Biomechanical corneal response measurement after manual insertion of intrastromal rings in patients with keratoconus

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PURPOSE: To evaluate the changes in corneal hysteresis before and after the insertion of intrastromal rings in keratoconic eyes.

SETTING: Fundación Oftalmológica del Mediterráneo. Cornea and Refractive Surgery Unit, FOM, Valencia, Spain.

MATERIAL AND METHODS: We studied 27 eyes with keratoconus: seven of them were stage II, fourteen stage III, and six stage IV, according to the Amsler-Krumeich classification. Two Keraring® rings (Mediphacos) were implanted in four eyes, while only one ring was implanted in the rest of the eyes. The following was analysed: visual acuity with and without correction, keratometry, pachymetry, and the corneal biomechanical parameters determined by the Ocular Response Analyzer Reichert (ORA), among which were: corneal compensated intraocular pressure (IOPcc), intraocular pressure correlated with Goldmann (IOPg), overall corneal resistance factor (CRF), and corneal hysteresis (CH). The determinations were performed before surgery and three months after intrastromal ring implantation.

RESULTS: Mean visual acuity improved from 0.41 ± 0.21 preoperatively to 0.58 ± 0.18 three months postoperatively (p<0.01). The mean keratometric values decreased. At three months of follow-up, the K1 value changed from 48.55 ± 4.58 preoperatively to 45.69 ± 4.42 (p<0.01). Likewise, the K2 went from 54.07 ± 5.91 to 51.01 ± 5.64 (p<0.01). The difference between spherical, cylindrical, and axial refraction values, preoperatively and postoperatively was not statistically significant (p>0.01). Changes in central pachymetry of the cornea prior to and post implantation of the rings were not statistically significant either (p>0.01). Comparing the preoperative and postoperative values obtained by the ORA, the OIPcc, the IOPg, the CRF and the CH values were higher, but not statistically significant (p>0.01).

CONCLUSIONS: The ORA performs determinations at the centre of the cornea, not at the periphery where the rings are inserted, therefore it does not appear to be able to predict the biomechanical changes in this area. By knowing the differences in IOPcc, IOPg, CRF, and CH with regard to the depth of the insertion of the ring, we can predict the postoperative IOPcc, IOPg, CRF, and CH values.

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INTRODUCTION

Keratoconus is a corneal ectasia characterised by progressive thinning and protrusion of the central and paracentral cornea1-5 that gives rise to irregular myopic astigmatism and a decrease in visual acuity. It is generally a bilateral process, however it presents and develops asymmetrically6,7.

The cornea of patients with keratoconus has a weakened, softer structure than normal, therefore keratoconic eyes can undergo applanation more easily than myopic eyes8,11.
Many studies published in the literature guarantee the efficacy of intrastromal rings in the treatment of myopia by ablation of the corneal centre. Consequently, it was thought that the ocular surface of patients with keratoconus could be flattened, made regular, and stabilised, and in this way delay corneal transplantation. Intracorneal rings could be an additional technique that would reinforce the cornea and delay progressive thinning in patients with ectasia.

Although intracorneal rings in the treatment of corneal ectasias have proved to be effective from the clinical viewpoint, we cannot tell to what degree they reinforce the cornea biomechanically. The Ocular Response Analyzer Reicerrt (ORA) uses a dynamic bidirectional applanation process to determine the intraocular pressure (IOP) of the eye and a corneal biomechanical properties indicator called Corneal Hysteresis (CH), which is the result of the viscous property of the corneal tissue. Determination of the CH provides a basis for two other new parameters, the corneal compensated intraocular pressure (IOPcc) and the corneal resistance factor (CRF).

The purpose of the present study was to compare the significant changes in the corneal biomechanical properties before and after the intrastromal rings surgery.

**MATERIAL AND METHODS**

There are several models of commercialised intracorneal rings, depending on their geometric shape, implant area, material, etc... All the rings used in this study are manufactured by Keraring® (Mediphacos). They are made of an acrylic material called Perpex CQ (Polymethylmethacrylate, PMMA) and have a triangular transversal section. The base of the triangle is 600 µm for all thicknesses and diameters, and it is inserted deeper down and very close to the corneal endothelium.

Its thickness varies between 150 and 350 microns, increasing in steps of 50 microns. Several arch length measurements are also commercialised: 90°, 120°, 160°, and 210°. These rings are implanted forming a 5 mm diameter at approximately 2.5 mm from the optic centre.

Twenty-seve eyes of 27 patients with keratoconus were studied, 7 of them with stage II, 14 with stage III, and 6 with stage IV according to the Amsler-Krumeich classification (Table 1). The nomogram used for Keraring-Ferrara ring implantation is based on the distribution of the ectasic area (EA) and the spherical equivalence (SE) (Table 2).

The refraction, visual acuity, keratometry, pachymetry and the IOPcc, IOPg, CRF and CH measurements were determined both preoperatively and three months after intrastromal ring implantation.

The refraction was measured using the power vector method of Thibos and Horner, any spherocylindrical refractive error can be expressed by 3 dioptric powers: M, J₀, and J₄5; M is a spherical lens equal to the spherical equivalent of the given refractive error, and J₀ and J₄5 are Jackson crossed cylinders equivalent to the conventional cylinder. These numbers are the coordinates of a point in a 3-dimensional dioptric space, being the power vector, the vector from the origin of this space to the point (M, J₀, J₄5).

Thus, the length of this vector is a measure of the overall blurring strength (B) of a spherocylindrical refractive error. Manifest refractions in conventional script notation (S [sphere], C [cylinder] x α [axis]) were converted to power vector coordinates according with the distribution of the ectasic area (AE) and the spherical equivalence (SE) (Table 2).

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The refraction was measured using the power vector method of Thibos and Horner, any spherocylindrical refractive error can be expressed by 3 dioptric powers:
Goldmann’s Applanation Tonometry (GAT)\textsuperscript{17}. Basically, IOPcc is not correlated with the corneal central thickness (CCT) in normal eyes and it remains relatively constant after LASIK surgery.

\textbf{IOPg:} Goldman-correlated intraocular pressure (mean of 2 IOP measurements).

\textbf{CRF:} Indicator of the overall resistance of the cornea. It is significantly correlated with the corneal central thickness (CCT) and with Goldmann’s applanation tonometry (GAT), but not with intraocular pressure compensated according to the cornea (IOPcc).

\textbf{CH:} Measurement of the viscose property of the corneal tissue. Is calculated as the difference between the 2 pressure values at the 2 applanation processes.

\section*{SURGICAL TECHNIQUE}

Surgery on all the eyes was performed manually under topical anaesthesia. The first step in this technique consists of locating the geometric centre of the cornea and marking it with a Sinskey hook. The reflection of the microscope light is used as a reference point. Then the optical areas required are marked forming a 5 mm diameter with a circular Ferrara marker using methylene blue dye so as to create two concentric circles which indicate the ideal position of the insertion canal of the rings\textsuperscript{18}. The radial incision is made with a calibrated square-edged diamond blade, at a depth of 80\% of the local corneal thickness. It is advisable to perform an intrastromal pocket dissection initially to increase the depth of the tunnel using a Suárez spatula and thus facilitate the insertion of a Ferrara spatula which will create two concentric stromal tunnels with an internal curvature radius of 2.5 mm where the rings are implanted. The incisions were sealed in all cases by hydrosuture with a lacrimal cannula. Topical corticoids, antibiotics, non-steroid anti-inflammatory drugs, and artificial tears were applied postoperatively. A therapeutic soft contact lens was applied to the eye for 48 hours.

\section*{STATISTICAL ANALYSIS}

The mean values of these data, with their standard deviations, were determined with the Microsoft Excel (Windows) program, as was the statistical analysis. The T-Test was used; this calculates the probability associated with Student’s T-test as the population sample was relatively small. Data that presented a $p < 0.01$ were considered statistically significant.

\section*{RESULTS}

Two rings were implanted in four eyes of patients included in the study, while one single ring was implanted in the rest. The total of Keraring rings implanted was 31, all with a 160° arch length, with a mean thickness of $220 \pm 44.72 \mu m$, and inserted at a mean depth of $395.74 \pm 35.49 \mu m$.

The results were analysed in terms of refraction, visual acuity, keratometry, pachymetry, and the aforementioned ORA parameters. Table 3 shows the results obtained after determining the preoperative measurements and postoperative measurements after the ring implantation.

Table 4 shows the determinations registered by the ORA both prior and after surgical implantation of the intrastromal rings.

\section*{Refractive Measuremen}

The difference between the pre- and postoperative refraction values (spherical, cylindrical, and axial) and vectorial values ($M$, $J_0$, and $J_{45}$) are not statistically significant ($p>0.01$). According to our results, there is no improvement in the patients’ refraction after Keraring ring implantation.

\section*{Visual Acuity}

The mean best corrected visual acuity (BCVA) went from $0.41 \pm 0.21$ preoperatively to $0.58 \pm 0.18$ three months after surgery ($p<0.01$). Visual acuity improved 41\% postoperatively.

\begin{table}[h]
\centering
\begin{tabular}{|l|c|c|c|c|c|c|c|c|}
\hline
& \textbf{PRE} & & & \textbf{POST} & & & \\
& \textbf{MEAN} \pm \textbf{SD} & \textbf{FROM} & \textbf{TO} & \textbf{MEAN} \pm \textbf{SD} & \textbf{FROM} & \textbf{TO} & \\
\hline
\textbf{SPHERE (D)} & $-3.96 \pm 4.58$ & 2.75 & $-14.50$ & $-3.01 \pm 4.33$ & 4.75 & $-15.50$ & \\
\textbf{CYLINDER (D)} & $-3.84 \pm 3.20$ & 5.25 & $-11.00$ & $-2.43 \pm 1.53$ & 0.00 & $-5.75$ & \\
\textbf{AXIS (°)} & $69.30 \pm 53.57$ & 170.00 & 0.00 & $90.37 \pm 60.32$ & 180.00 & 0.00 & \\
\textbf{M} & $-5.88 \pm 5.12$ & 2.63 & $-17.50$ & $-4.22 \pm 4.30$ & 4.00 & $\pm 16.00$ & \\
\textbf{J0} & $0.29 \pm 1.52$ & 2.89 & $-2.88$ & $-0.04 \pm 1.00$ & 1.84 & $-2.11$ & \\
\textbf{J45} & $0.08 \pm 1.99$ & 4.76 & $-3.57$ & $0.08 \pm 1.05$ & 2.83 & $-2.11$ & \\
\textbf{B} & $6.66 \pm 4.75$ & 17.76 & 0.00 & $5.00 \pm 3.62$ & 16.01 & $0.73$ & \\
\textbf{BCVA} & $0.41 \pm 0.21$ & 0.80 & 0.05 & $2.28 \pm 8.92$ & 46.90 & 0.20 & \\
\textbf{k1 (D)} & $48.55 \pm 4.58$ & 59.00 & 42.75 & $46.46 \pm 2.88$ & 53.00 & $39.40$ & \\
\textbf{k2 (D)} & $53.07 \pm 5.91$ & 65.75 & 44.25 & $51.08 \pm 5.50$ & 65.75 & $42.75$ & \\
\textbf{PACHYMETRY (µm)} & $455.37 \pm 62.34$ & 561.00 & 277.00 & $454.74 \pm 73.08$ & 588.00 & $263.00$ & \\
\hline
\end{tabular}
\caption{Comparison of pre- and post-operative results}
\end{table}
Keratometry

Postoperative keratometry decreased significantly after ring implantation. The mean K1 values went from $48.55 \pm 4.58$ preoperatively to $45.69 \pm 4.42$ (p<0.01) three months after surgery, and K2 values went from $54.07 \pm 5.91$ to $51.01 \pm 5.64$ (p<0.01) also three months postoperatively. There was a 6% reduction in the case of K1 and a 5.5% reduction in the case of K2, which means that implantation of Keraring rings appears to be effective in flattening the corneal surface.

Pachymetry

Central corneal pachymetry was determined prior to and after implantation of the rings using the Ilz Orbscan topographer. The difference did not prove to be statistically significant as the value was p>0.01 (Figure 1).

Biomechanical values (ORA)

The postoperative results obtained from the ORA regarding IOPcc, IOPg, CRF, and CH are higher preoperatively than three months after intracorneal rings implantation, however they cannot be considered as statistically significant (p>0.01) (Figure 2).

Table 4: Comparison of pre- and post-operative results of the determinations provided by the ORA

<table>
<thead>
<tr>
<th></th>
<th>MEAN ± SD</th>
<th>PRE FROM</th>
<th>TO</th>
<th>MEAN ± SD</th>
<th>POST FROM</th>
<th>TO</th>
</tr>
</thead>
<tbody>
<tr>
<td>IOPcc (mmHg)</td>
<td>13.83 ± 2.96</td>
<td>19.70</td>
<td>6.30</td>
<td>15.66 ± 4.60</td>
<td>27.30</td>
<td>6.40</td>
</tr>
<tr>
<td>IOPg (mmHg)</td>
<td>10.11 ± 3.25</td>
<td>17.00</td>
<td>2.90</td>
<td>12.25 ± 5.75</td>
<td>35.50</td>
<td>7.50</td>
</tr>
<tr>
<td>CRF (mmHg)</td>
<td>6.65 ± 2.30</td>
<td>12.20</td>
<td>2.90</td>
<td>7.50 ± 3.46</td>
<td>21.00</td>
<td>3.50</td>
</tr>
<tr>
<td>CH (mmHg)</td>
<td>7.91 ± 2.16</td>
<td>12.90</td>
<td>4.70</td>
<td>8.18 ± 2.95</td>
<td>17.30</td>
<td>3.70</td>
</tr>
</tbody>
</table>

Implantation of 1 or 2 rings

The IOPcc, IOPg, CRF, and CH values provided by the ORA prior to and after implantation of one ring (Figure 4) did not undergo significant changes, the same as the eyes with two rings implants, where the values were not statistically significant (p>0.01) (Figure 5).

Moreover, we compared these postoperative values in the case of having one or two rings and the changes in this case were not statistically significant either.

ORA versus Depth values

We studied the connection that exists between the depth at which the intrastromal rings are inserted and the differences in IOPcc, IOPg, CRF, and CH values. The deeper the ring was inserted, the greater the difference there was between the preoperative and postoperative IOPcc values. However, the difference between
the IOPg values decreased when the rings were inserted deeper. The changes in the CRF and CH values also decreased as the depth at which the ring was inserted became greater, as shown in Figures 6, 7, 8, and 9.

The dispersion of the data should be noted as it is considerable. The R2 values are very low.

**ORA versus thickness values**

Finally, we decided to analyse the connection between the ORA values and the thickness of the ring that was inserted. Since all the rings in this study had the same arch length (160º), the differences between said values, depending on the thickness of the ring inserted, did not prove to be statistically significant (p>0.01) (Figures 10 and 11).
DISCUSSION

The human cornea is a viscoelastic tissue that can be described by two main properties: a static resistance component (characterized by the corneal resistance factor – CRF) for which deformation is proportional to applied force and a dynamic resistance component (characterized by corneal hysteresis – CH) whose relation between deformation and applied force depends on time. The tissue response in the presence of a force does not only depend on the force magnitude, but also on the speed of the force application.

The ORA not only provides corneal biomechanical values, but also IOPcc values (an intraocular pressure that is less affected by the corneal properties than other methods of tonometry, such as Goldmann’s Applanation Tonometry) and IOPg values (a repeatable value of the intraocular pressure correlated with Goldmann’s).

Some studies have shown that subjects with keratoconus, Fuchs’ dystrophy or who had undergone corneal refractive surgery presented significantly decreased corneal hysteresis when compared with normal subjects. This value is used to obtain the compensated IOP with the ORA and is independent of the IOP obtained with Goldmann’s tonometry.

In our study, these corneal properties were determined prior to and after insertion of Keraring rings in a sample of 27 keratoconic eyes.

BCVA improved 41% after insertion of the rings in this analysis. Published results bear out the efficacy of this surgical procedure in the improvement of visual acuity. Miranda et al. gained two or more lines of corrected visual acuity in 87.1% of their cases at twelve months in a series of 36 eyes; similarly, Kwitko et al. also obtained an 86.4% improvement in their cases. Largely outcomes vary according to the evolutionary degree of the keratoconus. BCVA significantly improved in 68.3% of cases in the Colin and Malet study and remained stable (within 2 lines) between 1 year and 2 years in almost 90% eyes. In the Piñero et al. study the 38.89% of eyes gained 2 or more lines of BCVA at 6 months after surgery, whereas this percentage increased to 60% at 24 months.

The original concept of the intracorneal ring dates back to 1978 when Reynolds, while studying the effects of corneal topography on visual acuity, conceived the idea of placing a ring in the periphery of the cornea to adjust its anterior curvature. We know that the addition of tissue to the peripheral cornea brings about applanation, and the diameter of the ring determines the degree of applanation of the cornea. Such implantation involves an addition of volume, with a displacement of the collagen lamellae in the peripheral corneal stroma, giving rise to a reduction in the arch length of the central cornea, i.e., an applanation of the central corneal curvature with the consequent change in corneal dioptric power.

This study shows that there was a 6% decrease in K1 values and a 5.5% decrease in K2 values, which means that implantation of Keraring rings is effective in the applanation of the corneal surface. In 2005, Alió et al. investigated the effect of implanting one or two corneal rings, oriented according to the topographic pattern to correct keratoconus. After one year, visual acuity, both with and without correction, had improved. On the other hand, Rabinowitz et al. compared eyes with one- and two-ring implants, but they found no statistically significant differences between the two groups in any of the determinations, as occurred in our study. Therefore, it seems that the biomechanical properties of the cornea do not depend on the number of rings implanted in the patient’s eye. The changes in IOP values after surgery determined by the ORA are due to the biomechanical properties of the cornea, however, the intraocular pressure of the eye stays the same postoperatively even if the IOP value has changed. According to Liu and Roberts, corneal elasticity could cause an error of up to 17mmHg in the population of IOP determinations. They also observed that the influence of the central corneal thickness in the determination of IOP by applanation depended on the viscoelastic properties of the cornea.

This study shows that the difference in IOPcc values increases according to the depth at which the ring is inserted, while the difference in the IOPg, CRF, and CH values decreases. These results will make it possible to predict changes the IOPcc, IOPg, CRF, and CH depending on the depth of insertion of the ring, i.e. we will be able to know, for example, what the postoperative IOPcc value will be when we insert the ring at 350
microns and what it will be when it is inserted at 400 microns. However, the dispersion of the aforementioned data must be taken into account.

In 1966, Blavatskaya verified that the dioptic correction obtained with ring implantation is directly proportional to its thickness and inversely proportional to its diameter. Less diameter, more thickness, more correction. But the changes in the IOPcc, IOPg, CRF, and CH values are not significant whatever the thickness of the ring that is implanted, which makes us suppose that said values are independent of the thickness of the ring. Corneal hysteresis in keratoconic eyes is lessened, as is the central corneal thickness. Moreover, we know that intrastromal rings flatten the cornea. In view of this, we could suppose that both corneal hysteresis and corneal pachymetry should be affected after surgical insertion of intrastromal rings.

The ORA measurements are determined at the centre of the cornea, but the ring is inserted in the periphery, which is why the corneal hysteresis values should perhaps be determined at the area where the ring was inserted and not in the corneal centre. However, Reichert’s Ocular Response Analyzer only measures the central area.

Our opinion is that the ORA does not seem to be useful for predicting changes in corneal hysteresis when intrastromal rings are inserted since it cannot determine measurements in the appropriate area. We hope, improve software of the machine in the future will determine more accurate values in corneal hysteresis. Further long-term studies in the future would be needed to demonstrate this.

REFERENCES