Technique of simultaneous femtosecond laser assisted Myoring implantation and accelerated intrastromal collagen cross-linking for management of progressive keratoconus: A novel technique

Mehrdad Mohammadpour*, Hassan Hahemi, Mahmoud Jabbarvand

Eye Research Center, Farabi Eye Center of Excellency, Tehran University of Medical Sciences, Faculty of Medicine, Tehran, Iran

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A B S T R A C T
Purpose: To describe a novel surgical technique for the management of progressive keratoconus by simultaneous femtosecond laser-assisted Myoring implantation and accelerated corneal intrastromal collagen cross-linking with Dextran Free Riboflavin.

Methods: After creating a corneal pocket with femtosecond laser, Dextran Free Riboflavin was injected into the intrastromal pocket. Then the Myoring was implanted in the corneal pocket and accelerated corneal intrastromal collagen cross-linking was performed with no epithelial debridement.

Results: The cornea remained clear and the central keratometry was decreased significantly with marked improvement in uncorrected visual acuity up to two years following treatment. Anterior segment OCT revealed good centration and intended implant depth with desirable increase in the corneal stromal reflectivity confirming effective collagen cross-linking.

Conclusion: Simultaneous femtosecond laser-assisted Myoring implantation and accelerated corneal intrastromal collagen cross-linking with Dextran Free Riboflavin is a safe and effective technique for management of keratoconus and improving vision.

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1. Introduction

Keratoconus (KC) is a non-inflammatory corneal ectasia, that usually starts at adolescence and progresses until the third to fourth decades of life [1]. It can also occur after refractive surgery [2]. In the case of contact lens intolerance, several surgical options are available to improve visual acuity, including intracorneal rings (ICR) including segments (intacs and Ferrara) and continuous rings (Myoring), toric phakic intraocular lens implantation, deep anterior lamellar keratoplasty and finally penetrating keratoplasty [3–10].

ICR have been shown to improve contact lens tolerance and visual acuity in a selected group of patients with mild to moderate KC. However, long-term follow-up shows that ICR fails to provide a permanent flattening effect especially in progressive cases [2,4].

In 1998, Spoerl et al. introduced collagen cross-linking (CXL) by the photosensitizers riboflavin and ultraviolet A light as the first treatment that changes the intrinsic biomechanical properties of corneal collagen. Although this treatment may stop progression of keratoconus, the ability to achieve visual rehabilitation for improved visual outcome is limited. Therefore, combining corneal cross-linking (CXL) with visual rehabilitation methods—such as intracorneal implants, may improve the long-term visual outcomes in patients with keratoconus [11–14].

The standard CXL treatment requires epithelial debridement, which results in pain and discomfort for the patient. Leaving the epithelium untouched, however, may significantly impair the efficacy of the cross-linking process. However, retained epithelium may limit diffusion of riboflavin to the corneal stroma. The inability of the dye to penetrate the intact epithelium sufficiently also increases the risk of UV damage to the eye. However, bypassing the epithelium by injecting riboflavin directly into an intracorneal pocket seems to be safe and effective, preserving the epithelium and avoiding pain and discomfort seen after epithelial removal [15–20].

Herein, we present a technique for management of progressive keratoconus with intrastromal accelerated CXL with Dextran Free Riboflavin without epithelial debridement combined with continuous corneal intrastromal ring (Myoring) implantation.

2. Surgical technique

The surgical technique is characterized by a 4-step procedure:

1. Femto-assisted 10 mm corneal pocket creation with a femto laser machine in depth of 300 microns (Fig. 1).
femtolaser machine (Femtec TECHNOLAS Perfect Vision GmbH, Bausch + Lomb, USA). Then sterile Dextran-Free Riboflavin (0.1%) MEDIOCROSS M (Huenberg, Switzerland) was instilled into the corneal pocket via standard canula of 0.3-mm diameter through the incision tunnel. The instillation of the dye resulted in a “yellowish turbidity” in the anterior and the posterior stroma indicating that the dye distributes both anteriorly and posteriorly through the pocket. A flexible MyoRing intracorneal implant (DIOPTEX GmbH) was inserted into the corneal pocket. The cornea was subjected to a 10-min irradiation treatment with UV-A light of 365 nm (UV-X) and UV intensity of 9 mW/cm². A bandage contact lens Air Optix® (AQUA, Ciba Vision, Duluth, GA, USA) was placed on the cornea for 5 days allowing the self-sealing corneal incision to be healed and decreasing ocular discomfort [20].

3. Report of a case

A 23-year-old female was referred for decreased vision in her left eye. Her uncorrected visual acuity (UCVA) was 20/120 and her best spectacle-corrected visual acuity (BCVA) was 20/80 with −6.00–5.75@130. Ocular examinations and imaging revealed advanced progressive keratoconus. She underwent simultaneous femtosecond laser assisted Myoring implantation and accelerated intrastromal collagen cross-linking. Her UCVA and BCVA 3 months after surgery reached to 20/40 and 20/30, respectively. After 24 months, both UCVA and BSCVA improved to 20/30 and the refractive error was unremarkable (+0.37–0.12@30). The cornea was clear even in the early postoperative phase. (Fig. 4) The mean K flattened by 7 diopters (D) after 3 months and was stable 2 years after surgery. The changes in topography between preoperative status and one year after surgery are shown in Figs. 5 and 6. Two years after surgery the vision was stable and the cornea remained clear (Fig. 7).

High resolution optical coherence tomography (Casia anterior segment OCT) one year after surgery, showed desired effect of CXL on the corneal stroma and appropriate depth of the ring (Fig. 8).

Specular microscopy pre-operatively and also one year after surgery showed an endothelial cell count of near 3000 cells per mm², average cell area of 300 micron and coefficient variation of 20 with no significant difference between pre-operative and post-operative endothelial cell count, size and hexagonality. The small increase in the cell count after surgery is due to the flattening effect of the Myoring on the center of the cornea that causes slight crowding of endothelial cells in corneal center post-operatively (Figs. 9 and 10).

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2. Instillation of Dextran-Free Riboflavin into the corneal pocket (Fig. 2).
3. MyoRing implantation into the corneal pocket (Fig. 3).
4. Accelerated UV irradiation without epithelial debridement with UV-X (IROC Innocross AG, Bahnhofstrasse, Switzerland) UV intensity of 9 mW/cm² for 10 min.

After topical anesthesia, an intracorneal pocket in the depth of 300 micron was created via a small incision tunnel by means of a
4. Discussion

Collagen cross linking is now the preferred method to stabilize the keratoconic cornea; however, its efficacy to improve visual acuity is limited. On the other hand ICR have gained increasing use for decreasing irregular astigmatism in keratoconus, however, their potency to halt the progression of disease is in debate. There are three options to mix their effect to achieve both stability of the keratoconus and improvement on visual acuity including pre-, simultaneous and post operative CXL and ICR implantation each with its benefits and drawbacks [11–13].

The main concerns with transepithelial CXL are that riboflavin cannot penetrate an intact epithelium and that the intact epithelium will block approximately 20% of the UVA light from reaching the stroma. The advantages of the epi-on CXL method are less pain, a more comfortable postoperative course, faster recovery, a lower risk of infection, and a faster return to contact lens wear [14].

Our technique of combining CXL with Myoring uses a corneal pocket for bypassing the epithelium to apply intracorneal riboflavin and implanting a flexible full-ring implant.

Standard riboflavin solution (VibEx) contains the same formulation of the original riboflavin formula used in the first cross linking studies and protocols (Dresden and Siena); 0.1% riboflavin with 20% dextran. The drops contain 20% dextran 500,000 Da molecular mass in order to make the otherwise hyperosmolar 0.1% riboflavin solution iso-osmolar with the corneal stroma, thus preventing intraoperative corneal swelling after removing the epithelium [18,19].

Mohammadpour et al. [20] reported corneal crosslinking and visual rehabilitation in keratoconus in one session without epithelial debridement.

However, our technique differs in several ways:

First, we made the corneal pocket with a femtosecond laser in depth of 300 microns which is more accurate than the pocket maker that they used.

Second, we created a 10 mm pocket which helps wider diffusion of riboflavin and therefore a wider collagen cross linking.

Third, we used Dextran-Free Riboflavin for its faster diffusion and less possibility of inducing corneal haziness as a presumed antigen that may stimulate corneal stromal immune reaction and cause diffuse lamellar keratitis.

Fourth, we used accelerated collagen cross linking with 10 min duration that may cause more patient comfort and decrease the operating time.

These two latter may be in favor of lack of corneal haziness and faster visual recovery in the early postoperative period in our case.

Recent studies showed that the biomechanical properties of porcine corneas after accelerated (10 mw/cm², 9 min) versus standard treatment can be considered as equivalent to the standard procedure in terms of an increase in corneal stiffness causing a 1.3-fold increase as measured by the Young modulus [21,22].

Although confocal microscopy findings have shown that accelerated CXL has comparable effect when compared with that of the conventional CXL [23].

Regarding the safety of this procedure on corneal endothelial cells, we performed serial specular microscopy examinations before and after treatment which showed no significant change in endothelial cell count during follow up period.

It should be noted that further studies are being performed in our center with confocal microscopy examinations of all corneal layers to evaluate safety of this procedure. Our preliminary results shows that insertion of Myoring with or without CXL causes
apoptosis of stromal kerocytes and rarefaction of nerve fiber layers that recovers near totally after 6 months. There was no significant change regarding endothelial cell density, size and hexagonality (unpublished data).

Wollensak et al. [24] aimed to assess the biomechanical efficacy of transepithelial collagen crosslinking using the femtosecond laser pocket technique compared with that using the standard crosslinking (CXL) technique in forty ex vivo porcine eyes divided into 4 groups with 10 samples each. Group 1 comprised the untreated controls. Group 2 was the standard CXL group with debridement, instillation of 0.1% riboflavin-dextran solution for 15 min before and every 5 min during the 30 min of irradiation with ultraviolet A (UVA) light of 370 nm and an irradiance of 3 mW/cm². Group 3 pertained to the femtolasr pocket control with an intrastromal pocket but without riboflavin/UVA. Group 4 was the femtolasr pocket CXL group with an intrastromal pocket of an 8-mm diameter at a 180-μm depth, riboflavin/dextran application for 15 min and subsequent exposure to UVA light for 30 min. Postoperatively, biomechanical stress-strain measurements were performed. They concluded that the biomechanical effect of CXL using the femtolasr pocket technique is about 50% less pronounced than that after standard CXL and suggested further studies to show whether the efficacy of the technique can still be improved and whether the clinical effect is sufficient for stabilizing ectatic corneas. However, their experiment was limited to the non-ectatic porcine cornea without ring implantation. We think that CXL has a synergistic effect with Myoring especially in keratoconic eyes and may increase its stabilization. Nevertheless even fifty percent effect is desired to be added to the ring effect to lock it.

Chan et al. [25] showed that the addition of CXL to the Intacs procedure resulted in greater keratoconus improvements than Intacs insertion alone. However, their technique differs from ours as the riboflavin application consisted of a 30-min application of ultraviolet-A (UVA) light (3.0 mW/cm² at 370 nm) to the central 7.0 mm of the cornea combined with topical application of riboflavin solution (0.1% riboflavin-5-phosphate and Dextran) every 3 min, and they used corneal tunnels for inferior-segment Intacs segments insertion rather than continuous Myoring implantation into a 10 mm corneal pocket.

Ertan et al. [26] has also evaluated the efficacy of transepithelial cross-linking (CXL) in 25 keratoconic eyes after Intacs implantation.
and concluded that collagen cross-linking has an additive effect on Intacs implantation in these eyes and may be considered as an enhancement/stabilizing procedure.

Our previous work between two different depths and the long term follow up of patients showed that the best corneal depth for Myoring insertion is 300 micron. It causes less foreign body sensation and lower risk of extrusion and also have similar effect on corneal flattening as 250 micron depth [5].

It should also be mentioned that Myoring insertion without crosslinking has been shown to improve the corneal profile and be stable at least 1 year after surgery [27] and so to prove that its combination with crosslinking is more stable needs a comparative trial which is now performing as an ongoing study in our center to compare the outcomes of Myoring implantation in keratoconic eyes with and without simultaneous CXL.

In conclusion, combined femto-assisted Myoring implantation and accelerated corneal intrastromal collagen cross-linking with Dextran Free Riboflavin may be a safe and effective technique for management of advanced progressive keratoconus and yields fast and stable visual recovery with minimal discomfort. This technique has both advantages of epi-on (no pain, no epithelial debridement, decreased risk of haze and infection) and epi-off CXL (good distribution of riboflavin and effective cross-linking) while lacks their drawbacks. It also corrects most of the refractive error of the patient by implanting an annular ring. It may be a useful method for locking in the treatment effect of the Myoring, however, more data is required with more cases to validate this benefits.

References


