# EFFECT OF DOUBLE ANAESTHETIC COLICURSI® (TETRACAINE 0.1% AND OXIBUPROCAINE 0.4%) ON CENTRAL AND PARACENTRAL CORNEAL THICKNESS

# EFECTO DE LA INSTILACIÓN DEL COLICURSI® ANESTÉSICO DOBLE (TETRACAÍNA 0,1% Y OXIBUPROCAÍNA 0,4%) SOBRE EL ESPESOR CORNEAL CENTRAL Y PARACENTRAL

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## ABSTRACT

**Objective:** To study the effect of 1 drop of combined topical anaesthesia (tetracaine 0.1% and oxybuprocaine 0.4%) on central corneal thickness (CCT) values and at 2.5 mm from the corneal centre in nasal, temporal, superior and inferior hemi meridians, monitored by Orbscan over a period of 16 minutes.

**Materials and methods:** The corneal thickness of 12 right eyes of 12 young healthy men was determined using the Orbscan Topography System. Values were determined at the centre and paracentral regions 2.5 mm from the centre every 2 minutes for 16 minutes before and after the administration of 1 drop of double anaesthetic Colircusi® which contains tetracaine 0.1% and oxybuprocaine 0.4%.

**Results:** There was no obvious trend of central and paracentral corneal thickness value change before and after administration of Colircusi® (paired ANOVA, p>0.05). Although corneal thickness variation was not statistically significant, higher differences were observed at the 6 minute time-

## RESUMEN

**Objetivo:** El objetivo del presente trabajo es estudiar el efecto sobre el espesor corneal central (ECC) y paracentral a 2,5 mm del centro en los hemimeridianos nasal, temporal, superior e inferior, de la anestesia tópica en la que se combinan el clorhidrato de tetracaina 0,1% y el clorhidrato de oxibuprocaina 0,4%.

**Material y método:** Se determinó el espesor corneal central y paracentral a 2,5 mm del centro de la córnea en los ojos derechos de 12 varones jóvenes mediante Orbscan. Las medidas se realizaron cada dos minutos durante un periodo de 16 minutos previo y posterior a la instilación del anestésico.

**Resultados:** El análisis estadístico muestra que no existe variación en el espesor corneal central y paracentral antes y después de la instilacion del anestésico Colircusi® anestésico doble con clorhidrato tetracaina 0,1% y clorhidrato de oxibuprocaina 0,4% (ANOVA para medidas repetidas, p>0,05). Aunque no fueron estadísticamente significativas la

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point for CCT and at 8 minutes for nasal paracentral corneal thickness.
**Conclusions:** One drop of double anaesthetic Colircusi® with tetracaine 0.1% and oxibuprocaine 0.4% does not produce any significant change in central corneal thickness or in paracentral regions 2.5 mm from the centre (nasal, temporal, superior and inferior hemi meridians) *(Arch Soc Esp Oftalmol 2009; 84: 23-30).*

**Key words:** Cornea, corneal thickness, pachymetry, tetracaine, oxybuprocaine, topical anaesthesia.

mayor variación de espesor se observa para el ECC a los 6 minutos y para el paracentral a los 8 minutos en el hemimeridiano nasal.
**Conclusiones:** Una gota de Colircusi® anestésico doble con clorhidrato tetracaina 0,1% y clorhidrato de oxibuprocaina 0,4% no produce una variación significativa del ECC ni paracentral a 2 mm del centro en los hemimeridianos nasal, temporal, superior e inferior.

**Palabras clave:** Córnea, espesor corneal, paquimetría, tetracaina, oxibuprocaina, anestesia tópica.

## INTRODUCTION

Corneal thickness is a marker of ocular health and integrity. Variations in this thickness indicate the metabolic condition of the cornea. An increased thickness could be linearly correlated with increased hydration (1). It is an outstanding indicator to assess the success or failure of the adaptation of contact lenses. It is also crucial in diagnosing some corneal pathologies, and for the pre-surgical evaluation and follow-up of refractive surgery as well as for the effect of some ocular and systemic medications have on the corneal thickness.

Topical corneal anesthesia is utilized in a number of visual explorations such as ultrasound biometry, applanation tonometry and ultrasound pachymetry. Previous studies on the effect of various topical anesthetics on corneal thickness made with several pachymetric studies focused on the central corneal thickness (CCT) with different results: while in some cases the patients exhibited a temporary corneal thickness increase, others did not find significant variations in the CCT (2-5). As regards the para-central thickness variations induced by topical anesthesia, Asensio et al (6) observed with the Orbscan that there were not significant variations in corneal thickness 3 minutes after applying 0.4% oxybuprocaine.

The objective of the instant paper is to study the effect of topical anesthesia combining tetracaine clorhydrate 0.1% and oxybuprocaine clorhydrate 0.4% on the central and para-central corneal thickness, establishing the following thicknesses; nasal (NCT), temporal (TCT), superior (SCT) and inferior (ICT) at 2.55 mm from the centre in the nasal half-meridians (NCT). This was done utilizing Orbscan, an instrument widely utilized in ophthalmological practice in Spain.

## SUBJECTS, MATERIAL AND METHOD

Twelve young men participated in the study (mean age 22.5 years) having refraction values between +2,00 D and –3,00 D, corneal astigmatism was under 1,00 D, and with a visual acuity equal to or above 20/20. All the subjects were healthy, without contact lens or ocular surgery history and were not receiving any type of topical or systemic medication. In order to avoid hormonal effects on the corneal thickness and curvature (7) no women were included in the study sample. This study was carried out in accordance with the ethical standards set in the Helsinki declaration. After explaining the procedures to the patients they were asked to sign the informed consent.

The anesthetic utilized in this study was Colircusi ® dual anesthetic with tetracaine tetracaine clorhydrate 0.1% and oxyburpocaine clorhydrate 0.4%, agents which are usually utilized at 0.5% and 0.4% respectively when administered as the sole anesthetic agent. The preserving agent in said anesthetic was chlorbutanole.

The thickness data were determined by Orbscan II® optical scan pachymetry at the corneal centre and in 4 para-central locations, i.e., 2.5 mm nasal. 2.5 mm temporal. 2.5 mm superior and 2.5 mm inferior from the centre of the cornea.

**Table I. Mean value in µm (mean ±SD) of central and paracentral corneal thickness (nasal, temporal, superior and inferior at 2.5mm from the cornea centre) in a sample of n=12 subjects before and after the administration of anesthetic (base value) at 2- minute intervals**

| | *Central* | *Nasal* | *Temporal* | *Superior* | *Inferior* |
|---|---|---|---|---|---|
| Basal | 558 SD 43 | 647 SD 43 | 591 SD 32 | 649 SD 39 | 620 SD 43 |
| 2 minutes | 556 SD 44 | 644 SD 48 | 592 SD 34 | 653 SD 44 | 614 SD 45 |
| 4 minutes | 557 SD 45 | 647 SD 42 | 589 SD 33 | 649 SD 42 | 621 SD 44 |
| 6 minutes | 554 SD 44 | 642 SD 45 | 588 SD 36 | 642 SD 45 | 620 SD 46 |
| 8 minutes | 556 SD 43 | 640 SD 42 | 590 SD 32 | 650 SD 39 | 618 SD 40 |
| 10 minutes | 555 SD 44 | 646 SD 43 | 595 SD 39 | 648 SD 33 | 616 SD 49 |
| 12 minutes | 555 SD 46 | 636 SD 61 | 599 SD 32 | 645 SD 45 | 617 SD 39 |
| 14 minutes | 557 SD 42 | 643 SD 48 | 595 SD 34 | 645 ±43 | 617 SD 45 |
| 16 minutes | 556 SD 44 | 640 SD 49 | 595 SD 33 | 644 ±45 | 624 SD 50 |

SD: Standard Deviation.

First, the central and para-central corneal thickness were determined without anesthetic, for 16 minutes at 2-minute intervals, after which one drop of anesthetic was administered (tetracaine at 0.1% and oxibupracaine clorhydrate at 0.4%, dual anesthetic Colircusí, Alcon Cusí SA, Barcelona). Subsequently, pachymetry was performed again with Orbscan every 2 minutes for a 16-minute period after instillation.

For the statistical analysis of the influence of the anesthetic on the central and para-central corneal thickness, the SPSS® Professional Statistics 14.0. (SPSS for Windows, Chicago, Illinois, USA) computer application was used. To study the corneal thickness variations during the 16 minutes prior to the anesthetic, or any spontaneous variations, an ANOVA test was applied for repeated measurements in the central area and for each of the para-central areas, establishing in each case the base corneal thickness value. To study the corneal thickness variations after instilling the anesthetic, we compared the base value with all the thickness values at each point utilizing once again the ANOVA test for repeated measurements. The central tendency parameters were the mean and standard deviation (SD). In addition, to obtain 95% of probability of the thickness variations, we also determined the interval of 95% of the differences (IC 95%), by means of the expression: *mean ± 1.96 X SD* . The statistically significant level of this study was established at 5% ($p \leq 0.05$).

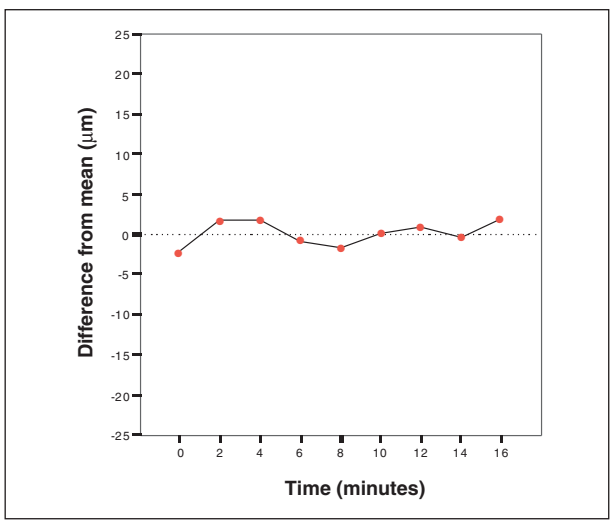


*Fig. 1: Mean spontaneous variation of CCT, measured every 2 minutes during a period of 16 minutes prior to instilling the anesthetic.*

## RESULTS

The analysis of thickness variations in corneal locations studied during the 16-minute interval prior to the administration of anesthetic shows the absence of variation in the central and para-central corneal thickness during said period (ANOVA of one factor for repeated measurements, $p>0.05$). Therefore, fore each subject and each corneal area we considered the mean values obtained during the period prior to administration of the anesthetic as the base value, against which we compared the successive thickness values after instilling the anesthetic (table I). The minimum and maximum para-central corneal thickness values were observed at the temporal and superior locations respectively. The spontaneous central and para-central corneal thickness variations are shown in Figures 1 and 2, respectively.

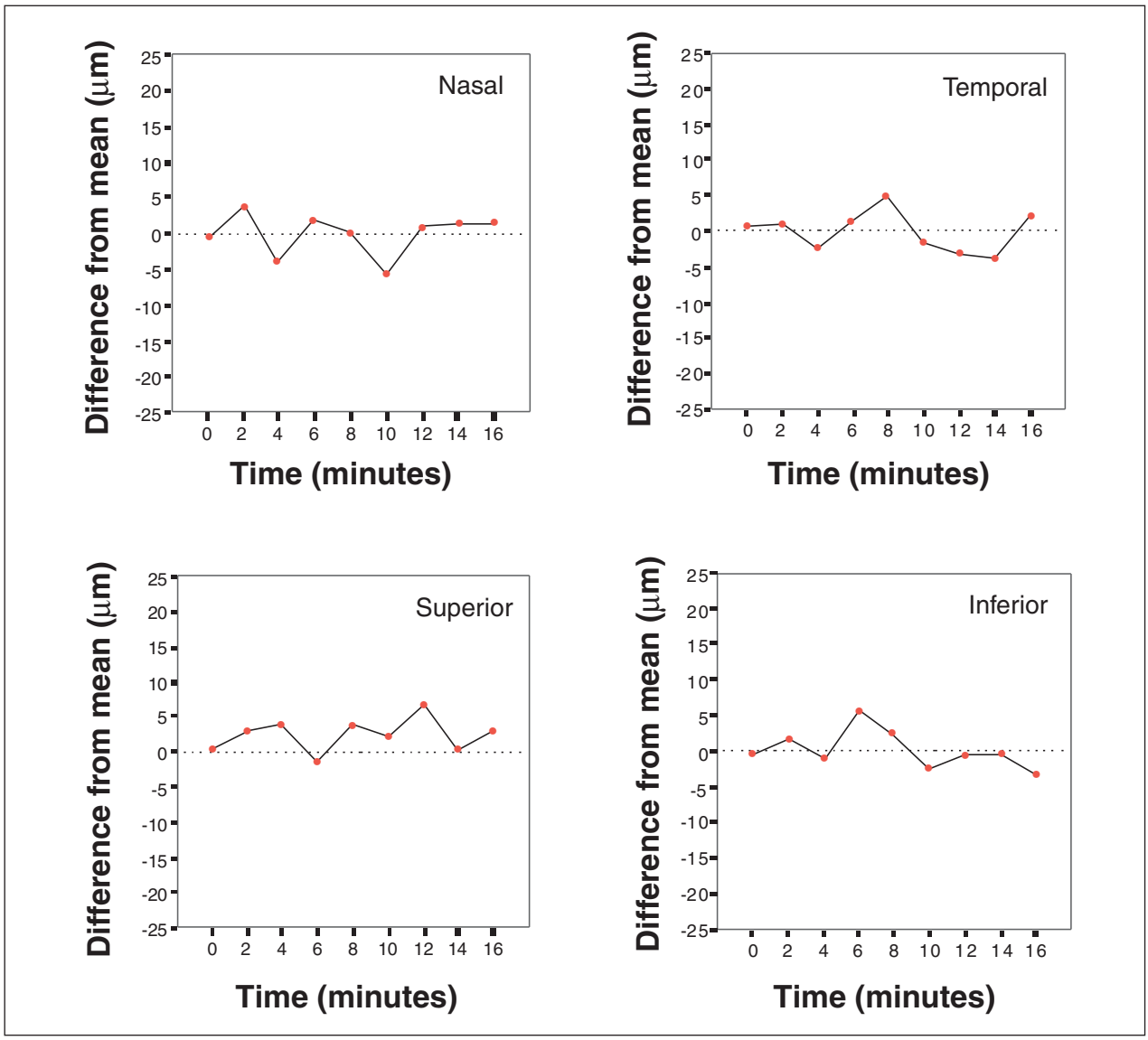


*Fig. 2: Mean spontaneous variation of NCT, TCT, SCT and ICT, measured every 2 minutes during a period of 16 minutes prior to instilling the anesthetic.*

Table I also shows the mean values for each corneal location, obtained at 2-minute intervals for a 16-minute period after instillation of Colircusi ® dual anesthetic with tetracaine clorhydrate 0.1% and oxyburpocaine clorhydrate 0.4%.

No statistically significant differences were found for each corneal area between the base values and those obtained after administration of the anesthetic in any of the measured times (ANOVA for repeated measurements, $p>0.05$). Table II shows the mean variation and the 95% CI corresponding to each measurement for the central and para-central corneal thickness. It can be seen that the largest variation is for the CCT at 6 minutes and at 8 for the para-central in the nasal half-meridian. The graphical representation of the variations (mean, SD) in the 16 minutes after the administration of the dual anesthetic (oxyburpocaine 0.1% and tetracaine 0.4%) are shown in figures 3 for the CCT and figure 4 for the para-central corneal thickness.

**Table II. Mean difference (μm) and CI of 95% for base CCT and para-central base (NCT, TCT, SCT and ICT) corresponding to 12 subjects with the values obtained at different times after administration of the anesthetic**

| | CCT | NCT | TCT | SCT | ICT |
|---|---|---|---|---|---|
| 2 min | –1.08 SD 9.25 | –2.54 SD 18.79 | 0.82 SD 19.54 | 5.00 SD 17.70 | –5.17 SD 19.93 |
| 4 min | –0.50 SD 10.59 | –1.90 SD 19.82 | –2.09 SD 22.03 | 1.54 SD 19.31 | 1.83 SD 17.14 |
| 6 min | –3.17 SD 6.62 | –3.90 SD 17.20 | –2.09 SD 15.09 | –1.91 SD 25.79 | 0.083 SD 14.80 |
| 8 min | –1.17 SD 13.55 | –6.90 SD 17.34 | –1.73 SD 17.81 | 0.45 SD 21.10 | –1.33 SD 20.54 |
| 10 min | –2.42 SD 12.32 | 0.45 SD 14.83 | 4.18 SD 23.74 | –3.00 SD 21.49 | –3.83 SD 22.56 |
| 12 min | –2.25 SD 12.48 | –5.18 SD 20.09 | 4.00 SD 21.52 | –2.09 SD 21.78 | –2.25 SD 18.61 |
| 14 min | –0.92 SD 8.42 | –3.36 SD 18.32 | 5.36 SD 18.03 | –2.54 SD 22.04 | –2.42 SD 25.48 |
| 16 min | –1.17 SD 15.45 | –6.09 SD 22.99 | 5.45 SD 20.91 | –6.27 SD 23.55 | 4.00 SD 27.17 |

SD: Standard deviation.

## DISCUSSION

The base CCT value found in this study (558 SD 43 μm) is close to the value found by other authors (3,5,6,8) and even though it differs from other studies (2,4), the difference could be due to different measurement procedures as well as the differences in the study samples. As regards the base corneal thickness observed at 2.5 mm from the centre of the nasal, temporal, superior and inferior cornea, the values of our study match those referred by other authors who also used the Orbscan (6,8), with the lowest thickness being at the temporal location and the highest thickness at the superior area. In what concerns the usefulness of the Orbscan for measuring corneal thickness, previous studies have demonstrated that the Orbscan provides higher values than optical and ultrasonic pachymeters (9,10). However, Marsich and Bullimore (9) observed that the Orbscan exhibited repeatability in central (CI 95% from–10 to +17 μm), as well as peripheral measurements, better than optical and ultrasound pachymetry. Its usefulness has also been demonstrated for measuring corneal thickness in research and clinical practice (11,12). On the other hand, Cho and Cheung (13) observed CIs of 95% similar to those obtained by Marsich and Bullimore (9) as regards the CCT, they questioned the clinical application of said instrument when finding CI of 95% in the temporal, superior and inferior para-central locations of between 25 and 30 for the upper limit and –27 and –34 for the lower one. Said intervals were greater in the nasal location. This means that thickness variations of 30 microns, measured with the Orbscan, may not indicate an actual change.

Topical corneal anesthesia is utilized in different visual explorations such as ultrasound biometry, Goldmann's applanation tonometry and ultrasound pachymetry. In addition, the effect of topical anesthetics on the corneal thickness is important in assessment s prior to refractive surgery because the corneal thickness is one of the main parameters to be considered in prescribing this type of surgery. Previous studies indicate that the residual corneal thickness after ablation is a critical factor in the development of a post-surgery corneal ectasia, which would produce an increased myopia, irregular astigmatism and visual acuity reduction (14-16).

Even though the effect of anesthetics on the corneal epithelium, stroma and endothelium is well known with the ensuing edema, in our study we did not encounter said effect. It was observed that the Colircusi ® dual anesthetic with tetracaine clorhydrate 0.1% and oxyburpocaine clorhydrate 0.4% hardly influences the corneal

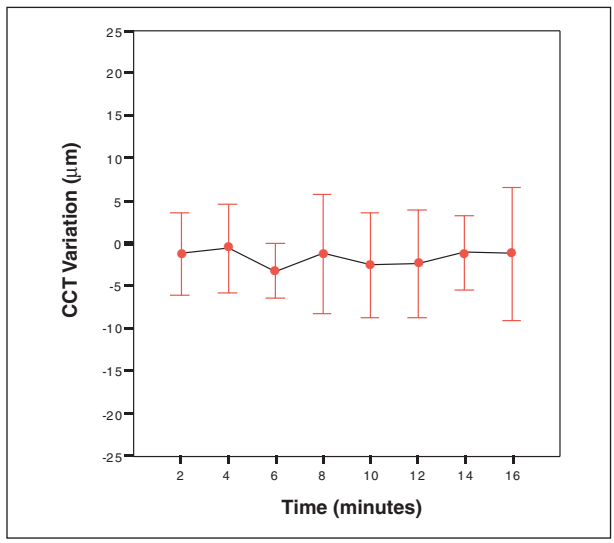


*Fig. 3: CCT Variation (mean ± SD), measured every 2 minutes during a period of 16 minutes after instilling the anesthetic.*

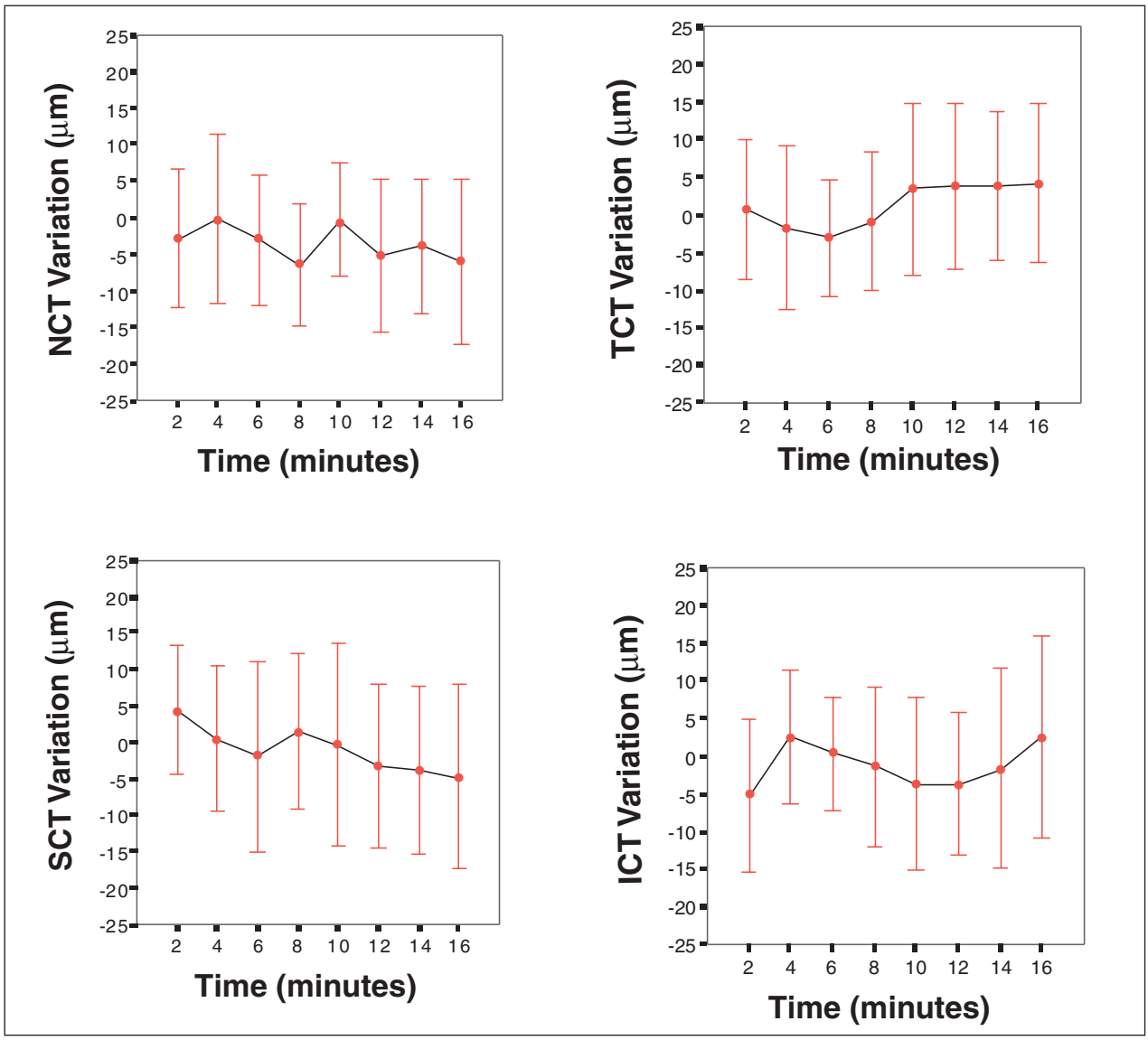


*Fig. 4: Variation of NCT, TCT, SCT and ICT (mean ± SD), measured every 2 minutes during a period of 16 minutes after instilling the anesthetic.*

thickness because no statistically significant differences were found in the central and para-central corneal thickness when instilling anesthetic. Herse and Siu (2), observed that a drop of propacaine 0.5% caused a slight CCT increase which recovered in 2 minutes. This effect became statistically significant when instilling 2 drops of said anesthetic (an increase of approximately 15 microns). Said authors attributed this increase (which took 8-10 minutes to recover) to a temporary edema of the corneal stroma (2). Also utilizing the Orbscan, Alemán et al (3) studies changes in corneal thickness after applying tetracaine 0.5%, and observed a corneal thickness increase of 9.4 microns, slightly greater to that found by Herse and Siu (2) after the administration of one drop of propacaine. Nam et al (4) applied mirror microscopy to measure the CCT and found that both benoxinate 0.4% and propacaine at 0.5% produced a mean temporary increase of 9 microns in the CCT. Even though this value returned to base within 80 seconds, the observed an equally temporary increase 5 minutes after instilling propacaine. They observed that the corneal thick-

ness is unstable during the 5 minutes after the instillation of propacaine but not in the case oxyburpocaine, probably due to edema or lachrymal film instability. In accordance with the results of our study, Lam et al (5) did not observe any tendency in CCT changes measured with Pentacan and mirror microscopy after the administration of one drop of propacaine 0.5%. The thickness variations from base values were under 5 microns. In this study, the mean CCT variation is also under 5 microns, which matches the findings of Lam et al (5). However and on the basis of the CI of 95% (Table II), a greater variability in the results was observed. This could have been due to the lower number of subjects in this study.

As regards the effect of anesthetics on the para-central corneal thickness, our findings match those of Asensio et al (6) who, utilizing Orbscan, studied the influence of two drops of oxybupracaine 0.4% on the corneal thickness at the cornea centre and at 3 mm from the visual axis in the nasal, temporal, upper temporal, lower temporal, super nasal and lower nasal locations. Although in some subjects they observed an important thinning and in other a thickening of the cornea, the corneal thickness changes were not statistically significant. In this study, the dual anesthetic Colicursi did not produce statistically significant variations in the para-central corneal thickness (ANOVA for repeated measurements, $p>0.05$), although the range corresponding to the CI of 95% (Table III) is greater than that observed in the central measurements. In fact, the variations observed in some cases and/or measurement times are close to the 95% CI found by Cho and Cheung (13) in corneal thickness measurements with Orbscan. Accordingly, the results must be interpreted with some caution.

The possible adverse pharmacological effects of topical anesthetics include reduction of tear stability, lachrymal secretion alterations, epithelial and endothelial toxicity, microbial contamination and allergic reactions (17). In the case of oxybuprocaine and tetracaine the side effects were infrequent and, even though toxicity was rare, some reactions could be a burning feeling, descaling of the corneal epithelium and allergic symptoms (6). In addition, the preservatives utilized in ophthalmological solutions can also cause lachrymal instability and structural/functional alterations at the epithelial and/or endothelial levels of the cornea (18,19). The anesthetic utilized in this study, dual Colircusi ®, the preservative is chrlobutanole which has minimum effects on the cornea and conjunctiva, above all compared with those produced by benzalconium chloride (20.21).

By way of conclusion, one drop of dual Colircusi ® anesthetic with tetracaine clorhydrate 0.1% and oxyburpocaine clorhydrate 0.4% does not cause a significant variation of the central and para-central corneal thickness, measured at 2.5 mm from the centre in the nasal, temporal, superior and inferior hemi-meridians.

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