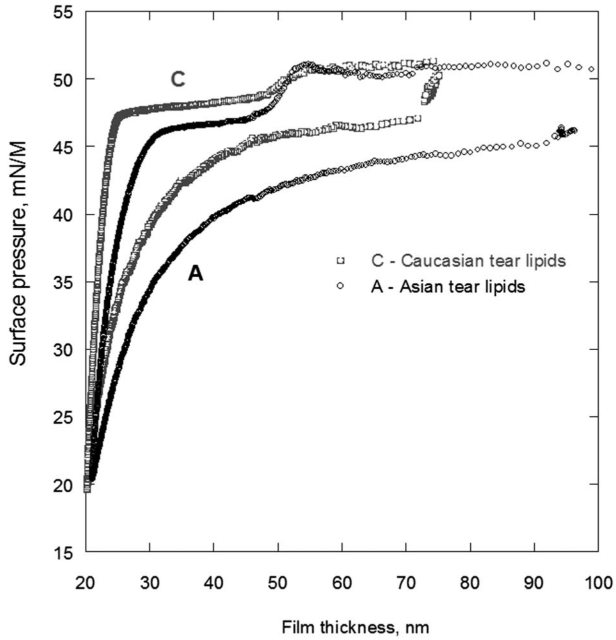

FIG. 4. Dynamic interfacial pressure as a function of tear lipid film thickness. A, Asian tear lipids; C, white tear lipids.

Sufficient production of tear aqueous is also important to maintain tear film stability. Unfortunately, there is little ethnicity-related information on this topic except for one study, which showed that with the phenol red thread test, Asian eyes produced significantly less wetting than white eyes in all age groups.[73] However, the variation found in this study could not be linked to either a decreased aqueous production or anatomic differences in the conjunctival sac or lid margin. Further studies are needed to determine if differences in aqueous production exist among ethnic groups because it can significantly impact tear film stability, ocular surface health, and ultimately the success of contact lens wear.

Tear–aqueous osmolarity is mostly proportional to the concentration of inorganic salts in tears and is relatively uniform, as measured by commercially available technology used in a clinical setting, across different ethnic populations.[64] However, current clinical techniques for measuring tear osmolarity have limitations. A major drawback of osmolarity measurement exists because of the location of tear sample collection from the inferior tear lake. In a healthy eye, there is a prominent presence of the black line that isolates the perched tear film from the upper and lower menisci.[74] During osmolarity measurements, a diluted tear lake due to reflex tearing in the prolong interblink period makes the measured value taken from the inferior meniscus lower in salt content compared with that of the perched film, resulting in lower-than-expected sensitivity and specificity of the instrument. In contrast, in patients with dry eye symptoms, the black line may be obscured because of conjunctival chalasis, resulting in a continuous film without separation between the central film and the inferior meniscus. For this reason, an osmolarity measurement taken from inferior meniscus in cases of conjunctival chalasis shows a higher salt content, leading to improved sensitivity and specificity of the measuring device.[75] Another possible reason for a higher salt content measured in cases of conjunctival chalasis is poor tear mixing, in the presence of redundant conjunctival tissues, which leads to an accumulation of salts in the inferior meniscus. More in-depth study of how a contact lens affects prelens tear film distribution and mixing can further our understanding of the impact of osmolarity on the ocular surface during contact lens wear, while being mindful about the limitation of tear osmolarity measurement location with today's commercially available technology.

SYMPTOMATOLOGY: DRYNESS, AND DISCOMFORT WITH CONTACT LENS WEAR

Despite constant advances in contact lens design and manufacturing, discontinuation of contact lens wear continues to be a challenge for practitioners. Prior studies have cited discomfort and dryness as the primary causes for patients to discontinue lens wear[76] despite the introduction of silicone hydrogel and daily disposable contact lens modalities.[3] Discomfort is a broad term used to include several sensations, such as dryness or lens awareness, and thus it is difficult to define. Even so, researchers have been able to tease out differences in both objective findings and subjective reports of discomfort between different ethnic groups.

Dryness without contact lens wear is prevalent worldwide. Studies conducted in China and Japan reported a much higher prevalence of dry eye syndrome (DES) than in previous reports,[12,13] suggesting that Asians may be more predisposed to DES than non-Asians.[11] In addition, Hispanic and Asian women in the United States were more likely to report severe dry eye symptoms when compared with white women.[77] Another research group came to a similar conclusion for Asian subjects. Their results showed that Asians demonstrated shorter NITBUT and fluorescein tear breakup times, which were correlated clinically with more severe dry eye symptoms and signs.[64] Since Asians experience more severe dryness even without contact lens wear, it is not surprising that they also experience more dryness with lens wear.[5,6]

Dryness is also a common complication after laser in situ keratomileusis (LASIK), a commonly performed surgical procedure to correct refractive error.[78] The trauma to the corneal surface from this procedure results in myopic or hyperopic correction, but also presents an increased risk for dry eye.[79,80] There is little evidence comparing LASIK outcomes for different ethnic groups, but one study observed an increased risk of chronic dry eye in Asians post-LASIK.[80] Both before and after the procedure, Asians exhibited greater ocular surface staining, poorer tear film stability, and lower tear film volume. Asians also reported a higher severity of dryness symptoms and a slower return to preoperative values for ocular surface staining, tear volume, and corneal sensation than non-Asians. Again, the differences in response to trauma between Asian eyes and non-Asian eyes are similar to the differences in response to contact lens wear.

One of the challenges contact lens wear presents to clinicians is the frequent disagreement between clinical signs and symptoms. Corneal staining is a perfect example. Conflicting results about the relationship between corneal staining observed in contact lens wearers and their corresponding symptoms have been examined by many investigators.[5,6] A large database study[6] identified years of contact lens wear and ethnicity as two significant confounders of this relationship between corneal staining and dryness. From this study, we learned that Asians experience more severe dryness symptoms and more severe corneal staining compared with non-Asians. In non-Asian eyes, dryness is associated with years of contact lens wear and the presence of corneal staining. In contrast, no relationship was found among dryness, years of contact lens wear, or corneal staining for Asians. One possible explanation for these differences is that Asian eyes may have an inherently lower corneal sensitivity compared with non-Asians. Little information is available regarding the effects of ethnicity on corneal sensitivity. Millodot found that subjects with blue irides exhibited significantly more sensitive corneas than subjects with brown irides, and that sensitivity is lower in nonwhite subjects with darker pigmented eyes compared with whites with darker pigmented eyes.[81–83] In a more recent study comparing LASIK-induced dry eye symptoms between Asians and Caucasians, corneal sensation at 3 and 6 months post-LASIK decreased more in Asians compared with whites.[80] If Asians have innately lower corneal sensitivity, then why do Asians report more dryness and discomfort during contact lens wear? Much research is needed to extend our knowledge of the functions and roles of corneal sensory receptors in normal and compromised ocular surfaces, especially for cases of post-LASIK and contact lens wear.

Furthermore, it is also important to note that even after accounting for known confounders, we must recognize that symptomatology is a multifaceted outcome. Cognitive modulation of dryness or discomfort is most likely perceived through complex and dynamic interactions among biological, psychological, and sociocultural processes.[84,85] Therefore, it is challenging to correctly interpret this individualized outcome variable. A recent study shows that factors such as ethnicity (i.e., Asians having greater pain sensitivity) and immigration status (i.e., immigrants having greater pain sensitivity) could affect how ocular discomfort is perceived and/or reported to clinicians or on medical questionniares.[86–88] Individual pain sensitivity provides a clinically relevant insight into the perception of symptoms of ocular dryness and discomfort.[85] Future work should include examining the relationship between signs and symptoms in subjects with a wide range of pain sensitivities.

FUTURE CONSIDERATIONS

Performance of a contact lens is intimately related to how it interacts with every component of the ocular surface, including the eyelids, tear film, cornea, and conjunctiva. There is not a lot of ethnicity-related information for the ocular surface. However, there seems to be sufficient evidence in the literature supporting the hypothesis that tear lipid biochemical properties are significantly different between ethnic groups.[62] These physical and chemical dissimilarities may be a significant culprit in the susceptibility of Asians to adverse events and/or symptoms of discomfort with lens materials and certain lens care solutions.[4] Thus, additional research is needed to elucidate the ethnicity-related differences in healthy human tear lipid compositions and biophysical properties to identify which biochemical alterations provoke discomfort and dry eye symptoms in general, and more specifically among contact lens wearers.

Variations in the mechanical lens–cornea interaction and physical fit of a contact lens are because of the obvious differences in ocular anatomy between Asians and non-Asians. Although an "acceptable" fit has a wide range of variability, an optimal lens for an Asian eye should have a smaller diameter and flatter BCR than would a lens for a white eye.[37] A better understanding of these ethnicity-based variations would help contact lens manufacturers and practitioners achieve personalized, targeted lens fitting for patients based on enhanced knowledge of their individual characteristics, and the impact of those characteristics on discomfort in contact lens wear.

However, a far more challenging aim is to develop a comprehensive understanding of the ethnicity-linked variability of human tears. It is possible that not only are the physical "mechanics" of lens fittings driving the disparities in ocular response to contact lenses, but also the intricate interplay of chemical interactions between tear film components and lens surfaces may be a far more important aspect of an "ideal fit." Detailed knowledge of tear component interactions with lens surface materials and lens care solutions as well as how these interactions differ for prelens and postlens tear films are all crucial for successful contact lens wear and comfort. Therefore, it is necessary for the contact lens industry to account for ethnicity-related factors and how they influence ocular surface health. If not, to improve moisture, wetting, lubrication, and comfort through changes in lens storage and lens care solutions, new artificial synthetic additives may continue to be introduced that could compromise ocular surface health and related comfort with contact lens wear.

Another area in which we are severely lacking in understanding involves ethnicity-related differences in the corneal sensory system and the mechanisms by which these differences lead to variability in tear aqueous production among ethnic groups, with or without contact lenses. More research is also needed to further our understanding of the interplay between corneal nerve density and sensitivity as well as the interplay between corneal sensitivity and subjective ratings of comfort. To understand the latter relationship, it would be prudent to elucidate how sociocultural, psychological, socioeconomic, questionnaire designs, and linguistics, both independently and collectively, contribute to the differences in subjective ratings between Asian and non-Asian subjects.

Furthermore, contact lens discomfort is a poorly defined term that may be influenced by many of the already discussed factors. It is imperative to better define contact lens discomfort to provide a more complete and universal understanding of its etiology. The key aspect to defining contact lens discomfort is the accurate differentiation between cases of lens-induced discomfort and cases of discomfort because of preexisting ocular surface diseases (e.g., meibomian gland dysfunction, blepharitis). In many cases, discomfort is dramatically alleviated or disappears completely after contact lens removal. These cases should be defined as true "contact lens-induced" discomfort. However, there are cases of contact lens discomfort that are not simply lens induced, but the presence of the lens in the eye pushes an already vulnerable tear film or ocular surface toward the threshold of discomfort.[89]

CONCLUSION

There are many inherent differences among patients that medical practitioners must often factor into their diagnoses, management, and treatments. Often, patients will compensate for these differences with learned behavior in a variety of environmental conditions, such as with stressful ocular environments during contact lens wear. Nevertheless, by using a human model that is ethnically diverse in study cohorts, we can more reliably assess the safety and efficacy of ophthalmic interventions. As there is a notable shift today toward more personalized medicine and targeted therapies, it is critical to understand inherent differences of ocular surface health among different ethnic groups. This approach is essential to greater success of contact lens wear and ophthalmic treatments, including therapies for dry eye disease, refractive surgeries, and effective penetration of topical ophthalmic drops into ocular surface tissues.

There are more questions than answers generated by this review. The intention is *not* to stereotype certain groups of people. Instead, the information is provided to inspire clinicians and researchers to recognize innate group differences in ocular surface integrity and understand how these differences interact with medical interventions, such as contact lens wear. Additionally, this review is meant to encourage researchers and industry sponsors to include ethnically diverse cohorts and incorporate detailed demographic information when publishing results from clinical trials. In doing so, the generalizability of the study results can be fairly assessed.

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