Title
Effects of Eye Rubbing and Breath Holding on Corneal Biomechanical Properties and Intraocular Pressure

Journal
Cornea, 30(8)

ISSN
0277-3740

Authors
Liu, Wan-Cherng
Lee, Shui-Mei
Graham, Andrew D
et al.

Publication Date
2011-08-01

DOI
10.1097/ico.0b013e3182032b21

Peer reviewed

Effects of Eye Rubbing and Breath Holding on Corneal Biomechanical Properties and Intraocular Pressure

Wan-Cherng Liu, MD,† Shui-Mei Lee, MD,†‡ Andrew D. Graham, MA,§ and Meng C. Lin, OD, PhD, FAAO§¶*

Purpose: To determine whether corneal biomechanical properties and intraocular pressure (IOP) are affected by eye rubbing and breath holding.

Methods: Corneal hysteresis, corneal resistance factor, corneal compensated IOP (IOPcc), and Goldmann equivalent IOP (IOPg) were measured on both eyes of 40 subjects. Measurements were taken at baseline before eye rubbing (ER_0) and before breath holding (BH_0), immediately after 2 episodes of eye rubbing (ER_1 and ER_2), and during 2 episodes of breath holding (BH_1 and BH_2).

Results: Corneal hysteresis, corneal resistance factor, and IOPg were significantly lower after ER_1 compared with ER_0 and were significantly lower after ER_2 compared with ER_1. In contrast, IOPcc did not decrease significantly. There were no significant differences among BH_0, BH_1, and BH_2 in any of the 4 outcomes.

Conclusions: Eye rubbing should be avoided before measurements of corneal biomechanical properties and IOPg. In contrast, breath holding during measurements is not likely to cause a significant change in IOPg and IOPcc or corneal biomechanical properties.

Key Words: corneal biomechanical properties, IOP, ORA, eye rubbing, breath holding, cornea

(*Cornea* 2011;30:855–860)

Eye rubbing is a common activity that occurs sporadically when awakening, before sleep, and throughout the day in response to fatigue, emotional stress, or ocular irritation.[1] Before and during an ocular examination, patients sometimes rub their eyes, thereby applying pressure to the cornea. Many studies have reported that frequent eye rubbing can contribute to the pathogenesis of keratoconus.[2–10] Recent investigations have demonstrated that values of corneal biomechanical measurements are significantly lower in keratoconic eyes than in normal eyes.[11,12] Although eye rubbing is associated with the pathogenesis of keratoconus, and keratoconus is associated with changes in corneal biomechanical properties, to our knowledge, there have been no investigations to determine directly whether eye rubbing alters corneal biomechanical properties. In addition, the effects of repeated eye rubbing on the cornea have not been studied to determine whether changes in corneal biomechanical properties persist or accumulate with repeated eye rubbing or recover quickly between eye-rubbing episodes.

Another common patient behavior that might affect clinical measurements is breath holding. Clinical observation indicates that patients often hold their breath during an ocular examination [eg, during intraocular pressure (IOP) measurements] and take either a deep or a shallow inspiration before holding their breath. Unfamiliarity with the procedures and nervousness could further promote this behavior. Vieira et al[13] reported that IOP increased significantly (mean IOP increased by 2.2 mm Hg) during a bench press exercise and found that breath holding during the bench press exercise led to a greater IOP increase (mean IOP increased by 4.3 mm Hg). It has also been shown that increases in IOP might be associated with increased corneal rigidity.[14] Nevertheless, no studies have investigated whether normal breath holding during clinical measurements affects IOP or corneal biomechanical properties.

Studies have tried to determine ocular rigidity[15–21] through in vitro measurements or mathematical calculations; neither methodology involves direct measurement of corneal biomechanical properties. With the recent introduction of the ocular response analyzer (ORA) (Reichert Ophthalmic Instruments, Depew, NY),[22] direct clinical assessment of biomechanical properties of the cornea is now possible. The ORA delivers a rapid air impulse, causing the cornea to deform inward, past applanation, and into slight concavity. Within approximately 20 milliseconds,[23] the air pump shuts off, pressure decreases, and cornea returns to its normal state. An electrooptical system captures the signal throughout corneal deformation and recovery, allowing the ORA software to calculate 4 parameters: corneal hysteresis (CH), corneal resistance factor (CRF), corneal-compensated IOP (IOPcc), and Goldmann equivalent IOP (IOPg). CH reflects viscoelastic

Received for publication April 12, 2010; revision received July 26, 2010; accepted August 11, 2010.
From the *Department of Ophthalmology, Taoyuan Veterans Hospital, Taoyuan, Taiwan; †School of Medicine, National Yang-Ming University, Taipei, Taiwan; ‡Department of Ophthalmology, Taipei Veterans General Hospital, Taipei, Taiwan; and §Clinical Research Center and School of Optometry, University of California, Berkeley, CA.
Supported, in part, by grant from the Taoyuan Veterans Hospital, Taiwan (960004643), and by an unrestricted research fund for clinical research fellows from the Clinical Research Center, University of California, Berkeley.
Parts of this research were presented, in abstract form, at the 2009 ARVO Annual Meeting, Fort Lauderdale, FL.
The authors report no commercial or conflicts of interest.
Reprints: Meng C. Lin, Clinical Research Center, School of Optometry, University of California, Berkeley, CA 94720-2020 (e-mail: mlin@berkeley.edu).

or damping properties of the cornea and is a measure of corneal capacity for energy absorption.[24] The value of CH forms the basis of a derived parameter, the CRF, which is a reflection of the overall corneal resistance to deformation.[25] IOPg is a Goldmann equivalent IOP, calculated as the average of 2 applanation pressures as the cornea is deformed inward and then as it recovers to convexity. The applanation pressures associated with corneal indentation and recovery are different, and the magnitude of this difference is CH, with greater CH indicating a more rigid cornea and a greater capacity for energy damping. The ORA also uses CH to calculate a corneal-compensated IOP (IOPcc) that is reportedly less influenced by corneal biomechanical properties.[25] The relationships among CH, CRF, IOPcc, and IOPg have been reported extensively elsewhere.

In the current study, the primary objective was to determine whether commonly observed patient behaviors of eye rubbing and breath holding affect measurements of corneal biomechanical properties and IOP and specifically whether CH and CRF decrease after eye rubbing. The application of shear force to the cornea by eye rubbing may result in changes to the viscoelasticity of corneal tissue, thereby changing corneal resistance to deformation pressure. A secondary aim of the eye-rubbing study was to examine the hypothesis that IOPg changes after eye rubbing because of the influence of corneal biomechanical properties, whereas IOPcc does not. We also determined whether a second episode of eye rubbing results in a further reduction in corneal biomechanical measurements or IOP, suggesting a cumulative effect of repeated eye rubbing over a short period.

We also tested the hypothesis that breath holding increases IOPg and IOPcc. Breath holding might increase choroidal blood volume through increased intrathoracic pressure and thus increase IOP. A secondary aim of the breath-holding study was to determine whether this patient behavior might also increase CH and CRF.

Overall, the goal of these analyses was to determine whether it is important for clinicians to monitor patients for eye rubbing and/or breath holding and instruct them to refrain from these sometimes unconscious behaviors to obtain accurate measurements of corneal biomechanical properties and IOP.

MATERIALS AND METHODS

Subjects

Eighty eyes of 40 healthy subjects (28 women and 12 men) free of glaucoma or corneal disease participated in this study. The mean age was 28 years (range, 18 to 58 years). Informed consent was obtained from all study participants after a full description of the study protocol. This study followed the tenets of the Declaration of Helsinki and was approved by the Institutional Review Board (Committee for Protection of Human Subjects, University of California, Berkeley, CA).

Procedures and Measurements

For each subject, one eye was randomly selected for the eye-rubbing test, the other eye for the breath-holding test. The eye-rubbing test preceded the breath-holding test because the effects of eye rubbing are local and only impact the tested eye, whereas the effects of breath holding are more systemic and could potentially affect both eyes.

The eye-rubbing test included 2 episodes, each lasting 20 seconds, with a 2-minute break between episodes. To simulate natural conditions, we instructed subjects to rub their eyes as they usually would if their eyes were itchy and to try to perform the eye rubbing in the same manner for both episodes of the test. The ORA measurements were performed at baseline before eye rubbing (ER_0), immediately after the first episode (ER_1), and immediately after the second episode (ER_2) of eye rubbing. The breath-holding test also included 2 episodes. During the first episode, subjects were asked to breathe normally and then to hold their breath during ORA measurement. During the second episode, subjects were asked to take a deep breath and then to hold their breath. The ORA measurements were performed at baseline before breath holding (BH_0), during the first episode (BH_1), and during the second episode (BH_2) of breath holding. For baseline and each experimental episode of eye rubbing or breath holding, 3 ORA readings were taken and averaged to reduce the possible effects of within-subject liability and measurement error. The duration of each ORA reading was long enough for a measurement to be taken but did not exceed 8 seconds. During the breath-holding test, subjects were given 30 seconds to rest in between the 2 experimental episodes. To avoid unintentional breath holding, subjects were reminded to breathe regularly while baseline measurements were being taken.

Statistical Methods

Multivariate repeated measures analysis of variance was employed to determine whether there were significant differences in each of the 4 outcomes (CH, CRF, IOPcc, and IOPg) among ER_0, ER_1, and ER_2 for the eye-rubbing test and among BH_0, BH_1, and BH_2 for the breath-holding test, while accounting for possible within-subject correlations because of repeat measurements on each subject. In addition to the main experimental effects of eye rubbing and breath holding, we examined the possible confounding effects of subject age, sex, ethnicity (Asian, Non-Asian), and history of contact lens wear (yes, no). The significance of the models was determined by analysis of variance F test, and diagnostic plots were examined to ensure that model assumptions were reasonably well met. In post hoc testing to determine which experimental episodes differed from baseline and from each other, the Tukey method was employed to construct multiple pairwise confidence intervals while maintaining a familywise confidence level of 95%.

RESULTS

CH, CRF, and IOPg were all significantly reduced after eye rubbing ($P < 0.001$), whereas IOPcc was not ($P = 0.057$) (Table 1). After the first episode of eye rubbing, CH and CRF were both significantly reduced, and the second episode of eye rubbing further reduced CH and CRF significantly (Table 2). IOPcc and IOPg were similar, on average, before eye rubbing (14.5 and 14.4 mm Hg, respectively). After 1 episode of eye

TABLE 1. Mean (SD) of IOPs and Corneal Biomechanical Properties in the Eye-Rubbing Test

	ER_0	ER_1	ER_2	*P*
IOPcc	14.5 (2.4)	14.3 (2.6)	14.0 (2.7)	0.057
IOPg	14.4 (2.9)	13.9 (2.7)	13.2 (2.6)	**<0.001**
CH	10.4 (1.7)	10.0 (1.7)	9.5 (1.4)	**<0.001**
CRF	10.3 (1.9)	9.9 (1.6)	9.3 (1.5)	**<0.001**

All variables are in units of mm Hg. Significant *P* shown in bold.

ER_0, baseline before eye rubbing; ER_1, immediately after the first episode of eye rubbing; ER_2, immediately after the second episode of eye rubbing; *P*, *P* value from repeated measures analysis of variance *F* test.

rubbing, neither IOPcc nor IOPg was reduced significantly; however, after the second episode of eye rubbing, IOPg reduced significantly to 13.2 mm Hg, whereas IOPcc only reduced to 14.0 mm Hg, which did not achieve significance at the 0.05 level. There were no significant effects on any of the 4 outcomes because of age, sex, ethnicity, or history of contact lens wear. Future studies with larger sample sizes are required to confirm these findings.

There were no significant changes in CH, CRF, IOPcc, or IOPg because of breath holding (Table 3). All the 4 outcomes remained virtually unchanged, on average, during breath holding with either a normal inspiration or a deep breath (Table 4). There were no significant effects on any of the 4 outcomes because of age, sex, ethnicity, or history of contact lens wear.

DISCUSSION

The human cornea is a viscoelastic tissue.[11,22,26] An elastic material is one that regains its original form in a completely reversible displacement along the stress–strain pathway when the imposed stress is removed. A viscous material flows when an external shear stress is applied and, unlike an elastic material, does not regain its original shape when the stress is removed. A viscoelastic material has elements of both viscosity and elasticity, and as a result, energy is dissipated by the material when stress is applied.[24] Collagen is the primary structural component of corneal tissue, and it has viscoelastic properties. Corneal collagen is contained primarily in the Bowman layer and in the stroma, the latter region constituting 90% of the total thickness of the cornea. The collagen fibrils in the corneal stroma are organized into flat lamellae. The ground substance, such as proteoglycan, may act as a glue to bind the collagen fibrils and lamellae together. The collagen lamellae and the ground substance in the corneal stroma provide the majority of the corneal viscoelastic rigidity. In this study, the CH and CRF values decreased after eye rubbing. What was happening at the cellular/tissue level during eye rubbing that could result in a decrease in corneal rigidity? The ground substance in the human cornea is thixotropic.[27] A thixotropic reduction in the viscosity of a gel or other form of pseudoplastic fluid occurs in response to agitation, shaking, squeezing, or other source of shear stress.[28] The agitation and shear force associated with eye rubbing may reduce the viscosity of the corneal proteoglycan ground substance.[29] As the ground substance acts to bind the collagen fibrils and lamellae together and provides resistance to corneal bending and bulging, the decrease in CH and CRF values after the eye-rubbing episodes in our study might be a result of a thixotropic reduction of the viscosity of the proteoglycan gel ground substance.

Prior studies have not investigated whether repeated eye rubbing has a cumulative effect on the cornea. We therefore designed the eye-rubbing test with 2 episodes and asked our subjects to rub their eyes in the same manner and with the same force during each episode. Our results showed that the CH and CRF values obtained from ER_2 were significantly decreased compared with those obtained from ER_1. This result suggests a cumulative effect on corneal biomechanical rigidity from short term repeated eye rubbing. This means that if the cornea is unable to resume its original biomechanical rigidity secondary to the short duration between the episodes of eye rubbing, the weakened cornea is more susceptible to the subsequent insult of repeated eye rubbing, hence further lowering corneal CH and CRF values. In this study, there was a 2-minute break between the eye-rubbing episodes. The 2-minute interval was an arbitrary pause between 2 eye-rubbing episodes that allowed us to study the effect of repeated eye rubbing within a brief time frame. Outside the laboratory setting, this interval varies greatly from person to person and depends on the nature of the stimulus to eye rubbing. Most people do not rub their eyes every 2 minutes, but those who suffer from severe allergies are more likely to rub their eyes within such short intervals. The time required for the CH and CRF values to recover from eye rubbing to baseline is unknown. The decrease in CH and CRF values after eye rubbing might be a result of the thixotropically reduced

TABLE 2. Mean Differences Between Episodes in IOPs and Corneal Biomechanical Properties in the Eye-Rubbing Test, and Confidence Intervals for the Differences Adjusted for Multiple Comparisons by the Tukey HSD Method

	$ER_0 - ER_1$		$ER_1 - ER_2$		$ER_0 - ER_2$	
	Estimated Mean Difference	95% CI	Estimated Mean Difference	95% CI	Estimated Mean Difference	95% CI
IOPcc	0.21	−0.42 to 0.84	0.29	−0.33 to 0.92	0.50	−0.12 to 1.13
IOPg	0.54	−0.15 to 1.22	**0.72**	**0.04 to 1.4092**	**1.26**	**0.57 to 1.94**
CH	**0.35**	**0.03 to 0.66**	**0.49**	**0.18 to 0.81**	**0.84**	**0.52 to 1.15**
CRF	**0.43**	**0.04 to 0.82**	**0.59**	**0.20 to 0.98**	**1.02**	**0.63 to 1.41**

All variables are in units of mm Hg. Significant pairwise differences shown in bold.

CI, confidence interval; ER_0, baseline before eye rubbing; ER_1, immediately after the first episode of eye rubbing; ER_2, immediately after the second episode of eye rubbing; HSD, honestly significant difference.

TABLE 3. Mean (SD) of IOPs and Corneal Biomechanical Properties in the Breath-Holding Test

	BH_0	BH_1	BH_2	P
IOPcc	14.4 (2.2)	14.3 (2.4)	14.1 (2.5)	0.395
IOPg	14.2 (2.4)	14.0 (2.4)	13.8 (2.5)	0.344
CH	10.3 (1.2)	10.3 (1.5)	10.2 (1.5)	0.500
CRF	10.1 (1.3)	10.1 (1.4)	10.0 (1.3)	0.505

All variables are in units of mm Hg.

BH_0, baseline before breath holding; BH_1, during the first episode of breath holding; BH_2, during the second episode of breath holding; *P*, *P* value from repeated measures analysis of variance *F* test.

viscosity of the proteoglycan gel ground substance. Prior studies have shown that thixotropic loss of viscosity is an active agitation-driven process, whereas recovery, on removal of the influence of agitation, is a passive process.[28,29] In some cases, the time scales involved can range from minutes, as in the case of thixotropic breakdown of viscosity, to hours for recovery.[28] Our results suggest that more than 2 minutes is necessary for corneal biomechanical rigidity to recover to baseline after an eye-rubbing episode. Further investigation is needed to determine the recovery time of corneal biomechanical rigidity from eye rubbing and the extent to which the effects of repeated eye rubbing accumulate.

Keratoconus is the most common ectatic dystrophy of the cornea.[30] In this disorder, the central or paracentral cornea undergoes progressive thinning and bulging, so that the cornea takes on the shape of a cone. It is a major reason for corneal transplantation in developed countries.[31,32] Numerous case studies have demonstrated that frequent eye rubbing is strongly associated with the development of keratoconus.[2–10] However, a strong association is not a sufficient condition for establishing a causal role.[29,33] Observational case reports usually have a low rank for inferring a causal hypothesis for keratoconus.[29,34] Testing the causal hypothesis between frequent eye rubbing and keratoconus is problematic because randomized clinical trials are contraindicated for ethical considerations.

In our study, the results showed that CH and CRF values decreased after eye rubbing and that there was a cumulative effect on corneal biomechanical rigidity from repeated eye rubbing. For a lamellar structure, such as the cornea, a useful analogy is a 500-sheet ream of copy paper that allows the layers to slide past each other when a shearing force is applied to the top of the stack.[35] Some laboratory studies[15,16] have demonstrated that the corneal stroma has less interlamellar cohesive strength (ie, reduced "glue" between the stacked "pages" or lamellae) in the central and inferior peripheral cornea than at any other location. The authors[15,16] believed that cohesive strength may be primarily dependent on the molecular binding strength of proteoglycan. The less rigid and less resistant inferocentral cornea is also the area where ectasia most commonly occurs in keratoconus.

Some clinical studies have found that the values for CH and CRF are significantly decreased in patients who underwent laser in situ keratomileusis (LASIK) surgery.[11,22] The biomechanical weakness of the cornea suggested by decreased CH and CRF values could be a cause of ectasia after refractive surgery.[11,22,35,36] This clinical finding has prompted refractive surgeons to consider corneal biomechanical measurement (CH and CRF) as a new indicator for screening the candidates who are likely to develop post-LASIK ectasia.[11,22]

These clinical studies show that corneas with lower biomechanical rigidity, as reflected in lower CH and CRF values, might be at greater risk for developing corneal ectasia (eg, keratoconus). Our results support the findings of previous studies that chronic habits of frequent eye rubbing could contribute to the pathogenesis of keratoconus.[2–10] When eye rubbing is frequent, and the interval between 2 episodes of eye rubbing is not long enough for the cornea to fully recover its original biomechanical rigidity, the weakened cornea could be more sensitive to additional eye rubbing, thus increasing the risk of developing keratoconus.

Prior studies have demonstrated that IOP measurement by Goldmann tonometry correlated with corneal biomechanical properties.[37] IOPg is a Goldmann equivalent IOP, and it has a strong correlation with the standard Goldmann applanation pressure measurement.[25] IOPcc is a new measurement of IOP that is less affected by corneal biomechanical properties than that provided by Goldmann applanation tonometry.[38] It has been reported that the decrease in IOPcc is lower than the decrease in IOPg after LASIK surgery.[11,37] This also suggests that the IOPcc parameter compensates for corneal properties. In our study, as with CH and CRF, the values of IOPg decreased significantly after eye rubbing. This result was similar to a previous study[39] that reported a 2.4-mm Hg decrease in mean IOP measured by Tono-Pen after 1 eye-rubbing episode. Yet, in our study, the change in IOPcc after

TABLE 4. Mean Differences Between Episodes in IOPs and Corneal Biomechanical Properties in the Breath-Holding Test, and Confidence Intervals for the Differences Adjusted for Multiple Comparisons by the Tukey HSD Method

	$BH_0 - BH_1$		$BH_1 - BH_2$		$BH_0 - BH_2$	
	Estimated Mean Difference	95% CI	Estimated Mean Difference	95% CI	Estimated Mean Difference	95% CI
IOPcc	0.06	−0.68 to 0.80	0.20	−0.54 to 0.94	0.26	−0.48 to 1.00
IOPg	0.09	−0.57 to 0.74	0.17	−0.48 to 0.83	0.26	−0.40 to 0.92
CH	0.01	−0.39 to 0.41	0.10	−0.30 to 0.50	0.11	−0.29 to 0.51
CRF	0.01	−0.39 to 0.40	0.10	−0.29 to 0.50	0.11	−0.29 to 0.51

All variables are in units of mm Hg.

BH_0, baseline before breath holding; BH_1, during the first episode of breath holding; BH_2, during the second episode of breath holding; CI, confidence interval; HSD, honestly significant difference.

eye-rubbing episodes was of small magnitude (0.2 to 0.5 mm Hg), not statistically significant. Because the IOPcc is less affected by corneal biomechanical properties than the IOPg, we speculate that the decrease in IOPg after eye rubbing, in our study, and the decrease in standard Goldmann IOP measured by Tono-Pen,[39] were influenced primarily by a decrease in CH and CRF after eye rubbing.

Elevated IOP during Valsalva maneuvers has been reported.[40,41] A Valsalva maneuver is a forced exhalation against a closed glottis leading to a sudden increase in intrathoracic pressure. When the intrathoracic pressure increases during a Valsalva maneuver, there is usually an increase in the intrathoracic venous pressure, which is transmitted through the jugular, orbital, and vortex veins to the choroid, bringing about vascular engorgement. An increase in the choroid volume could lead to an increase in IOP.[42,43] Activities like coughing, bearing down during defecation, heavy-weight lifting,[13] and playing wind instruments[43] are some Valsalva-like maneuvers that may lead to an increase in IOP.

In our study, breath holding did not induce a significant IOP increase from baseline, such as that observed during Valsalva maneuvers. We attribute this result to physiological differences between simple breath holding and Valsalva maneuvers. In our study, subjects were asked to hold their breath without exhaling forcefully to simulate patient behavior in a clinical setting. We know that patients often hold their breath during IOP measurements, but they do not typically exhale forcefully against a closed glottis. The expiratory effort, a component of Valsalva maneuvers but not part of our breath-holding test, is the main cause of increase in intrathoracic pressure and subsequent elevation of IOP, as shown by Rosen et al.[42] In their report, there was a correlation between the IOP increase and increased force of expiration during the performance of Valsalva maneuvers. From Rosen's findings and our results, we speculate that the increase in intrathoracic pressure induced by breath holding without forceful exhalation is much less than the increase during a Valsalva maneuver and is insufficient to cause a significant increase in IOP.

We did not find significant changes in IOP values between BH_1 and BH_2 in the breath-holding test. The IOP values during large lung volume breath holding (BH_2) should be higher than those during small lung volume breath holding (BH_1) because of increased venous pressure, assuming that during BH_2, subjects retain more air in their lungs by taking a deep breath before breath holding, leading to a greater intrathoracic pressure.[13] In contrast, when considering arterial pressure, Sakuma et al[44] found a differential effect on cardiac output between large and small lung volume breath holding. Cardiac output during large lung volume breath holding was significantly lower than that measured during small lung volume breath holding. Lower cardiac output decreases systemic arterial pressure. The decreased systemic arterial pressure during BH_2 could lead to decreased intraocular blood volume. It is possible that the changes in arterial and venous pressures take place in opposite directions during large lung volume breath holding. We therefore hypothesize a cancellation effect in which decreased intraocular blood volume mitigates the effect from engorgement of the intraocular vein because of increased intrathoracic pressure, with a net result of no significant difference in IOP values between BH_2 (large lung volume breath holding) and BH_1 (small lung volume breath holding).

Unlike in the eye-rubbing test, in which experimentally induced changes in the biomechanical properties of the cornea could be expected to influence the noncompensated IOPg measurement, in the breath-holding test, it is the experimentally induced changes in IOP that might be expected to alter corneal biomechanical properties. Thus, the observations that significant changes in IOP (IOPg and IOPcc) and corneal biomechanical properties do not occur with breath holding are consistent.

In summary, the biomechanical properties of the cornea (CH and CRF) were significantly decreased after eye rubbing. This decrease was cumulative with repeated episodes of eye rubbing over the short time scale of our study. Furthermore, the IOPg was also significantly decreased by eye rubbing but not the IOPcc, confirming that standard Goldmann IOP measures are affected by the biomechanical properties of the cornea. From a clinical perspective, patients should be instructed to avoid eye rubbing before measurements of corneal biomechanical properties and IOP. In contrast, breath holding of the type commonly observed in patients in the clinical setting is not likely to cause a significant change in IOP values (eg, IOPg, IOPcc) or corneal biomechanical properties and does not require monitoring by the clinician.

ACKNOWLEDGMENTS

The authors thank the staff of the Clinical Research Center, UC Berkeley School of Optometry for their contributions to this project.

REFERENCES

1. McMonnies CW. The evidentiary significance of case reports: eye rubbing and keratoconus. *Optom Vis Sci*. 2008;85:262–269.
2. Baum J. On the location of the cone and the etiology of keratoconus. *Cornea*. 1995;14:142–143.
3. Krachmer JH, Feder RS, Belin MW. Keratoconus and related noninflammatory corneal thinning disorders. *Surv Ophthalmol*. 1984;28:293–322.
4. Cameron JA, Al-Rajhi AA, Badr IA. Corneal ectasia in vernal conjunctivitis. *Ophthalmology*. 1989;96:615–623.
5. Boger WPIII, Petersen RA, Robb RM. Keratoconus and acute hydrops in mentally retarded patients with congenital rubella syndrome. *Am J Ophthalmol*. 1981;91:231–233.
6. Gasset AR, Hinson WA, Frias JL. Keratoconus and atopic diseases. *Ann Ophthalmol*. 1978;10:991–994.
7. Haugen OH. Keratoconus in the mentally retarded. *Acta Ophthalmol*. 1992;70:111–114.
8. Korb DR, Leahy CD, Greiner JV. Prevalence and characteristics of eye rubbing for keratoconic and non-keratoconic subjects. *Invest Ophthalmol Vis Sci*. 1991;32(Suppl):884.
9. Shapiro MB, France TD. The ocular features of Down's syndrome. *Am J Ophthalmol*. 1985;99:659–663.
10. Ridley F. Eye rubbing and contact lenses [letter]. *Br J Ophthalmol*. 1961; 45:631.
11. Ortiz D, Piñero D, Shabayek MH, et al. Corneal biomechanical properties in normal, post-laser in situ keratomileusis, and keratoconic eyes. *J Cataract Refract Surg*. 2007;33:1371–1375.
12. Shah S, Laiquzzaman M, Bhojwani R, et al. Assessment of the biomechanical properties of the cornea with the ocular response analyzer in normal and keratoconic eyes. *Invest Ophthalmol Vis Sci*. 2007;48: 3026–3031.
13. Vieira GM, Oliveira HB, Andrade DTE. Intraocular pressure variation during weight lifting. *Arch Ophthalmol*. 2008;124:1251–1254.

14. Ebneter A, Wagels B, Zinkernagel MS. Non-invasive biometric assessment of ocular rigidity in glaucoma patients and controls. *Eye*. 2009;23:606–611.
15. Smolek MK, McCarey BE. Interlamellar adhesive strength in human eyebank corneas. *Invest Ophthalmol Vis Sci*. 1990;31:1087–1095.
16. Smolek MK. Interlamellar cohesive strength in the vertical meridian of human eyebank corneas. *Invest Ophthalmol Vis Sci*. 1993;34:2962–2969.
17. Hartstein J, Becker B. Research into the pathogenesis of keratoconus: a new syndrome: low ocular rigidity, contact lenses and keratoconus. *Arch Ophthalmol*. 1970;84:728–729.
18. Edmund C. Assessment of an elastic model in the pathogenesis of keratoconus. *Acta Ophthalmol*. 1987;65:545–550.
19. Edmund C. Corneal rigidity and ocular rigidity in normal and keratoconic eyes. *Acta Ophthalmol*. 1988;66:134–140.
20. Elsheikh A, Wang D, Pye D. Determination of the modulus of elasticity of the human cornea. *J Refract Surg*. 2007;23:808–818.
21. Elsheikh A, Wang D, Brown M, et al. Assessment of corneal biomechanical properties and their variation with age. *Curr Eye Res*. 2007;32:11–19.
22. Luce DA. Determining in vivo biomechanical properties of the cornea with an ocular response analyzer. *J Cataract Refract Surg*. 2005;31:156–162.
23. Sullivan-Mee M. The role of ocular biomechanics in glaucoma management. *Rev Optom*. 2008;145.
24. Kotecha A. What biomechanical properties of the cornea are relevant for the clinician? *Surv Ophthalmol*. 2007;52:S109–S114.
25. Luce D. Methodology for corneal compensated IOP and corneal resistance factor for an ocular response analyzer. *Invest Ophthalmol Vis Sci*. 2006;47:e-abstract 2266.
26. Dupps WJ Jr, Wilson SE. Biomechanics and wound healing in the cornea. *Exp Eye Res*. 2006;83:709–720.
27. Hendrickson T. *Massage for Orthopedic Conditions*. Philadelphia, PA: Lippincott Williams & Wilkins; 2009:9.
28. Barnes HA. Thixotropy: a review. *J J Nonnewton Fluid Mech*. 1997;70:1–33.
29. McMonnies CW. Mechanisms of rubbing-related corneal trauma in keratoconus. *Cornea*. 2009;28:607–614.
30. Kennedy RH, Bourne WM, Dyer JA. A 48-year clinical and epidemiological study of keratoconus. *Am J Ophthalmol*. 1986;101:267–273.
31. Lois N, Kowal VO, Cohen EJ, et al. Indications for penetrating keratoplasty and associated procedures. *Cornea*. 1997;16:623–629.
32. Rabinowitz YS, Dong L, Wistow G. Gene expression profile studies of human keratoconus cornea for NEIBank: a novel cornea-expressed gene and the absence of transcripts fo aquaporin 5. *Invest Ophthalmol Vis Sci*. 2005;46:1239–1246.
33. Edwards M, McGhee CNJ, Dean S. The genetics of keratoconus. *Clin Exp Ophthalmol*. 2001;29:345–351.
34. Sharma S. Levels of evidence. *Evid Based Eye Care*. 2001;2:5–6.
35. Dupps WJ. Biomechanical modeling of corneal ectasia. *J Refract Surg*. 2005;21:186–190.
36. Guirao A. Theoretical elastic response of the cornea to refractive surgery: risk factors for keratectasia. *J Refract Surg*. 2005;21:176–185.
37. Pepose JS, Feigenbaum SK, Qazi MA, et al. Changes in corneal biomechanics and intraocular pressure following LASIK using static, dynamic and non-contact tonometry. *Am J Ophthalmol*. 2007;143:39–47.
38. Medeiros FA, Weinreb RN. Evaluation of the influence of corneal biomechanical properties on intraocular pressure measurements using the ocular response analyzer. *J Glaucoma*. 2006;15:364–370.
39. Mansour A, Haddad R. Corneal topography after ocular rubbing. *Cornea*. 2002;21:756–758.
40. Brody S, Erb C, Veit R, et al. Intraocular pressure changes: the influence of psychological stress and the Valsalva maneuver. *Biol Psychol*. 1999;51:43–57.
41. Whitacre MM, Stein R. Sources of error with use of Goldmann-type tonometers. *Surv Ophthalmol*. 1993;38:1–30.
42. Rosen DA, Johnston VC. Ocular pressure patterns in the Valsalva maneuver. *Arch Ophthalmol*. 1959;62:810–816.
43. Schuman JS, Massicotte EC, Connolly S, et al. Increased intraocular pressure and visual field defects in high resistance wind instrument players. *Ophthalmology*. 2000;107:127–133.
44. Sakuma H, Kawada N, Kubo H, et al. Effect of breath holding on blood flow measurement using fast velocity encoded cine MRI. *Magn Reson Med*. 2001;45:346–348.