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Contact Lens Care Solutions: A Pilot Study of Ethnic Differences in Clinical Signs and Symptoms

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Abstract

Objectives—To determine whether Asian and Caucasian subjects differ in clinical signs or subjective symptoms in response to use of different biguanide-preserved contact lens care solutions.

Methods—Forty-two subjects (15 Asian, 27 Caucasian) wearing lotrafilcon B silicone hydrogel contact lenses used a preservative-free lens care solution (Clear Care®, CIBA VISION, Atlanta, GA, USA) bilaterally for 2 weeks, then used 2 biguanide-preserved solutions (Solution 1: ReNu MPS®, Bausch & Lomb, Rochester, NY, USA; Solution 2: AQuify MPS®, CIBA VISION, Atlanta, GA, USA) contralaterally in randomly assigned eyes for 4 weeks. Comprehensive ocular surface exams were performed and symptomatology questionnaires were administered every 2 weeks. Investigators were masked as to solution assignment during examinations, while subjects were not in order to avoid potential difficulties in compliance with the protocol.

Results—With Solution 1, the majority of both Asian and Caucasian subjects had grade 2 or greater corneal staining after 2 weeks (67% and 59%, respectively) and 4 weeks (60% and 67%, respectively). With Solution 2, grade 2 or greater corneal staining occurred in 40% of Asians after 2 weeks and in 13% after 4 weeks, but in only 4% of Caucasians after 2 weeks and 0% after 4 weeks. Caucasians reported significantly better average comfort ($p = 0.046$) and less dryness ($p < 0.001$) than did Asians.

Conclusions—Asians and Caucasians differ in both ocular response to use of contact lens care solutions and in reporting of subjective symptoms. Racial and ethnic differences should be considered when evaluating and treating contact lens patients in a clinical setting.

Keywords

lens care solutions; soft contact lenses; corneal staining; ethnicity; conjunctival staining; race

There are a number of anatomical and physiological differences between Asian and Caucasian eyes. Anatomical characteristics specific to the Asian eye include an oblique angle of the palpebral fissure, a smaller vertical palpebral aperture, a smaller horizontal visible iris diameter, a flatter cornea and greater corneal toricity.^{1–4} Asian eyelids have greater herniation of the orbital fat in the upper and lower eyelids, combined with a narrower

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palpebral aperture, possibly resulting in higher lid tension.⁵⁻⁷ The physiology of the Asian eye differs from that of the Caucasian eye in having a shorter tear breakup time, smaller tear meniscus volume, and reduced pre-corneal tear film stability.^{8,9} (Yeh TN, Tran N, Graham AD, Green HM, Lin MC. Relationships among tear film stability, tear osmolarity, corneal staining history, and dryness symptoms. Invest Ophthalmol Vis Sci. 2013;54. ARVO E-Abstract 4332.)

Adverse responses to contact lens wear have been documented more frequently in Asian eyes than in Caucasian eyes. In controlled experimental settings, Hamano, et al. reported a higher incidence of endothelial bleb formation under hypoxic conditions in Asians compared to Caucasians and African Americans.¹⁰ Other studies have shown that Asians are more susceptible to micro-trauma during rigid gas-permeable contact lens extended wear, as well as after eight hours of closed-eye soft contact lens wear.^{4,11} In a clinical setting, Asian eyes exhibit a higher incidence of observable biomicroscopic signs, including limbal and conjunctival injection, corneal and conjunctival staining, and neovascularization.^{12,13} (Sanders TL, French HM, Yeh TN, Tran N, Green HM, Graham AD, Lin MC. Effects of irrigation on adverse events during continuous contact lens wear. 2010. AAO E-Abstract 105123.)

In recent years, researchers have focused on the relationship between solution toxicity and adverse ocular events during lens wear.¹⁴⁻¹⁹ Carnt, et al. found that eyes with solution-related staining are three times more likely to experience a corneal infiltrative event, suggesting that solution-related corneal staining could be a potential risk factor for developing low-level corneal inflammation. Although solution-related corneal staining has been well documented, the type of corneal staining reported has been mostly diffuse, superficial, and micropunctate in presentation, which is generally transient and asymptomatic. Lebow, et al. found that differences exist between different MPS with respect to the type, extent, and depth of solution-related corneal staining; however, the severity of staining, on average, was considered clinically insignificant.

Although several authors have examined the ocular response of the Asian eye to contact lens wear, none to date has studied racial differences in the ocular response to the use of lens care solutions. Of particular interest in the present study is the *moderate-to-severe* level of corneal staining that would prompt practitioners to recommend discontinuation of lens wear and possibly to implement clinical treatment. The degree to which this level of corneal staining occurs in response to contact lens solution toxicity has not been fully documented, nor is it known whether such solution-related staining is more common in Asian eyes. In addition, there have been differing reports of the relationships between lens care solutions and biomicroscopic signs other than corneal staining, depending on the type of solution investigated.^{14,20-22} Finally, racial differences in symptoms of discomfort or dryness are known to exist,²³⁻²⁵ but have not been investigated with respect to the use of lens care solutions. In the present study, we address these questions by examining the Asian and Caucasian ocular surface response and subject symptomatology with two biguanide-preserved contact lens care solutions used with daily silicone hydrogel contact lens wear.

MATERIALS AND METHODS

Study Protocol

In this study, the first 2 weeks served as a washout period during which all subjects used a preservative-free, hydrogen peroxide-based solution (Clear Care®, CIBA VISION, Atlanta, GA, USA) with lotrafilcon B contact lenses. At the 2-week follow-up visit, the subject surrendered the first pair of lenses and preservative-free solution, and was dispensed a fresh pair of lenses along with two preserved lens care products (Solution 1: ReNu MPS®, Bausch & Lomb, Rochester, NY, USA; Solution 2: AQuify MPS®, CIBA VISION, Atlanta, GA, USA) to be used contralaterally in randomly assigned eyes for 4 weeks. Solutions were assigned to eyes according to a pre-determined block randomization scheme. The two solutions are known to contain the same type and concentration of polyhexamethylenbiguanide (PHMB) preservative, but differ with respect to several other components, including buffering, viscosity, isotonicity, chelating and surface-active agents. Subjects were instructed to pre-rinse and not to rub lenses with either MPS. Subjects were questioned at each visit to ensure that lenses had been inserted 2 to 4 hours prior to the examination, the peak period for detection of any solution-induced corneal staining that may have occurred.¹⁷

After receiving Solution 1 (ReNu MPS) and Solution 2 (AQuify MPS), subjects returned for follow-up examinations at 2 and 4 weeks. At each visit, subjects were evaluated for proper contact lens fit, underwent biomicroscopic examinations, and completed a set of questionnaires. A lens fit and performance evaluation was conducted to ensure a good fitting relationship to the ocular surface and good subject comfort according to standard clinical guidelines. The evaluation included measurements of lens centration, post-blink lens movement, primary and upgaze lag, push-up test tightness, and grading of lens surface wettability and deposits. The lenses were then removed for slit lamp examination of the ocular surface, which included the use of sodium fluorescein dye observed under cobalt blue illumination with a Wratten #12 yellow filter. The primary objective outcomes included corneal and conjunctival staining, blepharitis, limbal, bulbar and palpebral hyperemia, infiltrates, Meibomian gland dysfunction, tarsal abnormalities (e.g., tarsal roughness, papillary conjunctivitis), neovascularization, microcysts, mucin balls, striae and anterior chamber reaction. Clinical outcomes were graded by a single experienced clinician (MCL) on a scale of 0 (none) to 4 (severe) according to the Efron N grading scales.²⁶

In addition to the clinical grading of lens performance and slit lamp findings, subjects completed a variety of questionnaires. Subjects expressed their level of agreement with a number of statements about their lens wearing experiences on a 5-point Likert scale (1 = Fully Disagree, 5 = Fully Agree). Items included clarity of vision, comfort on insertion, during the day and at end of day, dryness overall and at end of day, burning, itching, redness, lens awareness, satisfaction overall and specific to comfort, and ease of handling. Subjects also rated the performance of lenses and solutions for each of these items on a 10-point rating scale (1 = Poor, 10 = Excellent). Subjects indicated their preferences for Solution 1 or Solution 2 for overall comfort, end of day comfort, vision and handling, and were given the choice to indicate “No Preference”. Subjects were asked additional 5-point

Likert scale questions upon exit from the study covering the performance of the lenses for feelings of cleanliness and moistness.

Subjects 18 years of age and older requiring spherical distance correction between -1.00 and -6.00D with less than 1D of astigmatism were eligible to participate. Subjects with ocular abnormalities or disease, systemic conditions with ocular manifestations, a history of allergies, taking medications that could affect the ocular surface or tear film, or with ocular signs or symptoms likely to interfere with successful contact lens wear were excluded. Subjects selfreported ethnicity as being Asian or Caucasian. Subjects of Chinese, Japanese, Korean, or Vietnamese descent were eligible for the Asian sub-group. Subjects of mixed-race parentage were not eligible for this study.^{27,28} All subjects provided informed consent after a review of the study procedures, goals, risks, and benefits. Subjects were paid for their time participating in the study. This study adhered to the tenets of the Declaration of Helsinki and was approved by the University of California, Berkeley institutional review board (Committee for the Protection of Human Subjects). Data collection was completed in August, 2005.

Statistical Methods

After a thorough exploratory analysis, we employed a mixed effects modeling approach to account for possible correlations between eyes within subjects while estimating the effects on our main objective and subjective outcomes of solution type (Solution 1 vs. Solution 2), race, visit, and their interactions, along with a number of covariates including age, gender, corneal curvature measured by keratometry, hours per day of wear, and contact lens power. Models were compared by examining residual and other diagnostic plots, considering F-test p-values, and assessing whether estimated effect sizes were clinically meaningful. Nested models were compared by log-Likelihood and non-nested models by Akaike's Information Criterion. We also employed logistic regression analysis to estimate the odds of grade 2 or greater (G2+) slit lamp findings as a function of lens care solution (Solution 1 vs. Solution 2), race, and visit. With these two types of models, we were able to test hypotheses about clinical grades of corneal staining, and about the presence/absence of clinically significant staining (i.e., requiring discontinuation of lens wear). A test of proportions using Pearson's χ^2 statistic was employed to test the equality of the proportions of Asian and Caucasian subjects expressing a final exit preference for Solution 1 vs. Solution 2, among subjects expressing a preference.

RESULTS

A total of 20 Asian and 29 Caucasian subjects responded to recruiting efforts and were screened for eligibility. Subject ages ranged from 18 to 57 years (mean [SD]: 23.5 [6.3]), and were 76.2% female (32/42), 23.8% male (10/42). Of the Asian subjects, 4 presented with excessive cylinder and 1 with superficial punctate keratitis. Of the Caucasian subjects, 1 was a high myope outside the acceptable range defined for the study, and 1 was taking proscribed prescription medication. The 15 Asian and 27 Caucasian subjects who qualified all completed the study.²⁹ The Asian and Caucasian sub-groups did not differ significantly in terms of age (t-test $p = 0.099$) or gender (Fisher's exact test $p = 0.277$).

Clinical Signs

After using the preservative-free solution for 2 weeks, the grade of corneal staining significantly increased with the use of both biguanide-preserved solutions ($p < 0.001$). Grade of corneal staining was significantly greater overall among Asians ($p < 0.001$), with the difference between Solutions 1 and 2 being greater for Caucasians ($p < 0.001$). Higher corneal staining grade was also associated with flatter corneal curvature ($p = 0.019$). The proportion of eyes with G2+ corneal staining at entry into the study with their habitual lens care solutions was greater among Asian subjects (11/30, 37%) compared to Caucasian subjects (10/54, 19%). However, after the 2-week washout period during which all subjects used the same preservative-free lens care solution bilaterally, the proportion of eyes with G2+ corneal staining dropped in both the Asian (4/30, 13%) and Caucasian (6/54, 11%) groups, which were not significantly different ($p=0.558$). While using the preserved Solution 2, the proportion of Asian subjects with G2+ corneal staining initially increased to 40% (6/15) then decreased to baseline levels (2/15, 13%) after 4 weeks (Figure 1). There was 1 Caucasian subject having G2+ staining (4%) after 2 weeks with Solution 2, and none after 4 weeks. In contrast, nearly two thirds of both Asian (10/15, 67%) and Caucasian (16/27, 59%) subjects experienced G2+ corneal staining with Solution 1 after 2 weeks. The proportions remained high after 4 weeks for both the Asian (9/15, 60%) and Caucasian (18/27, 67%) groups. The odds ratio (OR) for having G2+ corneal staining was significantly greater for Solution 1 (OR = 4.79) and was lower overall for Caucasians (OR = 0.05), although the difference between solutions was much greater for Caucasians (OR = 19.1). Table 1 shows the logistic regression model fit, OR estimates and approximate 95% confidence intervals for the odds of having G2+ corneal staining.

Because the Asian subject group had a much higher proportion of clinically significant staining before the washout period than did the Caucasian group, and returned to a similar baseline level after 2 weeks with the unpreserved solution, it raised the possibility that differences in habitual solution use could confound the relationship between ethnicity and corneal staining after use of the study solutions. We therefore performed a post-hoc analysis, and found that past habitual use of study solutions was not a significant confounder.

Tarsal abnormality grades increased significantly over the 4-week wearing period ($p = 0.047$), and Caucasians had significantly higher grades of tarsal abnormalities than did Asians ($p < 0.001$). Greater tarsal abnormality grades were also associated with steeper corneal curvature ($p < 0.001$). There was no significant difference between the two study solutions. Nearly identical results were found when either vertical or horizontal keratometry was used as the measure of corneal curvature. Caucasians had a significantly greater risk (OR = 7.28) for G2+ tarsal abnormalities (Figure 2), and the risk increased from 2 weeks to 4 weeks of wear (OR = 2.22). Table 2 shows the logistic regression model fit, OR estimates, and approximate 95% confidence intervals for the odds of having G2+ tarsal abnormalities.

All subjects experienced some hyperemia during the course of the study. There was some suggestion that grade of bulbar redness was related to weeks of wear, although not significantly so ($p = 0.070$); the risk of G2+ bulbar redness was significantly lower after 4 weeks of wear (OR [95% CI] = 0.025 [0.09, 0.70]), possibly reflecting some adaptation to the solutions. Bulbar redness was not related to solution type ($p = 0.729$) or to race ($p =$

0.601). The risk of G2+ limbal redness was lower for non-Asians (OR [95% CI] = 0.36 [0.15, 0.85]), although grade of limbal redness was not significantly different between racial groups ($p = 0.691$), between the two study solutions ($p = 0.850$) or across visits ($p = 0.351$). Caucasians had somewhat higher grades of palpebral redness, although not significantly so ($p = 0.088$), and there was no significant difference between solution types ($p = 0.325$). Grade of palpebral redness did not reduce significantly over 4 weeks of wear ($p = 0.157$), although there was a reduced risk of G2+ palpebral redness at 4 weeks (OR [95% CI] = 0.50 [0.26, 0.96]), again, possibly due to adaptation.

Grade of conjunctival staining was significantly lower for Caucasians than for Asians ($p < 0.001$), as was the risk of G2+ conjunctival staining (OR [95% CI] = 0.34 [0.17, 0.69]). There was no significant difference between the two study solutions ($p = 0.104$). Although the difference between visits was statistically significant ($p = 0.036$), the magnitude of the difference was clinically negligible (approximately 0.23 lower on the 0-4 grading scale). Grade of conjunctival staining was lower with more hours per day of wear ($p = 0.004$).

Grade of contact lens back surface debris was significantly greater for Caucasians than for Asians ($p = 0.009$), as was the risk of having G2+ back surface debris (OR [95% CI] = 2.42 [1.24, 4.74]). Grade of back surface debris increased during 4 weeks of wear ($p < 0.001$), and there was not a significant difference between races in the rate of increase ($p = 0.103$). There was no overall difference between solution types (Figure 3).

No statistically significant or clinically important relationships were observed between solution type, race or weeks of wear and grades of blepharitis, infiltrates, Meibomian gland dysfunction, neovascularization, microcysts, mucin balls, striae, anterior chamber reaction, contact lens front surface deposits, non-wetting areas, or haze.

Subjective Symptoms

When subjects were asked if their lenses and solutions provided good comfort on a 5-point Likert scale (1 = Fully Disagree, 5 = Fully Agree), Caucasians reported stronger agreement than Asians for comfort on insertion ($p = 0.033$), during the day ($p = 0.046$) and at the end of the day ($p = 0.065$). There were no significant differences between visits, or between the two study solutions during and at the end of the day. However, both Asians and Caucasians agreed more strongly that Solution 2 provided good comfort upon insertion compared with Solution 1, with Asians reporting a significantly bigger difference between solutions ($p = 0.015$). Steeper corneal curvature ($p = 0.006$) and stronger prescription sphere power ($p = 0.004$) were also associated with stronger agreement that lenses and lens care solutions provided good comfort on insertion.

On a 10-point rating scale (1 = Poor, 10 = Excellent), comfort with Solution 2 was rated significantly higher than with Solution 1 overall ($p = 0.025$) and on insertion ($p < 0.001$). Solution 2 was also rated higher than Solution 1 on average, but not significantly so, for comfort during the day ($p = 0.118$) and at the end of the day ($p = 0.230$). Higher comfort ratings on insertion and overall were significantly associated with steeper corneal curvature ($p = 0.007$ and $p = 0.011$, respectively), stronger sphere power ($p < 0.001$ for both overall

comfort and on insertion) and more hours per day of wear ($p = 0.047$ and $p = 0.017$, respectively).

Caucasians more strongly agreed than did Asians that their lenses and solutions gave them no sensation of dryness, both overall ($p < 0.001$) and at the end of the day ($p < 0.001$). Agreement was stronger both overall and the end of the day with steeper corneal curvature ($p = 0.053$ and $p = 0.008$, respectively), stronger sphere power ($p = 0.005$ and $p = 0.049$, respectively) and increased hours per day of wear ($p = 0.003$ and $p < 0.001$, respectively). Using the 10-point rating scale (Table 3), Caucasians rated their lenses and solutions higher (i.e., less dry) than Asians, both overall ($p = 0.005$) and at the end of the day ($p = 0.001$). Both overall and at the end of the day, increased sphere power ($p < 0.001$ and $p = 0.001$, respectively) and hours per day of wear ($p = 0.012$ and $p = 0.006$, respectively) were also associated with better dryness ratings. There were no significant differences between the two study solutions or across visits.

Regardless of whether data were collected on the 5-point Likert scale or the 10-point rating scale, no statistically significant or clinically important relationships were observed between solution type, race, or weeks of wear and overall quality of vision, burning, itching, redness, ease of handling, or awareness of the lens.

On exit from the study, subjects were asked to rate the performance of each of the two lens care systems. There was no significant difference between solution types in end-of-day comfort. Solution 1 was not rated as highly as Solution 2 for feelings of cleanliness ($p = 0.001$) or for keeping lenses moist ($p = 0.019$). Asians gave higher ratings than Caucasians for feelings of cleanliness ($p = 0.016$). Caucasians ($p = 0.039$) and females ($p = 0.007$) gave higher ratings how moist the lenses felt than did Asians and males, respectively. Ratings for end-of-day comfort, cleanliness, and moistness were higher among those with steeper corneas ($p = 0.010$, $p = 0.010$ and $p = 0.006$, respectively) and more hours per day of wear ($p < 0.001$, $p = 0.024$ and $p = 0.004$, respectively). On exit from the study, Asians gave higher overall satisfaction ratings than did Caucasians ($p = 0.058$), and the two racial groups differed significantly in how they rated satisfaction with each of the solutions ($p = 0.040$). While both racial groups rated Solution 1 (ReNu MPS) lowest in satisfaction, Asians gave Solution 2 (AQuify MPS) somewhat higher ratings followed by the ratings given the unpreserved solution at baseline (Clear Care), in comparison to Caucasians who rated the unpreserved baseline solution and Solution 2 roughly equal in satisfaction. Nearly identical results were found when either vertical or horizontal keratometry was used as the measure of corneal curvature.

Subjects also performed a direct preference comparison of the two study solutions upon exit from the study. A greater number of subjects who did express a preference chose Solution 2 over Solution 1 for overall comfort, end-of-day comfort, quality of vision, handling, as well as overall. After two weeks of wear, Solution 2 was significantly preferred overall by Caucasians ($p = 0.046$). In general, however, preferences were not statistically significant because subjects were permitted to select "No Preference", which many subjects did. Of note is that after 2 weeks of wear, there were no Asian subjects who preferred Solution 1 for end-of-day comfort, quality of vision, handling, or overall.

A graphical summary of the significant and clinically important relationships between race and the various objective and subjective outcomes is presented in Figure 5. The main racial and ethnic differences observed in this study were as follows: (1) both the mean grades of corneal and conjunctival staining, and the odds of G2+ corneal and conjunctival staining, were significantly greater among Asians; (2) both the mean grades of tarsal abnormalities and back surface debris, and the odds of G2+ tarsal abnormalities and back surface debris, were significantly greater among Caucasians; (3) Caucasians found the lenses and lens care solutions to be significantly more comfortable and less dry than did Asians; (4) Asians gave significantly higher overall satisfaction ratings on exit from the study, in spite of having more corneal and conjunctival staining and lower comfort and higher dryness ratings.

DISCUSSION

This pilot study is the first to provide evidence that Asians respond to lens care solutions differently than do Caucasians, both in terms of clinical signs and subjective responses. Greater proportions of both Asian and Caucasian eyes exhibited *moderate-to-severe* corneal staining related to the use of Solution 1 (ReNu MPS) as compared to Solution 2 (AQuify MPS) or the non-preserved baseline solution (Clear Care). These cases of G2+ staining in this study required temporary discontinuation of lens wear and follow-up until the condition resolved and lens wear resumed. The staining observed in this study was not mechanical in origin, but rather solution-related, and was generally diffuse rather than localized, typically macropunctate in presentation and in more severe cases coalesced, and often accompanied by symptoms. Although evidence linking solution-induced corneal staining and serious adverse events has been contradictory,³⁰⁻³² the presence and type of G2+ corneal staining is of significant concern to most clinicians and contraindicates continuing contact lens wear. Therefore, it is important to distinguish this type of staining from the recently reported asymptomatic “preservative-associated transient hyperfluorescence”.³³ The course of corneal staining with the two solutions over 4 weeks of use was different between the two racial groups, with Asians exhibiting elevated corneal staining levels compared to baseline with both Solutions 1 and 2 — albeit more so with Solution 1 — while Caucasians experienced elevated levels of staining only with Solution 1. It has been well established that the cytotoxic effects of lens care solutions depend on the combination of solution, contact lens material and fitting relationship. In this study all subjects wore the same lenses and all were fit according to established clinical standards. One study has suggested that Asian eyes are more prone to lens-induced epithelial trauma, resulting from excessive lens-corneal apical pressure created by smaller palpebral aperture and higher lid tension.⁴ In the presence of lower tear volume, poorer tear film stability, and reduced epithelial barrier function, the cytotoxic effects of lens care solutions combined with wear of certain lens materials could be exacerbated in Asian eyes. While this study was not designed to evaluate the clinical relevance of lens type, fit, and performance, these factors should be considered and further investigated in future studies.

In the current study, the incidence of moderate-to-severe corneal staining was lowest with the hydrogen peroxide-based, preservative-free solution (Clear Care), which was used in both eyes of all subjects during an initial 2-week washout period, in order to minimize any differences between subject groups due to their habitual lenses and lens care solutions.

Several authors have shown that preservatives in some MPS produce levels of cytotoxicity not found in preservative-free lens care solutions.^{14-20,34-36} Our results are in accord with other studies that have shown that a hydrogen peroxide-based lens care system induces the least amount of solution-related toxicity.^{14,18,37,38} We also found more clinically significant (i.e., grade 2 or greater) corneal staining with Solution 1 than with Solution 2. Jones, et al. have reported an increase in the severity of corneal staining with MPS containing higher concentrations of PHMB when used in combination with Group II lenses.¹⁵ In our study, Solutions 1 and 2 had identical concentrations of biguanide preservative, suggesting that other solution components may contribute to the difference in ocular response. It has been found *in vitro* that different buffering, isotonic, and surface-active agents exhibit different cytotoxic profiles in solutions preserved with identical concentrations of PHMB.³⁸ Recent studies have suggested that boric acid used as a buffer in biguanide-preserved MPS can cause significant disruption of the corneal epithelial tight junctions and can compromise epithelial barrier function.³⁹ Other studies have found that ethylenedinitrilo-tetraacetic acid (EDTA) disrupts normal epithelial cell function, exacerbates the cytotoxic effect of boric acid⁴⁰, and when used in higher concentrations, can cause clinically significant corneal staining.¹⁸ Possibly, concurrent use of boric acid and EDTA in Solution 1 resulted in the higher proportion of moderate-to-severe corneal staining observed in our study.

Chemical variations in the formulations of lens care systems can also affect lens absorption of biocides and their subsequent release onto the ocular surface, resulting in differing degrees of solution toxicity. Rosenthal, et al. previously reported that among various combinations of contact lenses and solutions, PHMB-preserved solutions used with group IV contact lenses resulted in the greatest amount of biocide absorption.⁴¹ They also demonstrated that corneal staining can be a marker of epithelial insult from abrupt exposure to high concentrations of biocides. Powell, et al. have shown that PHMB has higher absorption and slower release rates in ionic lenses as compared to non-ionic lenses.⁴² One proposed mechanism for differences between biocide uptake and release may relate to the lipid deposition capacity of a silicone-hydrogel lens surface. Several authors have suggested that increased levels of bound lipids could enhance the uptake of preservatives into the lens and affect the release rate.^{18,19,42}

It is interesting to note that with Solution 2 there was an increase in corneal staining from baseline to 2 weeks, and then a reduction in staining after 4 weeks. This recovery could reflect some type of physiological adaptation of the cornea to the prolonged presence of cytotoxic components in the solution. To our knowledge, there have been no direct studies to date on long-term adaptation of the cornea to MPS exposure, or suggestions for a possible mechanism. There has been some empirical evidence of corneal staining initially increasing and then recovering over time with certain lens-solution combinations,¹⁶ although other studies have found staining levels to remain relatively constant or to continue to increase with longer exposure.^{19,43} There is some evidence of recovery of the electrophysiological properties of the cornea exposed to toxic solutions over time from *in vitro* animal models.⁴⁴ This is an interesting topic requiring further study, in particular because of the clinical implications of corneal response to solution toxicity over long-term exposure.

The Caucasian group in the current study exhibited far more moderate-to-severe tarsal abnormalities with both Solutions 1 and 2 than did the Asian group, and the proportion of Caucasians with this level of tarsal abnormalities increased over 4 weeks of wear. In addition, Caucasians had significantly worse back surface debris on their lenses than did Asians. There have been conflicting reports as to whether solution type is associated with tarsal abnormalities^{19,20,22,45}; in the current study, we found no difference between Solutions 1 and 2 in terms of tarsal abnormalities. Most studies agree about the relationship between tarsal abnormalities and front surface deposits^{46,47}; in the current study we did not find a significant relationship between them, although this was due mainly to having relatively few subjects with anything more than mild deposits. We did find, however, in post-hoc analyses, that the grade of tarsal abnormality was significantly related to the grade of back surface debris, and that back surface debris was not correlated with front surface deposits. It is not clear from our data whether developing tarsal abnormalities resulted in discharge (e.g., mucus) that became trapped under the lens, or whether debris accumulating under the lens was the result of physiological processes (e.g., inflammatory reaction) that also resulted in tarsal abnormalities. Further study is needed to establish a causal sequence.

With a relatively small sample size, we were able to find clinically relevant and statistically significant differences in some clinical signs and subjective symptoms between Asians and Caucasians. A link between signs and symptoms has been found in some studies^{19,48} but not in others.⁴⁹ Although the current study was not designed to directly assess the impact of changes to the ocular surface on subjective response, there are some suggestions of such a relationship from these results. Asians exhibited more corneal and conjunctival staining overall than did Caucasians, and reported feeling less comfort and more dryness and gave lower ratings for feelings of lens moistness. Asians also exhibited increased corneal staining with both biguanide-preserved solutions, whereas corneal staining in Caucasians remained low with Solution 2 (AQuify MPS). This could be related to Asians rating both biguanide-preserved solutions significantly lower than the preservative-free baseline solution, whereas Caucasians rated Solution 2 similarly to the preservative-free solution and Solution 1 (ReNu MPS) lower. Asians did, however, report greater overall satisfaction and gave higher ratings for feelings of cleanliness, in spite of having worse comfort and dryness ratings and more corneal staining. This could be explained by cultural differences in compliance or in how subjects of different ethnicities respond to questionnaire instruments. It is also possible that the Asian group entered the study requiring stronger correction on average and were more under-corrected with their habitual lenses, and thus in spite of discomfort and corneal staining, had improved overall satisfaction with their visual experience in their new contact lenses. Although we did not collect data on subjects' habitual lenses and prescriptions, we did find that the Asian group required an average of 0.72 D stronger correction compared with the Caucasian group. Finally, there is some recent evidence that while Caucasians exhibit worse symptoms in the presence of corneal staining, Asians do not tend to exhibit a relationship between signs and symptoms,⁵⁰ and thus for the Asian group having more corneal staining may not have been an impediment to feeling greater overall satisfaction. These results highlight the need to conduct a large sample size investigation into the relationships between clinical signs and subjective symptoms in different ethnic groups, in order for clinicians to better interpret symptomatology in prescribing care for their patients.

One potential limitation of the study is that although investigators were masked as to solution type, subjects were not. Because subjects used two different solutions contralaterally, it was felt that solution-specific packaging helped to minimize potentially serious compliance problems (e.g., using the wrong solution for each eye, or inadvertently switching solutions during the trial). Although this study was completed prior to the outbreaks of MPS-related fungal and acanthamoebic keratitis, it is possible that a bias could occur with subject unmasking, particularly if a substantial proportion of subjects were familiar with, and strongly liked or disliked, one of the care solutions prior to enrolling in the study. However, it was felt that the advantages of the contralateral study design in terms of direct subjective comparison of solutions (as opposed to comparing comfort in a bilateral, crossover study with a washout period in between solutions) outweighed the risks of unmasking. Subjects were asked not to reveal the care system assigned to each eye to the investigator during clinical assessments. As it turned out, the subjective results were largely in agreement with the unbiased objective assessments, thus increasing our confidence in their validity; however, we do acknowledge the potential limitations in drawing broad conclusions from the subjective results.

A second limitation of the study is related to the sample size. The original sample size was based on a comparison of corneal staining grade between the two biguanide solutions. The completed dataset also allowed us to retrospectively examine differences between ethnic groups. To determine if the sample size was adequate for this new comparison, we performed a post-hoc power analysis. We found that our sample size allowed us to detect differences in corneal staining grade between ethnic groups of approximately 0.6, or slightly over half a grade on the 0-4 scale, with 95% confidence and 80% power. A larger sample size would be required to detect smaller differences in mean grade of corneal staining.

The results presented here potentially provide further insights into the ocular response of Asian eyes to contact lenses and lens care systems. The ultimate success of contact lens wear can depend on contact lens solutions and their differential impact on the tear film and the ocular surface of different racial groups. Furthermore, ethnic and cultural differences exist in the reporting of subjective symptoms by patients. It is, therefore, critical for practitioners to be considerate of ethnicity when selecting a lens care system that will be least cytotoxic and provide the patient with the most satisfying and successful treatment for refractive error.

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Figure 1.

The proportion of subjects with grade 2 or greater (G2+) corneal staining was greater with Solution 1 (ReNu MPS) for both Asians and Caucasians. Asians experienced more G2+ corneal staining with both solutions, whereas Caucasians experienced elevated staining only with Solution 1.

Figure 2.

The proportion of subjects with grade 2 or greater tarsal abnormalities increased among Caucasians over 4 weeks of use with both solutions, whereas Asians did not experience increased tarsal abnormalities.

Figure 3. Grade of back surface debris was significantly greater overall for Caucasians, increased significantly over 4 weeks of wear, and did not differ significantly by solution type.

Figure 4. Comfort after lens insertion was rated significantly higher with Solution 2 (AQuify MPS).

Figure 5.

Significant racial differences were found in corneal and conjunctival staining, tarsal abnormalities, back surface debris, comfort, dryness, satisfaction, and lens performance ratings.

Table 1

Logistic regression model of the odds of grade 2+ corneal staining. An Odds Ratio (OR) < 1 represents increased risk for Solution 2 (AQuify MPS), Asian race and the 2-week visit, which are arbitrarily used as baselines, and an OR > 1 represents increased risk for Solution 1 (ReNu MPS), Caucasian race and the 4-week visit. ORs whose confidence intervals do not include 1 are considered significant. The significant interaction term reflects the fact that the difference between solutions in the proportion of Grade 2+ corneal staining is greater for Caucasians.

$\log(\text{OR}) = 0.046 + 1.567*\text{Solution} - 2.964*\text{Race} - 0.304*\text{Visit} + 2.948*\text{Solution}*\text{Race}$			
Model Parameter	Odds Ratio (OR)	95% CI for OR	
		Lower Bound	Upper Bound
Solution	4.79	1.59	14.42
Race	0.05	0.01	0.44
Visit	0.74	0.34	1.59
Solution*Race	19.07	1.85	196.29

Table 2

Logistic regression model of the odds of grade 2+ tarsal abnormalities. An OR < 1 represents increased risk for Solution 2 (AQuify MPS), Asian race and the 2-week visit, which are arbitrarily used as baselines, and an OR > 1 represents increased risk for Solution 1 (ReNu MPS), Caucasian race and the 4-week visit. ORs whose confidence intervals do not include 1 are considered significant.

$\log(\text{OR}) = -4.232 - 0.496 * \text{Solution} + 0.799 * \text{Visit} + 1.986 * \text{Solution2} * \text{Race} + 2.565 * \text{Solution1} * \text{Race}$			
Model Parameter	Odds Ratio (OR)	95% CI for OR	
		Lower Bound	Upper Bound
Solution	0.61	0.15	2.46
Visit	2.22	1.10	4.49
Solution2*Race	7.28	2.49	21.30
Solution1*Race	13.00	3.86	43.72

Table 3

Mean (SD) of overall dryness ratings stratified on solution and race. Ratings were given on a 10-point scale, with 1 = Poor (i.e., very dry) and 10 = Excellent (i.e., not at all dry). A preservative-free solution (Clear Care) was used bilaterally for 2 weeks. Solution 1 (ReNu MPS) and Solution 2 (AQuify MPS) were used contralaterally in randomly assigned eyes for 4 weeks.

Visit	Asian		Caucasian	
	Solution 0 [OD, OS]		Solution 0 [OD, OS]	
2wks Solution 0	7.8 (1.9)	7.9 (1.9)	8.6 (1.5)	8.6 (1.6)
2wks Study Solutions	Solution 2		Solution 2	
	7.9 (1.8)	8.0 (1.7)	8.6 (1.7)	8.3 (1.8)
4wks Study Solutions	8.2 (1.9)	8.0 (1.7)	8.8 (1.1)	8.4 (1.8)