Keratoconus is a relatively rare disease; it can be described as an asymmetric, bilateral, progressive, noninflammatory corneal ectasia due to gradually increasing biomechanical instability of the cornea. Usually the condition starts at puberty and progresses until a patient’s mid-30s; in up to 20% of keratoconic patients, their corneas are affected to such an extent that BCVA is severely diminished and good vision is not achievable with any means of optical correction.

Once the patient is unable to use rigid contact lenses, there are few surgical alternatives for correction. Expectations are limited, and consequences may be unpredictable, both anatomically and functionally. In addition to lamellar and penetrating keratoplasty procedures, intrastromal corneal ring segments (ICRSs) provide us with new tools for managing keratoconus.

These vision-correcting devices attempt to regularize the front surface of the cornea and maintain the existing biomechanical status within the underlying stroma. In cases in which irregular astigmatism is progressive, such as in keratoconus, pellucid marginal degeneration, or laser-induced iatrogenic ectasia, the corneal stroma is structurally weakened, and some corneas may be further worsened following tissue ablation procedures.

Corneal collagen crosslinking (CXL) with riboflavin and ultraviolet-A (UV-A) for the treatment of keratoconus has been reported to be a safe procedure that appears to stop disease progression; this is achieved by increasing corneal tissue rigidity using riboflavin as a photosensitizer and UV-A to promote the formation of intra- and interfibrillar covalent bonds through photosensitized oxidation. CXL can stop the progression of keratoconus by providing corneal biomechanical stability, thereby improving spherical equivalent, astigmatism, and maximal keratometry (K). Wollensak et al reported the first in vivo controlled study of CXL for the treatment of patients with moderate or advanced keratoconus, concluding that CXL effectively stopped progression for up to 4 years. However, although CXL treatment for the management of patients with keratoconus has shown promise to reduce spherical equivalent, astigmatism, and maximal K, only modest improvements in visual acuity have been seen.

ICRSs regularize the front surface of the cornea by augmenting tissue in the mid-periphery and maintaining the biomechanical condition within the underlying stroma.
These devices significantly improve visual acuity, spherical equivalent, and K values without posing the risk of extensive complications. However, the inhibiting effect of ICRS implantation on the progression of keratoconus remains unclear.

Studies of ICRS implantation have established their safety and efficacy, with improvements in visual acuity and refraction and minimal potential complications. The Keraring (Mediphacos) is one such ring segment, characterized by a triangular cross section that induces a prismatic effect on the cornea.

**CXL AND ICRS IMPLANTATION**

Can a combination of CXL and ICRS implantation offer an enhanced treatment option in eyes with keratoconus? Although corneal transplantation is an established and effective treatment for patients with keratoconus who can no longer be treated with rigid contact lenses, the invasiveness of the surgical procedure and the risk of complications can be discouraging for patients. A combination of these two less invasive treatments could, therefore, theoretically provide optimal results because the benefits of the procedures would complement each other.

We studied the combination of ICRS implantation with CXL treatment in patients with keratoconus, implanting the Keraring in 21 eyes and performing CXL approximately 7 months later (Figure 1). Mean UCVA improved from 0.11 preoperatively to 0.26 after Keraring implantation and further improved to 0.32 after CXL. Mean BCVA improved from 0.22 preoperatively to 0.49 following Keraring implantation and 0.54 after CXL treatment. The spherical equivalent, cylinder, and mean K showed significant improvements after Keraring implantation and further improvements following CXL treatment, demonstrating the efficacy of the combined treatment (Figure 2).

In a retrospective case series, Chan et al compared the results of 12 eyes that underwent ICRS implantation alone with the results of 13 eyes that underwent a combined treatment of ICRS implantation followed by CXL. Significantly greater improvements in cylinder and maximal K values were reported in the combined treatment group.

**SEQUENCE OF TREATMENTS**

In our experience, we have performed CXL first, followed by ICRS implantation 6 months later, because we believed that the UV-A exposure in CXL could potentially damage the devices. We then investigated the effects of implanting the ICRS first, followed by CXL treatment in patients with progressive keratoconus and a corneal thickness of at least 400 μm. In this series of 21 eyes, we had to remove the ICRS from one eye because of superficial migration. To avoid migration in the second eye, which had the same corneal thickness, we performed CXL. It is now 1 year later, and there have been no further problems with migration, melting, or any other
complications in the second eye. We concluded that CXL can stop progression after ICRS implantation.

We then compared the results of both sequences. In a prospective study, 48 eyes of 43 patients with progressive keratoconus (grades 1 through 3) in the past 6 months were included. All patients were over age 18 years, were contact lens intolerant, and had a corneal thickness of at least 450 μm at the site of the ICRS corneal channel. Exclusion criteria included a K reading of more than 65.00 D, severe atopy, corneal dystrophies, corneal opacities, herpetic keratitis, grade 4 keratoconus, and concomitant systemic disease. A total of 27 eyes received CXL treatment followed by Keraring implantation (group 1), and 21 eyes received Keraring implantation followed by CXL (group 2). The mean interval between the two treatments for all eyes was 7 months, and the mean follow-up time after the second procedure was 6 months. For CXL treatment, following the abrasion of a 7-mm diameter area of the corneal epithelium, 0.1% riboflavin solution in 20% dextran was applied on the cornea every 3 minutes for 30 minutes (Figure 3A).

UV-A irradiation was performed for 30 minutes using Koehler illumination, with seven UV-A diodes with a potentiometer in series to enable the regulation of voltage (3 mW/cm² corresponding to a surface dose of 5.4 J/cm²; Figure 3B). For ICRS implantation, all segment channels were created with the 60-kHz IntraLase femtosecond laser (Abbott Medical Optics Inc.) in approximately 10 seconds. The channel depth was programmed to 80% of the thinnest point at the channel location; the corneal incision was made on the steep axis.

The mean outcomes for group 1 are detailed in Table 1. After CXL, the mean UCVA increased by more than 0.5 lines, and BCVA increased by 0.5 lines. The spherical equivalent (SE) decreased by 1.39 D (P<.05), cylinder decreased by 0.44 D, and mean K decreased by 0.88 D. After Keraring implantation, there were further improvements: UCVA and BCVA each increased by 1 line, SE decreased by 2.76 D, cylinder decreased by 1.32 D, and mean K decreased by 3.28 D (P<.001).

In comparing the two groups, it is apparent that group 2 experienced a greater improvement in UCVA, BCVA, cylinder, and SE; however, there was no significant difference between the two groups for the mean K astigmatism.

**CONCLUSIONS**

ICRS followed by CXL in patients with keratoconus achieved better results in our series than CXL followed by ICRS. This minimally invasive combined procedure entails fewer risks than corneal transplantation and still achieves excellent visual and refractive outcomes.

It is unnecessary to perform ICRS implantation and CXL treatment simultaneously, because healing at the incision site is extremely important. After femtosecond channel creation with a 1-mm incision, epithelialization and perfect healing can be achieved by the end of the first postoperative day. Perfect healing can decrease the risk of segment migration and corneal (Continued on page 24)
melting; on the other hand, wide epithelial defects can cause the healing process to lag. Incomplete tunnel creation is one of the most common complications of femtosecond laser channel creation, as bridges in the tunnel may cause problems during ICRS implantation. We suggest increasing the energy level or decreasing spot separation to avoid these complications. We have created channels and implanted segments successfully without changing the procedure’s parameters.

After ICRS implantation, we examine postoperative results at 1, 3, and 6 months. If the K readings have increased by greater than 1.00 D, CXL is performed to stop the progression and achieve further improvements in visual and refractive outcomes.

Certain conditions call for an alteration in the combined treatment to cater to the patient’s situation. If the patient is younger than 20 years, has a corneal thickness less than 400 μm with the risk of superficial migration of the segments, or cannot return for follow-up, we perform CXL treatment in the worse eye 1 month after ICRS implantation and then perform CXL in the second eye 1 month later.

We have found that ICRS implantation is an effective method for the improvement of UCVA and BCVA in keratoconic eyes. The inhibiting effect of ICRS on keratoconus progression is still unclear; however, the addition of CXL to the procedure stops the progression of the disease and provides greater improvements than Keraring implantation alone.

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