Effect of tear osmolarity on repeatability of keratometry for cataract surgery planning

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PURPOSE: To evaluate the effects of tear osmolarity on the repeatability of keratometry (K) measurements in patients presenting for cataract surgery.

SETTING: Three clinical practices.

DESIGN: Observational prospective nonrandomized study.

METHODS: Subjects were prospectively recruited based on tear osmolarity (Tearlab Osmolarity System); that is, osmolarity more than 316 mOsm/L in at least 1 eye (hyperosmolar) and osmolarity less than 308 mOsm/L in both eyes (normal). The baseline K value was measured, and a second measurement was taken on the same instrument (IOLMaster) within 3 weeks of the first. Variability in average K, calculated corneal astigmatism using vector analysis, and intraocular lens (IOL) sphere power calculations were compared between groups.

RESULTS: The hyperosmolar group (50 subjects) had a statistically significantly higher variability in the average K reading ($P = .05$) than the normal group (25 subjects) and a statistically significantly higher percentage of eyes with a 1.0 diopter (D) or greater difference in the measured corneal astigmatism ($P = .02$). A statistically significantly higher percentage of eyes in the hyperosmolar group had an IOL power difference of more than 0.5 D ($P = .02$). No statistically significant differences were present when the subjects were grouped by self-reported dry eye.

CONCLUSIONS: Significantly more variability in average K and anterior corneal astigmatism was observed in the hyperosmolar group, with significant resultant differences in IOL power calculations. Variability was not significantly different when subjects were grouped by self-reported dry eye. Measurement of tear osmolarity at the time of cataract surgery planning can effectively identify patients with a higher likelihood of high unexpected refractive error resulting from inaccurate keratometry.

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Accurate intraocular lens (IOL) power calculations are essential to ensure good uncorrected vision after cataract surgery. This is especially important when patients select advanced-technology IOLs as an accurate refractive outcome is critical to patient satisfaction. A key component of all IOL power calculation formulas is the anterior corneal curvature, measured by keratometry. The average corneal curvature will be a factor in determining the appropriate sphere power, while the measured anterior corneal astigmatism will be a factor in planning for a toric IOL.

One of the most commonly used devices for measuring keratometry (K) values at the time of cataract surgery is the IOLMaster (Carl Zeiss Meditec AG), which is based on partial coherence interferometry (PCI). The device has a built-in, automated keratometer that measures 6 spots approximately 2.5 mm from the center of the anterior cornea.[1–3] Partial coherence interferometry provides precise, reliable K readings in normal eyes.[4] Another commonly used device is the manual keratometer, which measures the central 3.4 mm of the cornea based on 2 mires.[3]

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Like PCI, manual keratometry has good reliability and precision in normal eyes.[5,6] An unreliable K reading can affect the accuracy of IOL calculations and result in suboptimum refractive results after cataract surgery.[7–10] A 1.0 diopter (D) error in the measured corneal power results in approximately a 1.0 D error in the postoperative refraction.[11]

Ocular surface disease results in hyperosmolarity, which in turn contributes to an unstable tear film, the hallmark of dry-eye disease. Keratometric measurements are sensitive to a poor tear film because standard keratometers in current use rely on a good reflection of mires from the corneal surface. An unstable tear film reduces the quality of corneal reflections and therefore can compromise K readings.[7] With tear-film instability, the quality of the refractive surface is unpredictable, often changing dramatically between blinks. This instability affects methods of biometry that rely on reflected light to map the ocular surface. Furthermore, dry-eye disease is more prevalent with increased age, making tear-film instability a common concern in the cataract surgery population.[8,12]

Tear osmolarity testing using the Tearlab Osmolarity System (Tearlab Corp.) is an objective measurement to help diagnose dry eye. It has been shown to be sensitive,[13] specific,[14] objective,[15,16] and accurate,[17,18] with good repeatability,[19] although 1 study reported a poor correlation between osmolarity and classic measures of dry eye and suggested further research was warranted.[20] Tear osmolarity is less variable than corneal staining, conjunctival staining, and meibomian gland grading when evaluating dry eye.[21] A threshold value of 308 mOsm/L appears to be the most sensitive value,[15,22] whereas 315 mOsm/L appears to be the most specific value.[15] In addition, recent data showed that eye-to-eye and temporal differences in osmolarity increase linearly with increasing disease severity.[15,21,23] Tear osmolarity is an ideal candidate for identifying tear instability because heightened osmolarity plays a causal role in the damage,[24] desquamation, and destabilization of the ocular surface.[25] Early-stage morphologic changes leading to tear instability (eg, loss of microplicae and a compromised glycocalyx) might not be readily visible using traditional clinical methods such as surface staining or slitlamp examination. We hypothesize that it is of considerable value to identify patients with a damaged ocular surface and associated tear-film instability before cataract surgery to increase the confidence in the K measurements.

The present study evaluated the variability of measurements taken at 2 different times to determine whether tear hyperosmolarity could help to identify patients who were more likely to have inaccurate K readings at the time of cataract surgery.

SUBJECTS AND METHODS

Subjects at 3 sites who were presenting for cataract surgery and were willing to participate were recruited for the study. The study followed good clinical practice guidelines and was approved by an institutional review board (Alpha IRB, San Clemente, California, USA). All subjects provided written informed consent. The study involved no treatment.

Exclusion criteria included a history of cataract or refractive surgery and the presence of lid deformities or corneal scarring. Subjects were excluded who had recently altered their ocular medications (within 14 days) when such medications were associated with dry eye, if they had active ocular or nasal allergies or corneal or conjunctival infection, or if they were using ocular cyclosporine.

Tear osmolarity was measured at a baseline visit using the Tearlab Osmolarity System following the manufacturer's recommendations for testing. Osmolarity was measured at the start of each visit before other testing or the use of eyedrops to avoid influencing the tear-film osmolarity measurement. On the basis of these results, subjects were recruited in a 2:1 ratio for a hyperosmolar group (tear osmolarity $\geq$316 mOsm/L in at least 1 eye) or a normal group (tear osmolarity $\leq$308 mOsm/L in both eyes), respectively.

Subjects enrolled at the first visit had their tear osmolarity remeasured at a second visit that could take place any time within 3 weeks of the first, including on the same day as the first visit. The subject was considered to have tear-film hyperosmolarity if the tear osmolarity was more than 316 mOsm/L in either eye.

Eyes were measured for cataract surgery using the IOLMaster PCI device at the enrollment visit and a subsequent visit. Some K measurements were taken using a manual keratometer (Bausch & Lomb). For each measurement in each eye, the mean K reading and the keratometric astigmatism were calculated. The difference between the mean K readings at the 2 visits was calculated, as was the vector difference between the 2 keratometric astigmatism values. Using the available K and axial length data from each eye, the Holladay 1 formula[26] was used to calculate the IOL power for an emmetropic refraction. Subjects

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were also asked whether they subjectively experienced dryness in their eyes.

Data were recorded in an Excel spreadsheet, from which they were imported into an Access database for data checking, collation, and preliminary analysis (both Microsoft Corp.). Statistical analyses were performed using the Statistica data-analysis software (version 12, Statsoft, Inc.). Statistical testing was performed using analysis of variance for continuous variables and appropriate nonparametric testing (eg, Fisher exact test) for categorical variables. The categorization of osmolarity was by subject; therefore, a test was performed to look for statistical bias related to the evaluation of eyes rather than subjects in this study. A P value of 0.05 or lower was considered statistically significant.

RESULTS

Data were collated from the hyperosmolar group (100 eyes of 50 subjects) and the normal group (50 eyes of 25 subjects) measured at the 3 sites. Each eye was measured 2 different times. The data analysis was performed on 144 eyes (72 subjects) after data for 3 subjects were removed, 1 (both eyes) because keratometric angle data were not available and 2 because a different keratometric measurement device was used at each visit.

Table 1 shows the demographics by site. There were no statistically significant differences in sex, age, or percentage of eyes measured as hyperosmolar between the 3 sites. The data were pooled for subsequent analysis. The measurements were categorized by the 2 visits in which they were performed; that is, visit 1 and visit 2. Both measurements of 22% of eyes (32/144) were performed on the same day, as permitted by the study method. Table 2 shows the mean and standard deviation for the osmolarity and change by visit for the 2 different groups.

Although the osmolarity was categorized by subject, the data were analyzed by eye, which had the potential to bias results. The 2 measurements of primary interest in this study, the difference in average K and the difference in corneal astigmatism between visits, were tested for intereye correlation. There was no correlation between the differences in corneal astigmatism by eye ($P > .05$). A statistically significant correlation was found between the average K by eye, but the correlation was driven by 1 of the 72 subjects. When the correlation was tested without that 1 outlier, there was no statistically significant difference ($P > .05$). As such, the level of bias from using data from each eye was considered minimal.

Average Keratometry

The difference in the average K readings from the 2 visits was calculated. The measurement device (PCI or manual keratometer) had no effect on the results ($P = .62$). There was also no effect from whether the visits were the same day ($P = .39$). The mean difference in the average K was 0.13 D in the normal group and 0.28 D in the hyperosmolar group.

In the normal group, 38 (86%) of 44 eyes had a difference of 0.25 D or less and 6 (14%) had a difference of 0.50 D or less. In the hyperosmolar group, 78 (78%) of 100 eyes had a difference of 0.25 D or less, 14 (14%) had a difference of 0.50 D or less, and 8 (8%) had a difference of more than 0.5 D, with a maximum difference of 3.75 D. The 8 eyes in the group with the highest difference were of 6 subjects. A Fisher exact test indicated that the percentage of eyes with a difference more than 0.5 D was statistically significantly higher in the hyperosmolar group ($P = .049$). Figure 1 shows a plot of the absolute difference in average K between visits against the mean K measured, by group. The increased variability in the hyperosmolar eyes is evident.

In the normal group, the difference between the calculated IOL powers was 0.5 D or less for all eyes. Ten (10%) of 100 eyes 8 subjects in the hyperosmolar group had a calculated IOL power difference of more than 0.5 D, the highest difference being 5.5 D. The percentage of eyes with an IOL power difference of more than 0.5 D was statistically significantly higher in the hyperosmolar group than in the normal group ($P = .02$).

Keratometry Cylinder

The vector difference in the corneal astigmatism measured was compared between groups. Vector differences in the corneal astigmatism measured can be related to differences in the magnitude or

Table 1. Subject demographics by site.

Site	Subjects			Age (Years)	
	All (n)	Hyperosmolar (%)	Men (%)	Mean ± SD	Range
1	21	67	43	68.7 ± 9.1	49, 88
2	28	75	36	71.9 ± 9.9	50, 93
3	23	65	30	72.1 ± 6.1	59, 88

Table 2. Mean osmolarity by study visit.

Group	Mean Osmolarity (mOsm/L) ± SD		
	Visit 1	Visit 2	Change
Hyperosmolar	327.8 ± 10.5	319.3 ± 14.1	−8.4
Normal	301.1 ± 4.9	303.3 ± 7.0	2.1

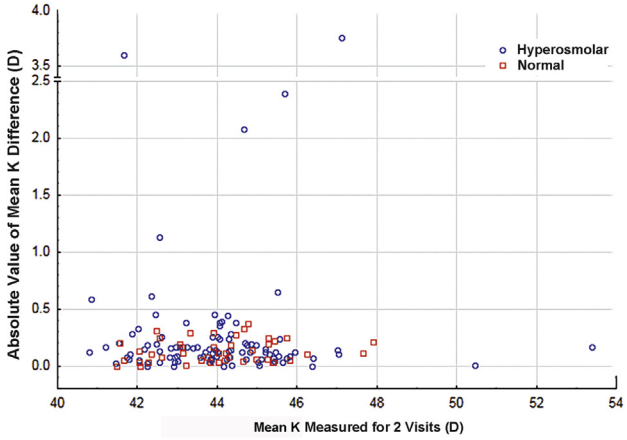

Figure 1. Absolute difference in mean K measured between visits.

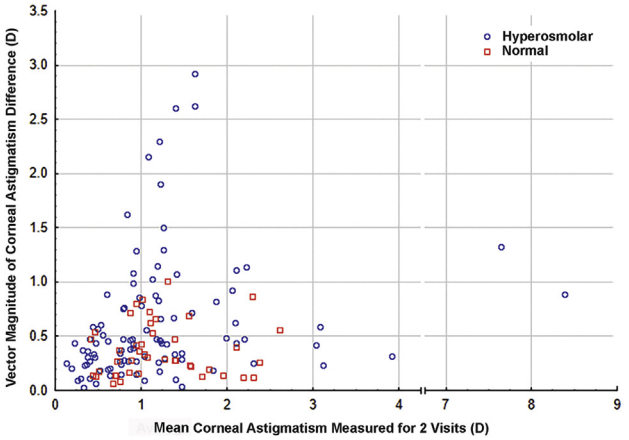

Figure 2. Vector magnitude of corneal astigmatism difference between visits.

the direction of the astigmatism, and the absolute magnitude of the corneal astigmatism measured affects which toric IOL can be implanted. To investigate the potential effect of differences in corneal astigmatism on IOL selection, the magnitude difference of the corneal astigmatism between visits was calculated. There was a statistically significant difference by group ($P = .02$), with the vector difference approximately 0.2 D higher on average in the hyperosmolar group. There was no statistically significant difference related to whether the visits were on the same day ($P = .21$). Figure 2 shows a plot of the absolute vector difference between visits by group, by the average corneal astigmatism measured. In the hyperosmolar group, 21 eyes (21%) in 19 subjects had an astigmatism magnitude difference of more than 0.5 D compared with 8 eyes (18%) in 8 subjects in the normal group; these ratios were not statistically significant ($P = .44$).

In the hyperosmolar group, 17 eyes (17%) of 15 subjects had a vector astigmatism difference more than 1.0 D, compared with only 1 eye (2%) in the normal group (actual value 1.01 D); this difference in percentages was statistically significant ($P = .01$). One eye in the normal group had an intereye osmolarity difference of 8 mOsm/L, which might be an early sign of dry-eye disease.

The difference in osmolarity values between eyes was also evaluated by group. The hyperosmolar group had a statistically significantly higher intereye difference than the normal group ($P < .01$). The intereye difference was 16.3 mOsm/L $\pm$ 12.2 (SD) (range 0 to 48 mOsm/L) in the hyperosmolar group and 4.8 $\pm$ 4.2 mOsm/L (range 1 to 19 mOsm/L) in the normal group. The intereye variability in the normal group was within the analytical variation of the osmolarity measurement system.

All subjects were also asked about symptoms of dry eye. The difference in the average K reading between visits was not statistically significantly different between subjects reporting dry-eye symptoms and those reporting no symptoms. ($P = .36$), nor was the difference in calculated IOL power ($P = .91$) or the vector difference in corneal astigmatism ($P = .06$).

DISCUSSION

In this study, statistically significantly more subjects with hyperosmolar tears showed poor repeatability of K values and thus poor repeatability of IOL power calculation than subjects with normal tear osmolarity. Keratometry testing that is repeatable and reliable is important to accurately calculate IOL power, especially when a toric IOL is being implanted.[9,10] Shammas and Chan,[1] who examined the accuracy of PCI, reported a median absolute difference of 0.14 D between K readings at 2 visits, which is consistent with the average absolute difference of 0.13 D in the normal group in the present study. Their median astigmatism difference was 0.2 D, which is similar to the results found here between the 2 groups, although they did not use vector math. Using optical biometry and standard IOL calculation formulas, they estimated that the relative contribution of keratometry to errors in IOL power calculation error was 20%.[1]

In a large dataset of cataract surgeries in Europe (>240 000 entries with follow-up data[27]), 91% of eyes were within $\pm$1.0 D of the intended target. In the present study, 10% of hyperosmolar eyes had an IOL power calculation difference of more than 0.5 D. It appears likely that hyperosmolarity is a significant contributing factor in refractive surprises in IOL power calculation.

Tear hyperosmolarity was associated with statistically significantly worse repeatability of K measurements in this study; however, patient self-reported dry eye was not. Patients presenting for cataract surgery do not generally verbalize any symptoms.[7] One theory is that the reduced sensitivity of the cornea from the damaging effects of keratoconjunctivitis sicca might be a contributing factor in the lack of symptoms,[28] despite advanced ocular surface signs.[23] This points to the need for objective testing for dry-eye disease at the time of cataract surgery. It might also be the reason a previous study[29] reported a poor correlation between osmolarity and patient self-assessment of dry eye.

One limitation of the present study is the lack of a treatment phase. Future research to evaluate the effects of treating hyperosmolar eyes is warranted to determine whether reducing the osmolarity of the eye also reduces the observed variability in K measurement. Another limitation is that alternative methods for diagnosing dry eye and/or tear-film stability (outside of patient self-reporting) were not evaluated. This aspect of the study was not comparative, but illustrated the potential value of measuring tear osmolarity in this patient group.

The high intereye difference (up to 48 mOsm/L) in the hyperosmolar group and the low intereye difference in the normal group in this study are consistent with the literature.[21,30-32] Other reports suggest that normal patients have low and stable osmolarity and with an intereye variability of 6.9 ± 5.9 mOsm/L,[31] whereas dry-eye patients have raised and variable measurements[21,30] and a between-eye difference of greater than 8 mOsm/L.[31,32] The subjects in the present study showed a similar pattern. As with the ability to objectively quantify osmolarity, the ability to measure these large intereye differences highlights the value of tear osmolarity as an indicator of ocular surface health and tear-film instability.

In conclusion, statistically significantly more variability in average K and anterior corneal astigmatism was observed in the hyperosmolar group, with statistically significant resultant differences in IOL power calculation. Variability was not statistically significantly different when subjects were grouped by self-reported dry eye. Measurement of tear osmolarity at the time of cataract surgery planning can effectively identify patients with a higher likelihood of refractive surprises from inaccurate keratometry. The results in this study suggest that the measurement of tear-film osmolarity at the time of cataract surgery and the treatment of dry eye before cataract surgery planning and IOL power calculation might improve the results of cataract surgery.

WHAT WAS KNOWN

- Dry eye affects keratometric measurements at the time of cataract surgery.
- Keratometry values are a significant factor in IOL power calculation.

WHAT THIS PAPER ADDS

- Objective measurement of tear osmolarity can identify patients at higher risk for a refractive surprise as a result of erroneous K readings.
- Tear osmolarity appears to provide more effective identification of such at-risk patients than self-reported dry eye.

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