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# Comparison of transepithelial corneal crosslinking with epithelium-off crosslinking (epithelium-off CXL) in adult Pakistani population with progressive keratoconus

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**Abstract:**

**PURPOSE:** The purpose of this study is to compare the safety and efficacy of transepithelial corneal crosslinking (CXL) with epithelium-off crosslinking (epithelium-off CXL) in the treatment of progressive keratoconus in adult Pakistani population.

**MATERIALS AND METHODS:** Sixty-four eyes of 64 consecutive patients of progressive keratoconus were included in this quasi-experimental study. Thirty-two eyes received transepithelial CXL with Peschke TE (0.25% riboflavin (Vitamin B2), 1.2% hydroxypropyl methylcellulose (HPMC), 0.01% benzalkonium chloride) and 32 eyes received epithelium-off CXL with Peschke M (0.1% riboflavin (Vitamin B2) 0.1%, HPMC 1.1%.) The cornea was then exposed to ultraviolet A light at an irradiance of 3 mW/cm$^2$ for 30 min. The primary outcome measure, clinical stabilization of keratoconus was defined as an increase of no more than 1D in $K_{max}$ at 1 year. Other parameters evaluated at baseline and 3, 6, 12, and 18 months postoperatively were uncorrected distance visual acuity (UDVA), corrected distance visual acuity (CDVA), spherical equivalent (SE), astigmatism (Ast), simulated keratometry, steep keratmetry (steep K), and corneal thickness at thinnest point (pachy thin).

**RESULTS:** Both epithelium-off CXL and transepithelial CXL groups showed a significant reduction in $K_{max}$, steep K, simulated K, corneal pachymetry at all test points ($P < 0.05$) with significantly greater reductions achieved in epithelium-off CXL group at 18 months follow-up. The mean UDVA, CDVA, SE, Ast significantly improved in both groups ($P < 0.05$). The mean postoperative UDVA and CDVA between the groups were not significant at 12 months ($P = 0.650$, 0.018, respectively). Clinical stabilization was achieved in 94% of eyes in epithelium-off CXL and 75% of eyes in transepithelial CXL. In epithelium-off CXL, three eyes exhibited stromal haze resolved by corticosteroid treatment. No complication was documented in transepithelial CXL group.

**CONCLUSION:** Transepithelial CXL is not recommended to be replaced completely by standard epithelium-off CXL due to continued ectatic progression in 25% of cases. However, thin corneas, unfit for standard epithelium-off CXL, can benefit from transepithelial CXL.

**Keywords:**

Adult Pakistani population, epithelium-off corneal crosslinking, progressive keratoconus, transepithelial corneal crosslinking

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## Introduction

Keratoconus is a noninflammatory, bilateral, frequently asymmetrical, and most common corneal ectatic disorder characterized by central corneal thinning, biomechanical weakening, and steepening of the corneal curvatures leading to



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substantial distortion of vision.[1] The estimated prevalence worldwide is 54.5 cases/100,000. It typically affects the young population with its onset at puberty, followed by continued progression with eventual stabilization toward the fourth decade.[2] Halting this progression was a daunting task until the introduction of an exciting and innovative technique of corneal crosslinking (CXL) in 2003 in Dresden, Germany. CXL promotes disease stabilization by increasing corneal rigidity and biomechanical stability. This is achieved by photopolymerization of collagen fibers, augmenting intrafibrillary and interfibrillary cross links induced by ultraviolet A (UVA) light in the presence of photosensitive riboflavin drops, saturating corneal stroma.[2]

The standard epithelium-off CXL achieved this corneal riboflavin concentration by removing central corneal epithelium as described by Wollensak and Iomdina[3] However, with epithelium debridement, complications such as severe postoperative pain, delayed healing, superficial punctate keratopathy, viral reactivation of herpetic keratitis, severe bacterial keratitis and central stromal scarring have been reported.[4] Transepithelial CXL with modified riboflavin containing epithelial permeability enhancers like EDTA and benzalkonium chloride promote riboflavin penetration and stromal saturation through intact epithelial barrier. However, a relatively superficial apoptotic effect of irradiance in anterior stroma was evidenced on confocal microscopy. It was thus estimated to achieve one-fifth of biomechanical rigidity compared to epithelium-off CXL.[5-8] Encouraging results in terms of improvement in visual acuity and topographic indices have been reported with transepithelial CXL and epithelium-off CXL as compared to untreated controls.[5,9,10] However, controversies exist in the international literature regarding comparative efficacy of transepithelial CXL and epithelium-off CXL in halting the progression of keratoconus. CXL is new treatment facility for keratoconus in developing countries like Pakistan with very limited studies in literature on Pakistani eyes. We aim to conduct a comparative study in adult Pakistani population, to evaluate the efficacy and safety of transepithelial CXL with Peschke TE in as compared to standard epithelium-off CXL in cases of progressive keratoconus to relate our clinical results with international trials. This will aid in establishing patient selection criteria and treatment guidelines for progressive keratoconus in adult Pakistani population.

## Materials and Methods

This quasi-experimental study was conducted at Armed Forces Institute of Ophthalmology, Rawalpindi, Pakistan from March 2014 to October 2016, after approval from the Hospital Ethical Review Board adhering to the tenets of the Declaration of Helsinki. A total of 64 eyes of 64 consecutive patients diagnosed with progressive keratoconus, eligible for CXL treatment were recruited in this study. Corneal pachymetry (pachymetry at the thinnest point of 400 μ or more) was allotted to either transepithelial CXL or epithelium-off CXL while corneas with pachy thin >375 μ and <400 μ, unfit for epithelial debridement procedure were scheduled for transepithelial CXL. Informed written consent was obtained from all patients. Inclusion criteria included a clear cornea, age between 18 and 33 years, documented progression of keratoconus evident on a minimum of two corneal topographies. Progression being defined as an increase of 1.00 D in central corneal astigmatism (Ast) or maximum apex cone curvature (apical K) over a period of 6 months. Patients with corneal scarring, active or previous ocular infections, autoimmune disorders, pregnancy, lactation, presence of any ocular or systemic associations of keratoconus, history of the previous CXL treatment, or any ocular surgery were excluded from the study.

All patients had a complete ophthalmic examination including uncorrected-distance visual acuity (UDVA), corrected distance visual acuity (CDVA) (Snellen visual acuity converted to logMAR notation), slit lamp biomicroscopy, scheimpflug topography, pachymetry (Galilei G4) and dilated fundus examination at baseline (preoperative) and postoperative follow-up visits at 3,6, 12 and 18 months. Contact lens users were advised to discontinue soft contact lens wear for 2 weeks and hybrid gas permeable lenses for 3 weeks before baseline evaluation.

### Surgical technique

Corneal collagen crosslinking was performed by same cornea specialist as a day care procedure under topical anesthesia 0.05% proparacaine hydrochloride (alkaline) and 1.0% pilocarpine in both transepithelial and epithelium-off CXL. Standard preoperative preparation with 5% povidone-iodine solution was done. Eyelid speculum was inserted after application of sterile surgical drapes covering the eyelashes. In epithelium-off CXL group, central 9 mm of epithelium was scraped off followed by the instillation of one drop of isotonic riboflavin (0.1% riboflavin (Vitamin B2) 0.1%, hydroxypropyl methylcellulose (HPMC) 1.1% (Peschke M, PESCHKE Trade GmbH) every 2 min for 20 min. The cornea was then exposed to UVA light of 366–370 μ at an irradiance of 3.0 mW/cm$^2$, total energy of 5.4 J/cm$^2$ for 30 min (CCL VARIO, PESCHKE Trade GmbH, Huenenberg Switzerland) at a distance of 55 mm from the eye, with continued instillation of riboflavin drops every 2 min. A bandage contact lens (Interojo, Korea) was applied and removed on 7$^{th}$ postoperative day if epithelium had healed.

In transepithelial CXL group, same surgical steps were followed as epithelium-off CXL except that epithelium was not removed, and a transepithelial riboflavin solution Peschke TE (0.25% riboflavin (Vitamin B2), 1.2% HPMC, 0.01% benzalkonium chloride) (PESCHKE Trade, GmbH) was used, which promotes the penetration of riboflavin through intact epithelium. Thin cornea of pachy thin <400 μ with epithelium on was treated with hypotonic riboflavin drops Peschke H (PESCHKE Trade GmbH) as per manufacturer's instructions, one drop every 5 s, till corneal thickness reached 400 μ measured with ultrasound pachymeter (REICHERT iPac PACHYMETER) before UV irradiation.

In both groups, postoperatively antibiotic eye drops (Vigamox 0.05%, Alcon) were advised for 1 week. Topical steroids (fluorometholone 0.1%, Allergan) were started in epithelium-off CXL group 1-week postoperatively and continued thrice a day for 2 weeks.

### Outcome measure

Primary outcome measure was clinical stabilization of keratoconus defined as maximum keratometry increase over preoperative or baseline $K_{max}$ of no more than 1 diopter at 1 year after CXL. Refractive outcome UDVA, CDVA, spherical equivalent (SE), Ast, topographic indices, simulated K, steep keratometry (steep K), and pachy thin were additional outcome parameters measured at test points 3, 6, 12, and18 months post-CXL.

### Statistical analysis

Data entry and analysis was done by using SPSS version 22. (SPSS Inc., Chicago, IL, USA). Quantitative variables were presented by using mean±SD. Normality of the data was tested with the help of Kolmogorov Smirnov test. Within the group, multiple-related samples were compared with Friedman ANOVA test. Related two samples comparisons were performed with paired two sample t-test for normally distributing data and Wilcoxon-matched pairs test for nonnormally distributing data. Between the group comparisons for normally distributing, data was done with independent sample t-test and Mann–Whitney U-test was applied to non-normal data. A $P$ value < 0.05 was considered as statistically signfiacnt.

## Results

Sixty-four eyes of 64 consecutive patients of progressive keratoconus (46 males, 18 females) who underwent CXL from March 2014 to October 2016 were included in this study. Thirty-two eyes were treated with transepithelial CXL, and other 32 eyes received standard epithelium-off CXL. All the patients recruited in this study attended follow-up visits till 12 months, however, owing to change of residence, or follow-up scheduled at nearby hospitals, six patients in transepithelial and eight in epithelium-off CXL group could not complete 18 months follow-up.

The mean age was 24.47 ± 4.90 years in transepithelial group and 24.81 ± 6.39 in epithelium-off CXL group, which was not statistically significant. Keratometric parameters (simulated K, steep K, $K_{max}$) and refractive data (Ast, SE) were comparable at baseline. Preoperative logMAR UDVA, CDVA, and pachy thin were significantly higher in epithelium-off CXL group ($P < 0.05$) [Table 1].

The mean postoperative logMAR UDVA and logMAR CDVA significantly improved at all test points of 3, 6, 12, and 18 months [Tables 2 and 3]. The difference in postoperative logMAR UDVA and CDVA was not statistically significant between the transepithelial and epithelium-off CXL groups at 12 months; however, CDVA was significantly better at 18 months in transepithelial CXL group.

The refractive Ast, SE, simulated K, steep K, $K_{max}$ showed significant reduction with both transepithelial CXL and epithelium-off CXL, the reduction being significantly higher in epithelium-off CXL group [Tables 2-4]. Significant flattening of $K_{max}$ from 53.7 ± 6.8D to 51.5 ± 0.9D ($P = 0.042$) was achieved in epithelium-off CXL at the end of 12 months follow-up ($P = 0.000$).

The mean baseline pachymetry ranged from 381 to 485 μ in transepithelial CXL group, and 420–550 μ in epithelium-off CXL, the corneas being significantly thinner in the transepithelial group ($P = 0.000$). Statistically, greater reduction in central corneal thickness to pachy thin was observed in epithelium-off CXL group ($P = 0.003$ at 12 months, $P = .042$ at 18 months) till the last follow-up.

The primary outcome measure, stabilization of disease was achieved in 94% (30) eyes in epithelium-off CXL group and 75% (24) eyes in transepithelial group. The preoperative pachy thin and $K_{max}$ of patients showing

**Table 1: Preoperative comparison of parameters**

| Preoperative | Epithelium | | $P^a$ |
|---|---|---|---|
| | On ($n$=32) | Off ($n$=32) | |
| UDVA | 1.10±0.54 | 0.78±0.58 | 0.033*,b |
| CDVA | 0.58±0.44 | 0.29±0.23 | 0.012*,b |
| SE | −6.39±2.34 | −6.74±2.78 | 0.586[a] |
| Astigmatism | −3.71±1.58 | −4.07±2.51 | 0.608[b] |
| Steep K | 51.00±3.06 | 49.51±3.43 | 0.075[a] |
| Sim K | 48.40±2.84 | 47.34±3.06 | 0.157[a] |
| $K_{max}$ | 54.32±3.54 | 53.65±4.76 | 0.529[a] |
| Pachy thin | 429.28±27.19 | 480.43±41.60 | 0.000*,b |

[a]$t$-test, [b]Mann-Whitney U-test, *$P$<0.05. UCDV = Uncorrected distance visual, CDVA = Corrected distance visual acuity, SE = Spherical equivalent, CCT = Central corneal thickness

**Table 2: Postoperative refractive and topographical data in Transepithelial CXL Group**

| *n* | Follow up Time period (Epi-On) | | | | | *P*[(a)] |
|---|---|---|---|---|---|---|
| | Pre-operative | 3 months | 6 months | 1 year | 18 months | |
| | 32 | 32 | 32 | 32 | 26 | |
| UDVA | 1.10±0.54 | 1.07±0.50 | 1.06±0.52 | 0.95±0.57 | 0.92±0.53 | 0.000* |
| CDVA | 0.58±0.44 | 0.59±0.41 | 0.51±0.39 | 0.50±0.37 | 0.54±0.39 | 0.009* |
| SE | -6.39±2.34 | -6.14±2.32 | -5.98±2.33 | -5.99±2.45 | -5.48±2.27 | 0.055 |
| Ast | -3.71±1.58 | -3.70±1.61 | -3.63±1.82 | -2.96±2.73 | -4.5±1.84 | 0.118 |
| steep K | 51.00±3.06 | 51.60±3.19 | 51.72±3.37 | 51.61±3.55 | 51.40±3.39 | 0.002* |
| Sim K | 48.40±2.84 | 49.89±2.38 | 49.95±2.54 | 49.67±2.78 | 49.77±2.74 | 0.299* |
| K max | 54.32±3.54 | 53.78±3.75 | 53.73±4.08 | 53.71±4.46 | 53.66±4.69 | 0.010* |
| Pachy thin | 429.28±27.19 | 427.43±26.70 | 427.15±27.80 | 425.93±26.80 | 423.76±26.31 | 0.000* |

Friedman ANOVA test, *$P$<0.05. UDVA=Un corrected distant visual acuity, CDVA=Corrected distant visual acuity, SE=Spherical equivalent, Ast=Refractive astigmatism, Steep K=Steep keratometry, Sim K=Simulated keratometry, Kmax=Maximum or Apex Keratometry, Pachy Thin=Pachymetry at thinnest point of cornea

**Table 3: Postoperative refractive and topographical data in Epithelium off-CXL Group**

| *n* | Follow up time period (epithelium-off CXL) | | | | | *P*[a] |
|---|---|---|---|---|---|---|
| | Pr-operative | 3 months | 6 months | 1 year | 18 months | |
| | 32 | 32 | 32 | 32 | 27 | |
| UDVA | 0.78±0.58 | 0.78±0.54 | 0.69±0.56 | 0.68±0.51 | 0.67±0.49 | 0.000* |
| CDVA | 0.29±0.23 | 0.36±0.20 | 0.30±0.21 | 0.27±0.20 | 0.32±0.28 | 0.001* |
| SE | -6.74±2.78 | -6.15±2.62 | -4.35±2.47 | -5.04±2.83 | -5.01±3.08 | 0.000* |
| Ast | -4.07±2.51 | -4.30±2.12 | -3.94±1.48 | -2.74±2.22 | -2.90±1.40 | 0.000* |
| steep K | 49.51±3.43 | 48.95±3.29 | 48.49±3.32 | 48.11±3.24 | 47.84±3.39 | 0.000* |
| Sim K | 47.34±3.06 | 46.71±2.98 | 46.50±3.11 | 46.07±2.95 | 46.48±3.19 | 0.000* |
| K max | 53.65±4.76 | 53.02±4.32 | 53.20±4.35 | 51.45±4.30 | 51.17±4.64 | 0.000* |
| Pachy thin | 480.43±41.60 | 455.40±48.32 | 461.34±68.22 | 453.65±69.22 | 446.59±66.35 | 0.000* |

Friedman ANOVA test, *$P$<0.05. UDVA=Un corrected distant visual acuity, CDVA=Corrected distant visual acuity, SE=Spherical equivalent, Ast=Refractive astigmatism, Steep K=Steep keratometry, Sim K=Simulated keratometry, Kmax=Maximum or Apex Keratometry, Pachy Thin=Pachymetry at thinnest point of cornea

**Table 4: Comparison of postoperative change of refractive and corneal parameters over baseline between two study groups**

| *n* | Follow Up (Postop-Preop) | | | | *P*-value at 12 months | *P*-value at 18 months |
|---|---|---|---|---|---|---|
| | Transepithelial CXL | | Epi-Off CXL | | | |
| | 12 months | 18 months | 12 months | 18 months | | |
| | 32 | 26 | 32 | 24 | | |
| UDVA | -0.147±0.23 | -0.22±0.27 | -0.104±0.29 | -0.12±0.34 | 0.650 | 0.305** |
| CDVA | -0.082±0.16 | -0.71±0.16 | -0.023±0.15 | 0.045±0.13 | 0.367 | 0.036** |
| SE | 0.403±0.763 | 1.04±1.59 | 1.70±0.90 | 1.89±0.96 | 0.000** | 0.005** |
| Ast | 0.753±2.23 | -0.68±2.68 | 1.33±3.11 | 0.89±2.17 | 0.001** | 0.002** |
| steep K | 0.617±1.01 | -0.45±0.98 | -1.40±1.71 | -1.72±194 | 0.000** | 0.008** |
| Sim K | 1.27±1.16 | 0.24±1.27 | -1.26±1.23 | -0.98±1.38 | 0.000** | 0.001** |
| K max | -0.61±2.03 | -0.59±2.19 | -2.19±1.33 | -2.66±1.36 | 0.000** | 0.000** |
| Pachy thin | -3.34±2.71 | 4.07±28.91 | 26.78±46.87 | 30.66±53.63 | 0.003** | 0.042** |

**$P$<0.05 (statistically significant). *Post-operative time period was the last follow up of patient after 12 months and 18 months, **$P$<0.05 (Statistically significant). UDVA=Uncorrected distant visual acuity, CDVA=Corrected distant visual acuity, SE=Spherical equivalent, Ast=Refractive astigmatism, Steep K=Steep keratometry, Sim K=Simulated keratometry, Kmax=Maximum Keratometry, Pachy Thin=Pachymetry at thinnest point of cornea

continued progression and disease stabilization in transepithelial CXL group is represented in [Table 5]. Twenty percentage of eyes in transepithelial CXL group with pachy thin below 400 μ showed clinical stabilization at 12 months [Table 5].

In epithelium-off CXL, three eyes exhibited corneal edema and stromal haze, two of which resolved with corticosteroid treatment by 6 weeks.

## Discussion

This comparative study analyzing the refractive, topographic, and clinical outcomes of transepithelial CXL against standard epithelium-off CXL in the treatment of progressive keratoconus in adult Pakistani population is the first study in literature on Pakistani population to the best of our knowledge. Both transepithelial and epithelium-off CXL showed

**Table 5: Preoperative transepithelial CXl - topographic and pachymetric data in relation to clinical progression or stablization**

| Transepithelial CXL *n*=32 | Preoperative Kmax Range | | Preoperative pachy thin | |
|---|---|---|---|---|
| | <55D | >55D | <400µ | >400µ |
| Progression | 2 (25%) | 6 (75%) | 3 (37.5%) | 5 (62.5%) |
| Disease stabilization | 15 (62.5%) | 9 (37.5%) | 5 (20%) | 19 (79.16%) |

improvement in UDVA, CDVA and topographic indices at 12 and 18 months follow-up. The flattening of keratometry ($K_{max}$, simulated K, steep K) and reduction in pachymetry was significantly superior in epithelium-off CXL group ($P < 0.05$) while improvement in UDVA and CDVA remained statistically insignificant between the groups. In terms of treatment success, clinical stabilization and regression were achieved in 94% of eyes in epithelium-off CXL and in 75% of eyes in transepithelial CXL group. Twenty percent of this 75% eyes had a pachy thin of < 400 µ. The transepithelial group showed progression in 8 (25%) eyes that were higher than epithelium-off CXL group which was only 6% at the end of 12 months. Patients lost to follow-up at 18 months, in each group limited us in reanalyzing the long term stability, owing to nonlinear trend of disease progression.

Transepithelial CXL offers several advantages over the epithelium-off CXL, such as faster visual rehabilitation, less postoperative pain, decreased incidence of keratitis, and epithelial healing problems. It utilizes a special riboflavin solution with EDTA and benzalkonium chloride which enhances penetration through intact epithelium. Still, the major limitation has been its relatively inefficacy in halting the progression of keratoconus which is attributed to reduced UVA transmittance and riboflavin stromal diffusion with intact epithelium as described by Bottos *et al*.[11] Wollensak *et al*. also reported that one-fifth of biomechanical effect was achieved with CXL if the epithelium was not debrided.[8]

Literature review on comparison of transepithelial and epithelium-off CXL revealed controversial results in different age groups and populations.[6,12-17] Magli *et al*. compared transepithelial and epithelium-off CXL in paediatric population with similar efficacy.[6,13] Buzzonetti and Petrocelli reported visual improvement at 18 months with no improvement in topographic indices.[14] Caporossi *et al*. described an initial temporary stabilization of keratoconus in 26 eyes of young patients between 11 and 26 years of age at 1-year posttransepithelial CXL. This was followed by progression and increase in *K* values at 24 months, requiring retreatment in 19% of cases. Çerman *et al*. described similar results in adult population.[15] Kocak *et al*. compared transepithelial and epithelium-off CXL at 12 months follow-up with no statistically significant change in UDVA and CDVA with progression in 11 out of 17 eyes in transepithelial CXL and deterioration in topographic indices in adult population.[16] Rossi *et al*. and Filippello *et al*. on the other hand reported clinical stability and similar refractive outcomes in both transepithelial and epithelium-off CXL at 12 months.[5,17] In our study, CDVA and UDVA improved significantly with no statistical significant difference between transepithelial and epithelium-off CXL group at 12 months which were comparable to the previous similar trials results of Çerman *et al*.[15,18] The mean reduction in corneal thickness in our study was 30 µ in epithelium-off CXL group and 4 µ in transepithelial group at 18 months postoperatively measured by dual Scheimpflug corneal topography in accordance with similar study.[15] Gutiérrez *et al*. proposed that this decrease in pachymetry reflects stromal collagen lamella compactness and dehydration and reported a reduction of 50 µ in average corneal thickness at 1-month postoperative which lasted till the end of 1 year.[19] This suggests that transepithelial CXL might not be as effective as epithelium-off CXL in bringing an anatomical or structural change. We achieved a 2.0D topographic flattening of maximum keratometry in epithelium-off CXL at 12 months which was comparable to 1.5D of Soeters *et al*.[18] and better than 0.27D flattening described by Kocak *et al*. in epithelium-off CXL at 1 year.[16] The flattening of keratometry achieved can be explained by a steeper preoperative $K_{max}$ values, 53.4D and 58D, respectively, against 48.97D, which are known to flatten more after CXL.[18] The average $K_{max}$ flattening achieved with epithelium-off CXL is statistically higher in our study, which suggests that transepithelial CXL is effective yet not comparable to epithelium-off CXL in reducing topographic keratometric indices, also indicated in the previous clinical trials.[15,18] Progression in 25% of eyes in transepithelial CXL combined with significantly less pronounced effect on flattening topographic keratometric indices, mean reduction of corneal pachymetry as compared to epithelium-off CXL at 12 months implies that transepithelial CXL is not as effective as epithelium-off CXL in halting the progression of keratoconus. These results were consistent with other comparative studies of transepithelial and epithelium-off CXL in adult population with progressive keratoconus.[15,16,18] Unavailability of confocal microscopy at our settings limited our ability to see stromal changes after CXL, which was reported by Touboul *et al*. with both conventional accelerated protocols of epithelium-off CXL, however, corneal stroma remains unaltered after transepithelial CXL.[20] This might be the reason for continued progression of disease in our patients in transepithelial CXL group. Moreover, the disease itself progresses very rapidly in Asian eyes, which again can contribute to relatively higher progression percentage in our study.[21]

The commercially different riboflavin solutions and different treating protocols might have resulted in variance of results.[5,11,18] Modification of UVA irradiation profile or shortening of the UVA irradiation with increase irradiation power is the new evolving grounds.[22-24] Ricrolin TE has been the most studied transepithelial riboflavin solution so far. We have used Peschke TE in our study achieving comparable results to Ricrolin TE clinical trials.[15,18] Limitations of our study are relatively small sample size and the nonequivalence of the transepithelial CXL group in terms of pachy thin. The purpose was to ethically provide a CXL treatment to halt the progression of disease in a young patient, unfit for standard treatment despite controversial efficacy, to prolong or prevent corneal transplants.

## Conclusion

We at present do not recommend a complete replacement of epithelium-off CXL with transepithelial CXL in corneas with more than 400 μ thickness in Pakistani eyes with progressive keratoconus. Transepithelial CXL can be offered as a rescue treatment in progressive keratoconus to halt the progression of disease in these young patients having thin corneas with pachy thin <400 μ, unsuitable for an invasive procedure, especially in our country due to ineffective cornea banks, and lack of surgical experience in selective layered keratoplasties. Penetrating keratoplasty offered for very progressive advanced disease has all its risks and complications.


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### Conflicts of interest
The authors declare that there are no conflicts of interests of this paper.

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