The effect of a combination of 0.1% tetracaine HCl and 0.4% oxybuprocaine HCl on human central corneal thickness measurements

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Summary

A combination of 0.1% tetracaine HCl and 0.4% oxybuprocaine HCl is used when carrying out morphometrical corneal studies in vivo by means of ultrasound pachymetry. The aim of this was to determine the effect of a combination of 0.1% tetracaine HCl and 0.4% oxybuprocaine HCl anesthetic eye drops on central corneal thickness values.

We carried out a prospective study involving 30 eyes of 30 healthy subjects. The mean age of the subjects was 26.13±2.62 years (age ranged from 20 to 30 years old). Central pachymetry was carried out prior to and three minutes after the instillation of two saline solution eye drops, and three minutes after the administration of a combination of 0.1% tetracaine HCl and 0.4% oxybuprocaine HCl anesthetic eye drops. The mean of three consecutive measurements of the central corneal thickness obtained with the Orbscan Topography System II (Orbscan, Inc., Salt Lake City, UT. USA) was used as the corneal thickness value.

No significant differences were found ($p=0.714$) in the mean central corneal thickness values before and three minutes after saline solution eye drops had been instilled. Nevertheless, after anesthesia there was a significant increase in mean central corneal thickness ($p<0.001$). Increases ranged from 22 to 131 micrometers, with a mean of approximately 47 micrometers.

Following the instillation of a combination of 0.1% tetracaine HCl and 0.4% oxybuprocaine HCl eye drops corneal thickness increase. Researchers must be aware of this effect of topical anesthetic eye drops on corneal morphometry in order to analyze corneal thickness results correctly.

Key Words: Central corneal thickness – Topical anesthesia – Cornea – Ultrasound pachymetry

Introduction

Ultrasound pachymetry is the most widely used technique for in vivo corneal thickness measurement (Doughty and Zaman, 2000). It is a technique in which the ultrasound probe must be in contact with the ocular surface. Morphometric study of corneal thickness by means of ultrasound pachymetry involves the application of one or two anesthetic eye drops directly onto the corneal surface in order to avoid pain when the ultrasound probe touches the ocular surface (Price et al., 1999; Sanchis Gimeno et al., 2001; Lleó et al., 2003). Thus, theoretically corneal thickness values could be affected by the use of anesthetic eye drops.

Nevertheless, there are only a few references regarding the effect that anestethetic eye drops have on corneal thickness values when carrying out morphometric studies in vivo (Herse and Siu, 1992; Asensio et al., 2003).

In a study by Herse and Siu (1992), an average increase of 2.9% was observed in central corneal thickness (CCT) about two minutes after instillation of two drops of 0.5% proparacaine. More recently, it has been observed that 0.4% oxybuprocaine HCl

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eye drops can induce interindividual changes in corneal thickness values (Asensio et al., 2003).

Nevertheless, a combination of 0.1% tetracaine HCl and 0.4% oxybuprocaine HCl anesthetic eye drops can also be used to anesthetize the cornea before ultrasound pachymetry. Currently, the effect of the instillation of these anesthetic eye drops on corneal thickness measurements remains unclear.

In light of the above, we were prompted to study the CCT changes induced by the instillation of a combination of 0.1% tetracaine HCl and 0.4% oxybuprocaine HCl anesthetic eye drops by analyzing CCT before and after topical anesthesia.

Material and methods

The work was performed in accordance with the World Medical Association's Declaration of Helsinki and written informed consent was obtained from all patients. Ethics approval from the Ethics Committee of the Faculty of Medicine of Valencia was obtained. We carried out a prospective study involving 30 eyes of 30 subjects. All subjects were healthy and none of them was taking any kind of topical or systemic medication. The manifest sphere ranged from -0.75 to -3.00 diopters (mean±SD, -2.27±0.39) and the mean cylinder ranged from 0 to -0.75 diopters (mean±SD, -0.38±0.26). The mean age of the subjects was 26.13±2.62 years (their ages ranged from 20 to 30 years old). Mean tonometry ranged from 12 to 19 mmHg (mean±SD, 16.10±1.78). Only the right eye of the subjects was analyzed. The choice of limiting the study to the right eye instead of the left eye was random.

Once the subjects had been chosen, all CCT measurements were determined on another day using the Orbscan II Corneal Topography System (Orbscan, Inc., Salt Lake City, UT, USA) following the procedures recommended by the manufacturer (Figure 1 and Figure 2).

Orbscan pachymetry was carried out prior to and three minutes after the instillation of two saline solution eye drops. Two drops of a combination of 0.1% tetracaine HCl and 0.4% oxybuprocaine HCl anesthetic eye drops were instilled immediately after the post-saline solution measurement had been carried out. Three minutes after the administration of the anesthetic eye drops, Orbscan pachymetry was carried out again. One physician took all corneal thickness measurements. The mean of three consecutive measurements of CCT was used as the corneal thickness value.

The statistical tests used in the work were the Kolmogorov-Smirnov test and after this the differences between data sample means were determined by a t-Test. P values of below 0.05 were considered statistically significant.

Results

The individual changes in CCT values before and after saline solution eye drops, before saline solution and after anesthesia, and after saline solution and after anesthesia can be seen in Figures 3, 4 and 5.

No significant differences were found (p=0.714) between the mean CCT values measured before (547±5 micrometers) and after the instillation of saline solution eye drops (548±6 micrometers).

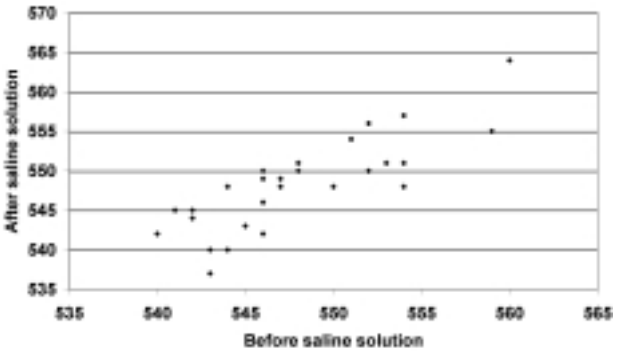

Fig. 3.- Scarttergraph showing the correlation between the pachymetric measurements obtained before and after saline solution eye drops (microns).

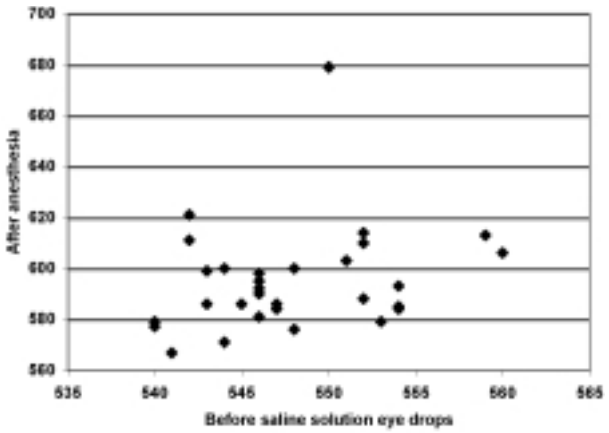

Fig. 4.- Scarttergraph showing the correlation between the pachymetric measurements obtained before saline solution and after anesthesia (microns).

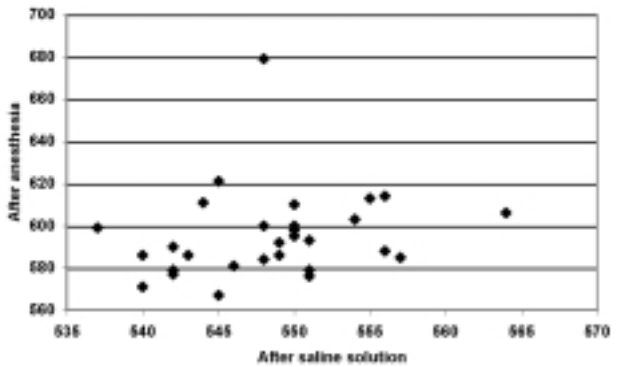

Fig. 5.- Scarttergraph showing the correlation between the pachymetric measurements obtained after saline solution eye drops and after anesthesia (microns).

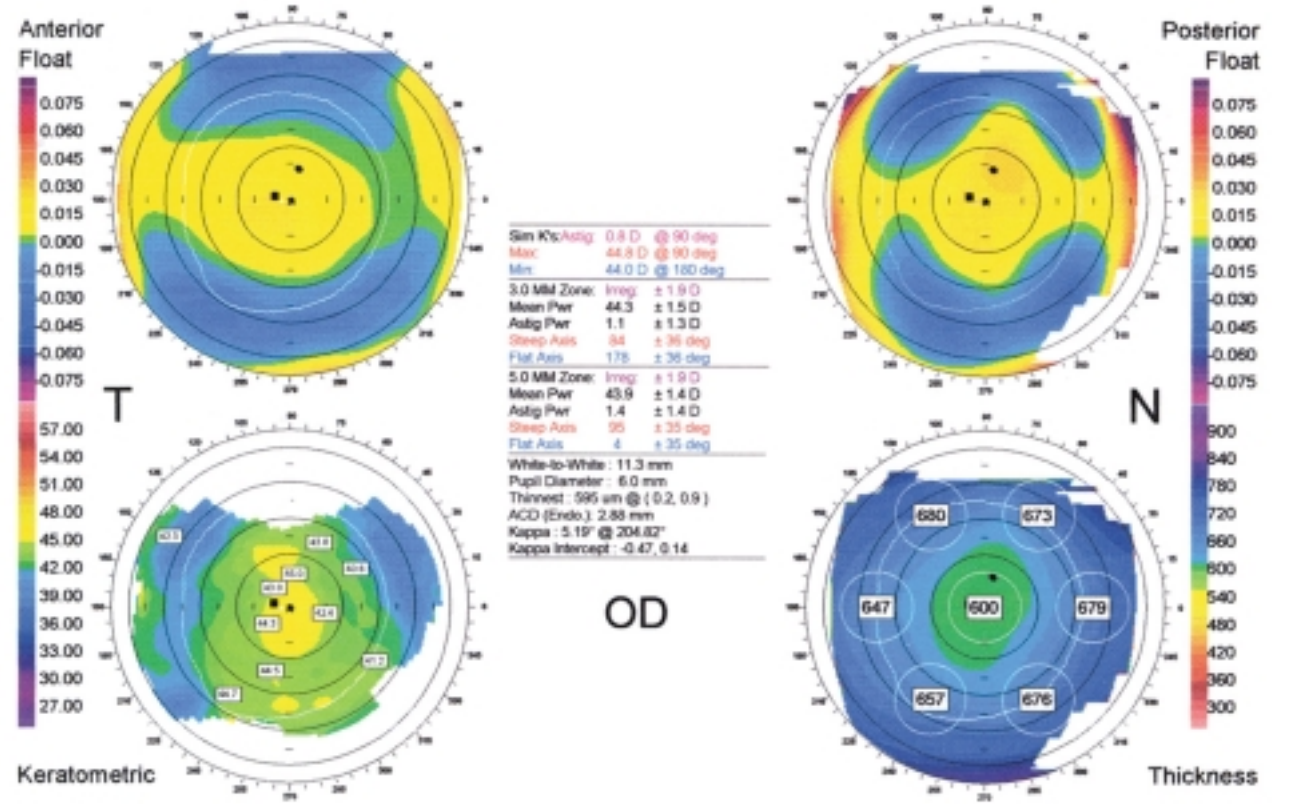

Fig. 1. The Orbscan system measures anteror and posterior corneal elevation (relative to a best-fit sphere), surface curvature, and corneal thickness using a scanning-slit mechanism. The images of the cornea are taken using the placido disc and are shown on the screen of the instrument. The subjects were asked to look at a blinking red light coaxial to the imaging system while the tracking system measured involuntary eye movements during the examination. Corneal thickness is obtained showing the differences in elevation between the anterior and posterior surfaces of the cornea.

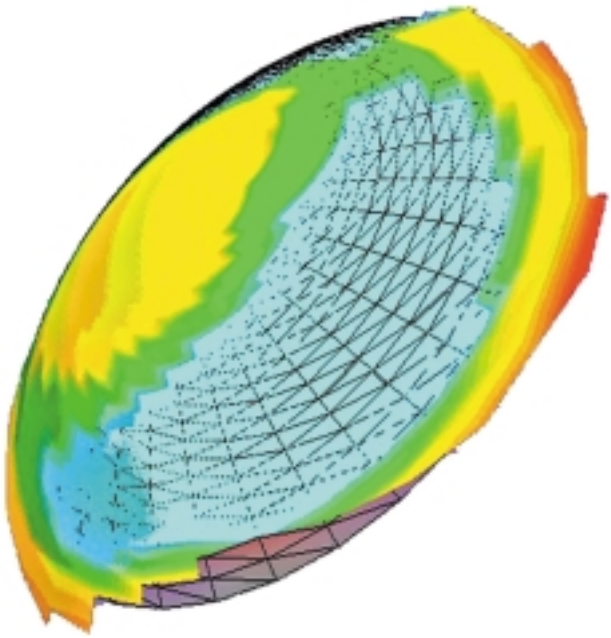

Fig. 2. With the Orbscan Topography System two scanning slit-lamps project beams at 45 degrees to the right or left of the instrument axis. Forty images –20 with slit beams projected from the left and 20 from the right– are obtained at two intervals, each lasting 0.7 seconds. Surface data points are measured on the x, y, and z axes, thus creating color-coded topographic maps.

The mean CCT after anesthesia was 595±21 micrometers. Significant differences were found ($p<0.001$) between the mean CCT values measured before saline solution eye drops and after anesthesia, and between the mean CCT values obtained after saline solution and after anesthesia ($p<0.001$).

The mean change in CCT values before and after saline solution instillation was 0.533±3.33 micrometers (range, -6 to 4 micrometers). After anesthetizing the cornea there was an increase of 47.26±20.14 micrometers (range, 26 to 129 micrometers) in CCT values with respect to the values obtained before saline solution eye drops. After anesthetic eye drops the CCT values were 46.73±20.42 micrometers higher (range, 22 to 131 micrometers) than those obtained after saline solution eye drops.

Discussion

The objective of this study was to determine the effect that a combination of 0.1% tetracaine HCl and 0.4% oxybuprocaine HCl anesthetic eye drops have on CCT. Our results revealed that after the instillation of a combination of 0.1% tetracaine HCl and 0.4% oxybuprocaine HCl there was a significant increase in CCT values.

Thus, these results seem to confirm that anesthesia by means of a combination of 0.1% tetracaine HCl and 0.4% oxybuprocaine HCl anesthetic eye drops can affect CCT measurements.

We used Orbscan pachymetry because it is a non-contact technique that can be used to obtain CCT values without using corneal anesthetic eye drops. Therefore, by analyzing CCT values before and after corneal anesthesia we were able to detect changes in CCT values associated with the instillation of anesthetic eye drops.

The literature does not explain the effect that anesthetic eye drops have on human corneal thickness, although Herse and Siu (1992) observed a significant increase in CCT (2.9% of the corneal thickness) about two minutes after instillation of two drops of 0.5% proparacaine, which was not found after instillation of 2 drops of artificial tear solution. We found similar results, although the increase in CCT values in our study was lower than that reported by Herse and Siu (1992).

However, another study that analyzed the effect of 0.4% oxybuprocaine HCl on corneal thickness values did not find significant increases in mean corneal thickness values, although an individual response to anesthetic eye drops was observed that was associated with increases or decreases of corneal thickness (Asensio et al., 2003). On the other hand, in this study we found no decreases in corneal thickness values after anesthesia. Thus, it seems that proparacaine, oxybuprocaine, tetracaine or a combination of these drugs can induce a different response in corneal thickness values.

In our study only one physician carried out all the Orbscan pachymetric measurements so that the differences could not be the result of different observers analyzing the CCT but rather the result of the effect of topical anesthesia.

It is known that when an anesthetic diffuses deep into the corneal stroma it may inhibit the cellular metabolism of the keratocytes and the posterior layers of the cornea (Penna and Tabbara, 1986). Moreover, it is known that the inhibition of the endothelial cell metabolism may lead to corneal edema (Penna and Tabbara, 1986) and this corneal edema can induce a change in corneal thickness. In fact, corneal edema was the reason attributed by Herse and Siu (1992) for the increased values they observed after topical corneal anesthesia.

Alterations in the degree of corneal hydration after topical anesthetics were observed in a study on the effects of cocaine, lidocaine, and benoxinate on the corneal epithelium of rabbits (Weeker, 1974). That study concluded that topical anesthetics caused an alteration of the Na^+/K^+ endothelium pump, resulting in increased osmotic pressure in the cornea and subsequent increased hydration of the stroma, which could explain an increase in CCT values.

Finally, an open question remains: should the effect of anesthetic eye drops on corneal thickness be ignored when carrying out corneal morphometric studies in vivo? Our results have shown that use of this kind of topical anesthesia when carrying out morphometric corneal studies in vivo by means of ultrasound can affect the cornea, causing increases in CCT. In addition, our results are similar to those of Herse and Siu (1992) but differ from others (Asensio et al., 2003), making it more complicated to ascertain how anesthetic eye drops affect CCT. Therefore, we believe there is evidence of a lack of knowledge regarding the effect and consequences that anesthetic eye drops have on the human cornea, and the present study should be complemented with further research.

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