ABSTRACT

Objective: Corneal topography and thickness has clinical importance in contact lens fitting and refractive surgery, however repeated measurement of corneal thickness and curvature is complicated by the natural phenomenon of diurnal variation. Our aim was to determine diurnal variations of central and paracentral corneal thickness and curvature over a period of ten hours.

Materials and methods: Corneal thickness and curvature of 10 right eyes of 10 young healthy men were determined by Orbscan Topography System and EyeSys videokeratoscope respectively. Both parameters were determined for central and paracentral regions 1 mm and 2 mm from the centre of the cornea at 2-hour internals for ten hours.

Results: The cornea was thickest and flattest on awakening. There was a difference in corneal thickness (ANOVA, Schfféc method p< 0.05) and curvature (ANOVA, Tamhane method p< 0.05) over time for all the corneal locations studied, with greater changes observed in the peripheral corneal data. The minimum value was 10 and 8 hours after eye opening for central and paracentral zones, respectively. Change in central and paracentral corneal

RESUMEN

Objetivo: La topografía y espesor de la córnea tienen una gran importancia clínica en la adaptación de lentes de contacto y en cirugía refractiva. Sin embargo, la repetibilidad en las medidas de estos parámetros se ve comprometida por el fenómeno natural de las variaciones diurnas. Nuestro objetivo es determinar las variaciones diurnas de espesor y curvatura corneal central y paracentral durante un periodo de 10 horas.

Material y método: Se determinó la curvatura y espesor corneal en los ojos derechos de 10 varones jóvenes mediante Orbscan y videoqueratoscopio respectivamente. Ambos parámetros fueron determinados para la zona central y paracentral a 1 y 2 mm del centro de la córnea, cada dos horas durante un periodo de 10 horas.

Resultados: La córnea presentaba su espesor máximo y curvatura mínima al abrir el ojo. Se observó una variación estadísticamente significativa de espesor (ANOVA, método de Schefféc p< 0,05) y de curvatura (ANOVA, método de Tamhane p < 0,05) a lo largo del día en todas las localizaciones estudiadas, si bien la variación y los rangos de valores en la zona paracentral eran mayores. Los valo-
thicknss was strongly correlated with corneal curvature, except for the 2 mm nasal and superior semi-meridians.

**Conclusions:** These data indicate a shift in corneal thickness and curvature that can be of clinical relevance as individual changes vary greatly (Arch Soc Esp Oftalmol 2008; 83: 183-192).

**Key words:** Cornea, corneal thickness, corneal curvature, pachymetry, diurnal variation.

**INTRODUCTION**

The determination of corneal thickness has gained relevance in recent years, partly due to the growing interest in the continued use of contact lenses (1,2) and refractive surgery (3-5). Corneal thickness provides valid information about its physiological condition and possible changes associated to diseases, traumas and hypoxia.

The diurnal variations of corneal thickness are an obstacle for repeated pachymetric measurements. The pattern of this variation is that the cornea attains maximum thickness upon awakening after night sleep (6-8). Optical and ultrasound pachymetry have been utilized to measure corneal thickness in periods of 12-48 hours (7-10). Utilizing the Haag-Streit optical pachymeter, Kiely et al (7) found a diurnal variation of 10 µm for the central thickness and 20 µm in the periphery at 40º.

The corneal curvature has also been considered in relation to refractive surgery, the adaptation of contact lenses and others. Several authors have studied the daytime change of the central corneal curvature which show that the cornea is flatter upon awakening, with a slight but statistically significant increase in curvature throughout the day (6,10,11). More significant variations are observed in the superior and inferior hemi-meridians (12), in addition to gender differences (13).

Kiely et al (7) studied the relationship between the curvature and corneal thickness and found a significant correlation between the diurnal thickness and curvature variations in the horizontal meridian. On the other hand, Rom et al (14) did not find a relationship between the variations of corneal thickness and topography.

This study determined the central and para-central corneal thickness and curvature values (at 1 and 2 mm from the centre) during a 10-hour period, with measurements being taken at 2 hour intervals. The aim was to determine the daytime corneal thickness and curvature values in the central and para-central locations as well as to study the relationship between the thickness and curvature variations.

**SUBJECTS, MATERIAL AND METHOD**

Ten young men took part in the study, having no history of contact lens use, ocular or systemic pathology or receiving at the time any type of topical or systemic medication. Women were not included in the study sample in order to avoid the effects of hormonal activity on the corneal thickness and curvature (15). After explaining the procedures to the patients, they were asked to sign the informed consent.

Immediately upon awakening and with the purpose of eliminating the effect of tear evaporation on the size of the cornea (8), each subject covered his right eye with a patch up to the first measurement. The thickness and curvature values of the right eye cornea were determined with the Orbscan Topography System (Orbscan II version 3.0) and with the EyeSys videokeratoscope (EyeSys Corneal Analysis System 2000. version 3.1; EyeSys, INC, Houston, TX), respectively.

Although previous studies have demonstrated that Orbscan yields higher values than the optical and ultrasonic pachymeters (16,17), its usefulness has been proved for measuring corneal thickness in investigation and in clinical practice with a preci-
sion in relation to gauge spheres of ±2 µm (range, 1.2 µm in the centre to 3.2 µm in the periphery) (10,16). Repeated measurements on individuals produced a mean standard deviation of 9.08 µm in the central 7 mm of the cornea (10). However, the repetitiveness and reproducibility of the Orbscan is low when measuring corneal curvature (18), for which reason the curvature values were determined by videokeratoscopy. Previous studies have shown a high repetitiveness in measurements taken with the videokeratoscope, with a standard deviation of ± 0.01 mm in humans and gauge spheres (19.20).

The thickness and curvature measures were taken in nine corneal locations: central and at 1 and 2 mm from the centre in the nasal, temporal, superior and inferior half-meridians. The first measurements were taken immediately after withdrawing the eye patch and at 2 hour intervals for a 10-hour period. The statistical analysis was made utilizing SPSS 6.1 (SPSS Inc., Chicago, Illinois, USA). For comparing the daytime thickness and curvature variations in said locations an ANOVA test was applied with an Univariate General Linear Model. The corneal thickness and curvature were considered as dependent variables whereas the central location, at 1 and 2 mm from the centre, meridians and the measurement time were considered as factors. As Levene’s test for equalizing variances was statistically significant for the thickness but not for the curvature, the Sheffé and Tamhane methods were utilized for thickness and curvature, respectively. The relationship between the thickness and curvature measurements were assessed by means of linear regression analysis.

RESULTS

Figure 1 and 2 show the corneal thickness and curvature measurements taken at the central and nasal, temporal, superior and inferior areas at 1 and 2 mm of the centre. The statistical analysis showed statistically significant corneal thickness variations in all the locations and period of the study (ANOVA, Schffé method, p < 0.05). The cornea exhibited its maximum thickness upon opening the eye after night sleep, which then reduced during the day in all the locations. The mean diurnal variation in central corneal thickness was of 14 µm (1.95%), with individual values in the range of 9-22 µm, and with the minimum value after 10 hours of said initial opening. The mean gradient of the pachymetric descent in the centre of the cornea was of -0.686. The thickness variations corresponding to the nasal, temporal, superior and inferior at 1 and 2 mm of the centre are shown in tables I and II, the minimum value being approximately 8 hours after opening the eye. The mean gradient of the pachymetric des-

![Fig. 1: Mean value of central and nasal, temporal, superior and inferior corneal thickness immediately after opening the eye and at 2-hour intervals in a 10-hour period: a) at 1 mm from the centre; b) at 2 mm from the centre of the cornea.](image-url)
cent for 1 and 2 mm measurements in the meridians are shown in table III, where the values corresponding to the nasal, temporal, inferior and superior locations at 2 mm from the centre indicate a larger pachymetric reduction than in the centre of the cornea (~0.686). In the case of the superior meridian, it can be seen that the mean gradient of the thickness variation 1 mm from the centre is slightly smaller than the central one, and the value obtained at 2 mm, even though it is bigger, fits in better with the pachymetric variation in the centre of the cornea. The smallest curvature was observed with the first opening of the eye after sleep, with a statistically significant difference when compared with the values obtained throughout the day (ANOVA, method of Tamhane p < 0.05). After an initial increase of the corneal curvature, it remains virtually stable through the day in all the locations of the study. The mean variation of central curvature observed in the period of the study was of 0.07 mm, with the smallest value being at 2 hours after opening the eyes. Table IV shows the values of the para-central measurements of the study.

No statistically significant differences were found between the thickness variations (ANOVA,

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Table I. Percentage of maximum corneal thickness diurnal variation at 1 and 2 mm of the cornea centre in the nasal, temporal, superior and inferior hemi-meridians

<table>
<thead>
<tr>
<th>Location from the centre</th>
<th>Nasal (%)</th>
<th>Temporal (%)</th>
<th>Superior (%)</th>
<th>Inferior (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mm</td>
<td>2.23</td>
<td>2.57</td>
<td>2.13</td>
<td>2.70</td>
</tr>
<tr>
<td>2 mm</td>
<td>2.97</td>
<td>2.80</td>
<td>2.66</td>
<td>3.14</td>
</tr>
</tbody>
</table>

Table II. Variations in corneal thickness at 1 and 2 mm of the cornea centre in the nasal, temporal, superior and inferior hemi-meridians during a 10-hour period after opening the eyes (mean values and range)

<table>
<thead>
<tr>
<th>Location from the centre</th>
<th>Nasal (µm)</th>
<th>Temporal (µm)</th>
<th>Superior (µm)</th>
<th>Inferior (µm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mm</td>
<td>22 (7-32)</td>
<td>22 (13-31)</td>
<td>24 (12-27)</td>
<td>20 (8-26)</td>
</tr>
<tr>
<td>2 mm</td>
<td>19 (10-40)</td>
<td>19 (12-47)</td>
<td>23 (12-36)</td>
<td>16 (13-44)</td>
</tr>
</tbody>
</table>

Table III. Mean gradient of pachymetric descent in paracentral location at 1 and 2 mm of the cornea centre in the nasal, temporal, superior and inferior hemi-meridians

<table>
<thead>
<tr>
<th>Location from the centre</th>
<th>Nasal (µm)</th>
<th>Temporal (µm)</th>
<th>Superior (µm)</th>
<th>Inferior (µm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mm</td>
<td>-0.994</td>
<td>-0.784</td>
<td>-0.603</td>
<td>-1.100</td>
</tr>
<tr>
<td>2 mm</td>
<td>-1.250</td>
<td>-1.247</td>
<td>-0.726</td>
<td>-1.426</td>
</tr>
</tbody>
</table>
Scheffé method, p > 0.05) or curvature variations (ANOVA, Tamhane method p > 0.05) observed in the centre of the cornea and at 1 and 2 mm from the centre in all the hemi-meridians measured. Similarly, no statistically significant differences were found between the thickness variations (ANOVA, Scheffé method p > 0.05) or between the curvature variations (ANOVA, Tamhane method p > 0.05) which were measured in the hemi-meridians of the study. The nasal, temporal, superior and inferior thickness and curvature variations at 1 and 2 mm from the center are shown in figures 3 and 4 respectively.

Table IV shows the results of the statistical analysis comparing the daytime variations in thickness and curvature in the corneal locations of the study. A high degree of correlation was observed between the variations in the center of the cornea (r = 0.983, r² = 0.967, p < 0.001) and in the other locations, excepting the nasal and superior areas at 2 mm from the center.

Table IV. Mean variation and value range of central and para-central curvature at 1 and 2 mm from the centre of the nasal, temporal, superior and inferior hemi-meridians (mm)

<table>
<thead>
<tr>
<th>Location</th>
<th>Central</th>
<th>Nasal</th>
<th>Temporal</th>
<th>Superior</th>
<th>Inferior</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mm</td>
<td>0.07 (0.05-0.1)</td>
<td>0.05 (0.01-0.10)</td>
<td>0.06 (0.03-0.11)</td>
<td>0.07 (0.03-0.11)</td>
<td>0.06 (0.03-0.12)</td>
</tr>
<tr>
<td>2 mm</td>
<td>0.07 (0.02-0.12)</td>
<td>0.07 (0.02-0.16)</td>
<td>0.06 (0.03-0.20)</td>
<td>0.07 (0.05-0.13)</td>
<td></td>
</tr>
</tbody>
</table>

DISCUSSION

The purpose of this study is to contribute to the knowledge about the effect of time on the corneal thickness and curvature in the course of the day. By establishing said changes in the central and para-central areas of the cornea, it would be possible to determine the time in which basal measurements should be taken.

The relevance and implications of knowing the diurnal variations of corneal thickness are particularly important in the clinical evaluation of PRK patients and in candidates for other keratorefractive surgeries. In fact, the most common contraindication for LASIK surgery is reduced central corneal thickness, which is also an important factor in the characteristics of the flap made during the intervention (21,22). Corneal curvature has also been considered in relation to refractive surgery due to its relationship with the thickness and diameter of the flap (23).

In this study, the maximum corneal thickness for all locations was measured immediately after opening the eyes in the morning. This finding matches those of other studies (5-10).

The reduced oxygen supply during sleep leads to anaerobic metabolism which causes and increase in lactic acid production, in turn leading to an increase in osmotic pressure which facilitates the diffusion of water from the aqueous humor to the stroma. This increases the corneal thickness (24). When comparing the corneal thickness obtained during a 10-hour process, we observe a statistically significant variation in all the locations of the study. Even though the mean daytime variation of the observed central corneal thickness (14 µm) was similar to that found by other authors (7,10,25), individual variations could be clinically relevant (range of 9-22 µm).

As can be seen in table III, the magnitude of thickness change and the range of values is larger in para-central data. This fact is also observed when comparing the mean gradient values of the central pachymetric reduction (-0.686) with the values of the nasal, temporal, inferior and superior paracentral data at 2 mm (table III). In the case of the superior meridian, it can be seen that the mean gradient of the thickness variation at 1 mm from the centre is slightly smaller than the central variation, and even when the value obtained at 2 mm is larger, it most closely matches the central value. This can be due to the fact that the superior cornea, both in eye clo-
sed and open conditions, is the area with the largest hypoxic stress, which leads to a smaller thickness reduction in open eye conditions (26-28).

The thickness increase in the periphery of the cornea and the greater thickness variation observed could imply changes in the regulating hydration capacity and in the specific control thereof, indicating the presence of a lateral hydration gradient extending outwardly from the apex (10). The hydration variations throughout the profile of the cornea could be a source of errors with some refractive surgery patients because the diurnal variation in pachymetry could be greater than the amount of tissue eliminated for each dioptre. In addition, many microkeratomes generate meniscus having different thicknesses, and therefore the corneal biomechanic

Fig. 3: Variation of corneal thickness at 1 and 2 mm of the centre of the nasal, temporal, superior and inferior hemi-meridians.
stress could be compromised if in certain locations the residual stroma is very low. If the minimum corneal thickness value is not adequately determined, in theory the measures could yield a higher spurious value, leading to an overestimation which could increase the risk of developing postop kerectasia.

The central and paracentral corneal thickness exhibited their lowest value 10 and 8 hours after opening the eyes. Previous studies have shown that the lowest corneal thickness values are obtained between 5 and 12 hours after opening the eye (7-9,25), in some cases obtaining a corneal thinning exceeding the base value. The differences between studies could be due to differences in the measurement intervals and frequencies. The thinning of the cornea beyond the base value has already been stu-
died (29), and even though its presence is proven it is an aspect of corneal hydration dynamics for which no explanation has yet been found. Odenthal et al (29) suggest that the most likely possibility that the rate of the endothelial pump is not constant and that hypoxic stress may activate a functional reserve in the capacity of the ionic pump delaying its activity at a normal level. When this situation occurs, the corneal thickness could be influenced by other factors such as the blinking frequency, the quality of the lachrymal film and diurnal variation in the production of tears and intra-ocular pressure. This could explain the increased thickness occurring after the cornea reaches its minimum thickness between 8 and 10 hours after the nightly eye closure (29).

In what concerns curvature, our results are consistent with those found by other researchers (7,11,13). Initially, in contrast with Kiely et al (7), we did not observe differences in the daily variations which occur in the horizontal and vertical meridians. Using the eyes in near focus and eyelid pressure could play a relevant role in the daytime changes of corneal curvature (12,30,31). For this reason, it is likely that the results of this study will differ from those found in other studies where the subjects used their eyes in near focus during the measurement period. In addition, in our study the effect of eyelids is not very probable when the measures are taken at 1 and 2 mm from the cornea centre. Read et al (12) suggest a correlation between the amount of work done in near focus and the curvature change values, with possible associated factors being corneal hydration, tear stability, blinking frequency, vertical eyelid aperture and the time elapsed between the near focus ocular activity and the measurement. Even though statistically significant differences between meridians were not observed, Figure 4 shows a curvature increase in the superior and inferior meridians 8 hours after opening the eyes. This finding matches agrees with other studies, which refer an increase in the curvature of the vertical meridian at the end of the day (11,12).

It has been suggested that diurnal corneal curvature thickness variations in normal eyes could be related to changes in the cornea thickness (7,32). MacRae et al (32) found that in normal eyes and in those treated with radial keratotomy there was a relationship between the corneal thickness and changes in its shape. However, they observed that said correlation was not statistically significant when the sample was divided in 3 groups (8 patients per group). In our study, the statistical analysis shows a strong correlation between corneal thickness and curvature changes (table V). These results can be seen graphically in the similarity existing between figures 2 and 4, and match other studies which include normal and radial keratotomy corneas (32,33). On the other hand, Kwitko et al (34), did not observe said correlation considering it was due to the small number of subjects in their sample, which limited statistical analysis and the detection of statistical correlations. Surprisingly, with the same sample size of Kwitko et al (34), we obtained statistical significance with a similar tendency to that found by MacRae et al (32) in which, when the thickness of the cornea is reduced, the curvature is increased. This relationship between thickness and curvature could be due to the greater thickness reduction which takes place in the para-central area of the cornea when compared to the centre. In other words, said difference in the thickness reduction could be the cause of the observed curvature increase.

REFERENCES