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Expanding Treatment Horizons: Efficacy And Safety Of Contact Lens-Assisted Collagen Cross-Linking In Thinner Corneas For Keratoconus Management In An Indian Cohort

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ABSTRACT

Background: Keratoconus is a progressive, non-inflammatory corneal ectasia causing irregular astigmatism and visual deterioration. Corneal collagen cross-linking (CXL) is a well-established procedure to halt keratoconus progression, but conventional CXL requires a minimum corneal thickness of 400 µm after de-epithelialization. Patients with thinner corneas are thus often excluded from this effective intervention. Contact lens-assisted CXL (CACXL) was introduced to overcome this limitation, but limited data exist on its outcomes in the Indian population.

Methods: This hospital-based, interventional study enrolled 75 eyes (48 patients) with progressive keratoconus and corneal thickness of 350–440 µm. After epithelial debridement, a soft contact lens soaked in 0.1% riboflavin was placed on the cornea to achieve a combined thickness ≥400 µm. Ultraviolet-A (UVA) irradiation of 30 mW/cm² was delivered for 3 minutes at 370 nm. Key parameters—minimum corneal thickness, steepest keratometry (Kmax), endothelial cell count, best-corrected visual acuity (BCVA), and manifest refraction—were recorded preoperatively and at 1, 6, and 12 months.

Results: Mean corneal thickness showed no significant change at 6 and 12 months compared to preoperative values ($p=0.304$, $p=0.433$). There was no significant increase in Kmax at one-year follow-up ($p>0.05$). Endothelial cell counts remained stable ($p>0.05$). A significant improvement in BCVA was observed at 6 and 12 months ($p=0.002$). No major intraoperative or postoperative complications were reported.

Conclusion: CACXL safely and effectively halted keratoconus progression in patients with thinner corneas, while preserving endothelial function and improving visual acuity. This approach expands treatment eligibility to corneas thinner than 400 µm and is easily adaptable using standard soft contact lenses.

Keywords: *Keratoconus, Collagen Cross-linking, Contact Lens-Assisted, Thin Corneas, UVA Irradiation*

1. INTRODUCTION

Keratoconus is a progressive, non-inflammatory ectatic disorder of the cornea characterized by corneal thinning, conical protrusion, and irregular astigmatism that impairs visual acuity. Corneal collagen cross-linking (CXL) with riboflavin and ultraviolet-A (UVA) light is a proven method to stabilize the cornea and arrest the progression of ectasia by increasing the biomechanical rigidity of corneal tissue [1]. Conventional CXL requires a minimum corneal thickness of 400 µm (post-debridement) to prevent endothelial damage from UVA irradiation [2]. However, in advanced keratoconus, the corneal stroma often measures less than 400 µm, creating an unmet need for alternative approaches.

Multiple techniques have been proposed to facilitate cross-linking in thin corneas. These include hypo-osmolar riboflavin instillation, transepithelial protocols, donor lenticule augmentation, customized epithelial debridement, and contact lens-assisted CXL (CACXL) [3]. In the hypo-osmolar approach, riboflavin without dextran is applied to swell the cornea artificially [4]. Although this can temporarily increase corneal thickness above 400 µm, the effect may not be sustained throughout the procedure, thus risking inadequate stromal saturation or UVA exposure [5]. Transepithelial CXL spares the epithelium but is associated with reduced riboflavin penetration and lower cross-linking depth [6]. Donor lenticule-based approaches require suitable lenticules from small-incision lenticule extraction (SMILE) surgeries, which may not always be readily available. Furthermore, lenticule thickness must match the extent of corneal thinning, increasing logistical complexity [7].

Contact lens-assisted CXL (CACXL), first described by Jacob et al. [2], employs a soft contact lens soaked in 0.1% riboflavin, placed on the debrided cornea to artificially augment corneal thickness to at least 400 µm. The process harnesses Lambert's law, leveraging a riboflavin film both pre-corneal and pre-contact lens to achieve sufficient UVA absorption and protect deeper corneal structures, especially the endothelium [2]. Because soft lenses do not intrinsically absorb UVA, they serve mainly as a scaffold, effectively raising corneal thickness. In addition, CACXL allows an earlier visual rehabilitation compared to techniques that rely on corneal edema.

Despite promising early results, only a few studies have assessed CACXL in larger cohorts over extended follow-up periods. In India, this technique has been explored only in limited series; hence, the long-term safety and efficacy data remain sparse. In this study, we aim to evaluate the effectiveness of CACXL in halting keratoconus progression in thinner corneas (350–440 µm) while monitoring for potential endothelial damage, changes in corneal curvature (Kmax), and improvements in best-corrected visual acuity (BCVA).

2. MATERIALS AND METHODS

This hospital-based, interventional study was conducted at the Department of Ophthalmology, S.M.S. Hospital & attached group of hospitals, Jaipur, between September 2017 and August 2018. Approval from the Institutional Ethics Committee was obtained, and the study adhered to the tenets of the Declaration of Helsinki. Written informed consent was secured from all participants.

Patient Selection

Seventy-five eyes of 48 patients, aged ≥18 years, with progressive keratoconus (Kmax increase of >1 D, manifest spherical equivalent ≥0.5 D change, and ≥2% thinning of central corneal thickness over two consecutive 6-month evaluations) and minimum corneal thickness between 350 and 440 µm were enrolled. Exclusion criteria included acute hydrops, corneal scarring, active ocular infection, and pregnancy.

Sample Size and Statistical Analysis

The sample size was calculated to be 73, with an alpha error of 0.05 and 80% power, expecting a detectable difference of 0.1 in mean pre- and postoperative uncorrected distance visual acuity (UDVA) with standard deviation of 0.3. Statistical analysis was performed using SPSS for Windows (Version 16.0, SPSS Inc., Chicago, IL, USA). Paired t-test was used for continuous variables. A p-value of <0.05 was considered statistically significant.

Surgical Procedure

Preoperatively, uncorrected distance visual acuity, best-corrected visual acuity (Snellen's chart), slit-lamp examination, manifest refraction, fundus evaluation, keratometry, endothelial cell count (Topcon SP-3000P), and central corneal thickness (ultrasound pachymetry) were recorded. Scheimpflug imaging was performed for corneal topography.

Under aseptic conditions, the central corneal epithelium was removed (hockey-knife). Riboflavin 0.1% solution was instilled every 3 minutes for 30 minutes onto both the de-epithelialized cornea and a soft contact lens. After 30 minutes, the riboflavin-soaked lens was placed on the cornea. Pachymetry confirmed a combined cornea-contact lens thickness ≥400 µm. UVA irradiation (370 nm) at 30 mW/cm² was then applied for 3 minutes. Finally, the contact lens was removed, the cornea was irrigated with saline, and a bandage contact lens was applied until re-epithelialization.

Postoperatively, patients were prescribed moxifloxacin 0.5% (until epithelial healing), loteprednol 0.5% (tapered over 3 weeks), and artificial tears for 3 months. Follow-up visits were scheduled at day 1, day 7, 1 month, 6 months, and 1 year. At each follow-up, BCVA, manifest refraction, CCT, endothelial cell count, and Scheimpflug imaging were repeated.

3. RESULTS

Overall Demographics and Procedure Profile

Seventy-five eyes of 48 patients (27 males, 21 females) underwent CACXL. The mean age was 19.88 ± 2.37 years (range, 18–26 years). Among these, 27 patients had bilateral CACXL, and 21 had unilateral treatment.

Corneal Thickness and Contact Lens Augmentation

The mean preoperative minimum corneal thickness after epithelial removal was 366.4 ± 21.03 µm. With the riboflavin-soaked contact lens in place, the minimum functional corneal thickness increased to 478.96 ± 27.39 µm, reflecting a mean absolute gain of 111.19 ± 8.87 µm.

Table 1 summarizes corneal thickness changes at follow-up. No significant thinning was observed from baseline (407.91 ± 23.15 µm) at 6 and 12 months (p=0.304 and p=0.433, respectively).

Table 1: Corneal Thickness	Mean (µm)	Std. Dev.	Std. Error	p-value
Pre-op	407.91	23.15	2.67	-
1 month	406.35	22.63	2.61	0.007
6 months	408.35	23.08	2.66	0.304
12 months	408.36	23.22	2.68	0.433

Corneal Topography (Kmax)

Steepest keratometry (Kmax) showed no significant increase over one year (p>0.05). Baseline Kmax was 58.99 ± 5.36 D and stabilized at 58.82 ± 5.45 D at 12 months (Table 2).

Table 2: Kmax	Mean (D)	Std. Dev.	Std. Error	p-value
Pre-op	58.99	5.36	-	-
1 month	59.20	5.45	0.072	0.005
6 months	59.11	5.37	0.081	0.140
12 months	58.82	5.45	0.107	0.111

Endothelial Cell Counts

No significant endothelial cell loss was noted at 6 or 12 months (p=0.150 and 0.110, respectively). Preoperative endothelial cell density averaged 2859.40 ± 205.45 cells/mm² and remained stable thereafter (Table 3).

Table 3: Endothelial Cells	Mean (cells/mm²)	Std. Dev.	Std. Error	p-value
Pre-op	2859.40	205.45	23.72	-
1 month	2857.89	205.05	23.69	0.054
6 months	2860.56	206.13	23.90	0.150
12 months	2860.69	205.79	23.76	0.110

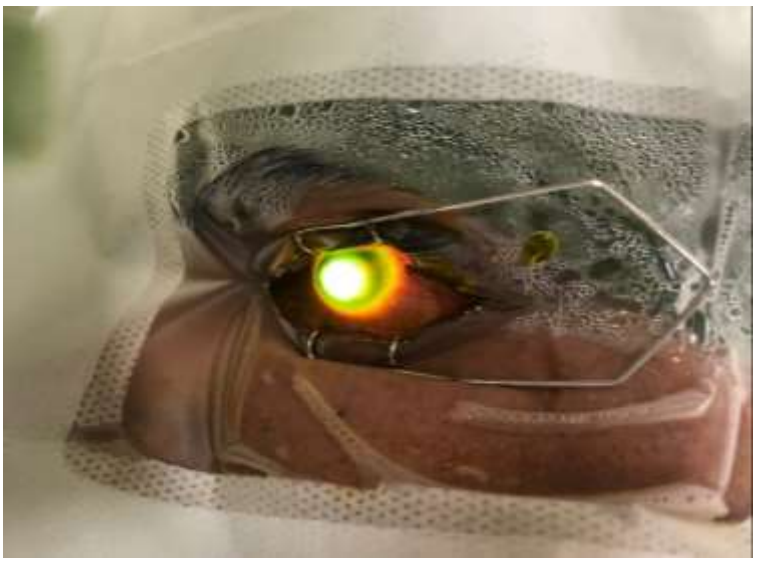
Visual Acuity and Refraction

BCVA (LogMAR) significantly improved from 0.65 ± 0.30 (pre-op) to 0.60 ± 0.29 at 6 and 12 months (p=0.002). Spherical equivalent similarly improved from 4.88 ± 2.44 D preoperatively to 4.75 ± 2.33 D at 12 months.

Table 4: BCVA	Mean (LogMAR)	Std. Dev.	Std. Error	p-value
Pre-op	0.65	0.30	-	-
1 month	0.62	0.29	0.008	0.009
6 months	0.60	0.29	0.013	0.002
12 months	0.60	0.29	0.013	0.002

FIGURE 1. APPLICATION OF 0.1% RIBOFLAVIN SOLUTION ON SOFT CONTACT LENS FOR 30 MINUTES.

FIGURE 2. UVA LIGHT (370 NM) AT 30 MW/CM² DIRECTED ONTO THE CORNEA WITH THE RIBOFLAVIN-SOAKED CONTACT LENS IN PLACE.



4. DISCUSSION

Conventional CXL requires a post-debridement corneal thickness of at least 400 µm to safeguard endothelial cells from potential UVA toxicity [1]. In advanced keratoconus, this threshold is frequently not met, which previously limited therapeutic options for patients with thin corneas. Multiple strategies have attempted to address this limitation. Hypo-osmolar riboflavin can momentarily swell the cornea to reach the safe threshold but may not sustain the thickness throughout the entire irradiation period [5]. Furthermore, transient edema can reduce the effective concentration of riboflavin within the stroma, potentially compromising cross-linking efficacy [6].

Transepithelial approaches maintain corneal epithelium but suffer from inconsistent riboflavin penetration, leading to a more superficial cross-linking effect. Some studies report minimal changes in keratometry and the depth of the demarcation line [8,9]. Other techniques—such as customized pachymetry-guided epithelial debridement and lenticule augmentation—show promise but either risk incomplete riboflavin penetration under partially intact epithelium or rely on donor tissues that may not be readily available [7,14].

Contact lens-assisted CXL (CACXL) was introduced by Jacob et al. [2] to overcome these hurdles. By placing a riboflavin-

soaked soft contact lens on the de-epithelialized cornea, the total thickness is effectively raised above 400 µm. The combination of a pre-corneal and pre-lens riboflavin film adheres to Lambert's law, allowing adequate UVA absorption within the superficial cornea, thereby sparing deeper structures, including the endothelium. This method does not depend on time-consuming corneal swelling, avoids the need for specialized lenticules, and allows more predictable and stable corneal biomechanics during the procedure.

In the present study, CACXL stabilized keratoconus progression in eyes with a minimum corneal thickness of 350–440 µm. Our one-year follow-up revealed no significant increase in Kmax, minimal endothelial cell loss, and significantly improved BCVA. These findings corroborate earlier studies, such as Jacob et al. [2], who reported no progression of keratectasia or endothelial damage in thin corneas post-CACXL. The improvement in BCVA at 6 and 12 months may be attributed to the stabilization of the corneal contour and reduction in irregular astigmatism. Although not all studies observe a statistically significant improvement in vision, halting disease progression alone can be a clinically meaningful endpoint [2].

Notably, CACXL does not induce significant corneal edema intraoperatively, in contrast to hypo-osmolar swelling protocols. This can translate into quicker visual recovery and better predictability of cross-linking depth. The current study's larger sample size (75 eyes) and a longer follow-up (12 months) provide stronger evidence supporting CACXL's safety and efficacy compared to previous smaller series [2].

Overall, CACXL is an attractive and cost-effective technique for treating keratoconus in corneas thinner than 400 µm. Future research with even longer follow-up and comparative cohorts (e.g., hypo-osmolar or transepithelial CXL) can help elucidate the long-term outcomes and refine patient selection criteria.

5. CONCLUSION

CACXL is a safe and effective procedure to arrest keratoconus progression in thin corneas (350–440 µm). By artificially augmenting stromal thickness using a riboflavin-soaked contact lens, adequate UVA absorption is achieved without compromising endothelial cell viability. Our study demonstrated stable corneal thickness, no significant endothelial cell loss, arrest of keratometric progression, and an improvement in BCVA at one year. This approach circumvents the limitations posed by other methods (e.g., lenticule unavailability, transient edema) and offers predictable intraoperative conditions. Hence, CACXL expands the treatment spectrum for patients with thinner corneas while preserving safety and achieving favorable visual outcomes.

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