CLINICAL AND EXPERIMENTAL
OPTOMETRY

RESEARCH PAPER

Effect of corneal cross-linking on contact lens tolerance in keratoconus

Clin Exp Optom 2017; 100: 369–374 DOI:10.1111/cxo.12470

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Submitted: 11 April 2016
Revised: 16 May 2016
Accepted for publication: 9 June 2016

Background: The aim was to investigate changes in corneal sensation and rigid gas-permeable (RGP) contact lens tolerance after corneal cross-linking (CXL) on patients with keratoconus.

Methods: Thirty eyes of 30 patients, who were RGP lens intolerant, were treated with CXL. The main outcome measures were corneal sensation evaluation by Cochet–Bonnet esthesiometry, sub-basal nerve fibre assessment by corneal *in vivo* confocal microscopy and RGP contact lens tolerance evaluation with the Likert scale and wearing time. All eyes were evaluated preoperatively and post-operatively at one, three and six months after CXL procedure.

Results: The mean age was 25.3 ± 6.2 years. Preoperatively, the maximum keratometry (Kmax) in study eyes was 56.89 ± 4.60 D. Six months after CXL, it reduced to 56.03 ± 4.85 D ($p = 0.01$). Preoperative mean corneal sensation was 0.44 ± 0.05 g/mm^2, (range: 0.40 to 0.55); it was significantly decreased at the first month and increased to preoperative values after six months. The sub-basal nerve plexus could not be visualised in 90 per cent of the patients by confocal microscopy at one month post-operatively. Gradual restoration of corneal innervation with almost similar preoperative levels at post-operative month six was noted. There were significant differences in Likert scores between preoperative and third and sixth months after CXL. Likert scale scores correlated significantly with corneal sensitivity.

Conclusion: It can be concluded that increased RGP contact lens tolerance after CXL may be associated with the potential role of decreased corneal sensitivity and corneal flattening after CXL.

Key words: corneal cross-linking, keratoconus, rigid gas-permeable contact lens, tolerance

Keratoconus is a progressive, asymmetric disease characterised by steepening and distortion of the cornea. While spectacles may provide acceptable visual acuity in the early stages of keratoconus, rigid gas-permeable (RGP) contact lenses are the primary method of visual correction in keratoconic patients; however, a considerable number of more advanced cases suffer symptoms of contact lens intolerance and the presence of the subepithelial nerve plexus may cause this problem.[1,2] Although all of these techniques correct the refractive errors of keratoconus, they do not treat the cause underlying the corneal ectasia and therefore, cannot stop the progression of keratoconus.[3] Corneal collagen cross-linking (CXL) is a unique and effective method which hardens the cornea and stops or delays progression of the disease.[4,5]

Corneal confocal microscopic studies have demonstrated a reduction in subepithelial nerve plexus density after CXL, which seems to return to the preoperative status several months after the procedure.[6–9] Recent studies have demonstrated a transient reduction in corneal sensitivity after epithelium-off CXL in keratoconic corneas up to six months after the procedure.[10,11] Damage to corneal nerves leads to diminished corneal sensitivity and possible transient or long-term alterations in the functional integrity of the ocular surface.[12]

To the best of our knowledge, no study is present in the literature reporting RGP contact lens tolerance after CXL. This study aims to investigate the changes in corneal sensitivity and subepithelial nerve plexus after CXL and to assess RGP contact lens tolerance in keratoconus patients after CXL.

METHODS

This study was performed as part of a clinical research project approved by the local Ethics Committee of Gazi University, Turkey, and written informed consent was obtained from all patients.

This present study included 30 eyes of 30 patients with progressive keratoconus who were not able to tolerate RGP lenses because of their irregular corneal astigmatism. An experienced practitioner fitted the RGP lenses prior to CXL and at one month post-CXL. The clinical diagnosis of keratoconus was based on topographic findings as well as biomicroscopic signs of keratoconus. All treated eyes had moderate keratoconus (grade II according to Amsler-Krumeich's classification,[13] with mean central keratometry readings of less than 53 dioptres, absence of corneal scarring and minimum corneal thickness of greater than 400 μm) with documented evidence of progression with reduced uncorrected distance vision or distance visual acuity by more than one line and/or worsening of refractive or corneal astigmatism, keratometry or cone apex power increased by

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0.75 D over the 12 to 24 months prior to CXL.

Exclusion criteria included advanced keratoconus, where corneal irregularity or scarring prevented acquisition of accurate refractive and topographic data, central corneal thickness less than 400 μm (with epithelium on), other ocular pathology, previous anterior segment surgery and diabetes.

The main outcome measures were corneal sensation evaluation by Cochet–Bonnet aesthesiometry, sub-basal nerve fibre assessment by corneal *in vivo* confocal microscopy and RGP contact lens tolerance evaluation with the Likert scale.[14] All eyes were evaluated preoperatively and postoperatively at one, three and six months after CXL procedure. RGP contact lens tolerance was not evaluated at one month.

The surgical procedure of corneal cross-linking induced by riboflavin and ultraviolet A light (UVA) was performed in all patients according to the Dresden protocol as described by Wollensak and colleagues.[5]

Corneal aesthesiometry

Corneal sensitivity was measured using the Cochet–Bonnet aesthesiometer (Luneau Ophthalmlogie, Chartres, France), which consists of a nylon filament 60 mm in length and 0.12 mm in diameter. Using it as a handheld instrument, the subject was instructed to fixate a point in front, while the nylon thread was directed toward the central cornea, perpendicular to the area of touch. The cornea was judged to have been touched when the clinician noticed the first visible bending of the thread. After each approach, the subject was asked to respond if the stimulus was felt. Measurements began using the lowest intensity stimulus, which corresponds to the longest thread length (60 mm). If the subject was unable to feel the stimulus, the thread was shortened by 5.0 mm. This procedure was repeated until the subject felt the filament. This length is converted into pressure (g/mm^2) using the table provided with the instrument.

Wearing time and subjective performance

RGP lenses (Rose K design, FreshKon, Shanghai, China) were prescribed one month after CXL. The patients were fitted with suitable RGP lenses and then assessed on a slit-lamp with fluorescein. The fit was judged to be good if there was apical clearance or mild apical touch, good centration and adequate edge lift. If the ordered lenses gave an acceptable fit, vision and comfort, the patient was scheduled for the next visit. Patients were asked to grade the performance of RGP lenses using a Likert scale[15,16] (in which 1 represents very poor and 5 represents excellent) with respect to foreign body sensation, comfort and overall satisfaction preoperatively and three and six months after the CXL procedure. Additionally, regarding lens wearing time, patients were asked to state how many hours a day they had been wearing the lenses.

In vivo confocal microscopy

All corneal sub-basal nerve fibre assessments were performed using scanning slit *in vivo* confocal microscopy (Confoscan 3, Nidek Technologies, Gamagori, Japan). The examinations were performed on 'full mode' to examine the full thickness of the cornea and the lateral solution (depth) of the images was 1.0 μm. The interval between images was 5.0 μm. Images of sub-basal nerves of the central cornea were acquired using the same illumination intensity and by focusing the microscope beneath the basal epithelium. Approximately five images were randomly selected for qualitative analysis from the basal epithelium. The sub-basal nerve fibre was assessed. The confocal images were selected and analysed by the same clinician (MU). The clinician was masked to the subjects and the time of the visits in both of the measurements of corneal sensitivity and sub-basal nerve fibre density.

Statistical analysis

SPSS version 12 for Windows (Chicago, Illinois, USA) was used for statistical analysis. Descriptive data were presented as mean and standard deviation and percentages. The data were tested for normal distribution using the Kolmogorov–Smirnov test. To compare the corneal sensitivity and RGP contact lens tolerance among the different visits, Wilcoxon's non-parametric test was considered. Spearman correlation analysis was performed to evaluate the relationship between Likert scale scores and corneal sensitivity values. The p-values less than 0.05 were considered statistically significant.

RESULTS

Demography

Thirty subjects with keratoconus (18 male) participated in this study. The mean age of the subjects with keratoconus was 25.30 ± 6.23 years (range: 12 to 36 years).

Corneal topography

Preoperatively, the mean keratometry in study eyes was 48.84 ± 2.99 D (range: 43.45 to 52.99 D). One month after CXL, it had increased to 49.29 ± 3.31 D (range: 43.80 to 54.70 D) ($p = 0.1$). Three and six months after CXL, the mean keratometric readings were 48.73 ± 3.14 D (range: 43.17 to 53.73 D) ($p = 0.271$) and 48.86 ± 3.78 D (range: 43.01 to 60.45 D) ($p = 0.17$), respectively.

Preoperatively, the maximum keratometry (Kmax) in study eyes was 56.89 ± 4.60 D (range: 49.02 to 66.50 D). One month after CXL, it had increased to 57.27 ± 4.79 D (range: 48.57 to 67.02 D) ($p = 0.181$). Three and six months after CXL, it reduced to 56.16 ± 4.63 D (range: 47.00 to 63.71 D) ($p = 0.08$) and 56.03 ± 4.85 D (range: 45.86 to 64.47 D) ($p = 0.01$), respectively.

Corneal sensitivity

The preoperative mean value for corneal sensation was 0.44 ± 0.05 g/mm^2 (range: 0.40 to 0.55 g/mm^2). One month after CXL procedure the mean value for corneal sensation decreased to 1.19 ± 0.72 g/mm^2 (range: 0.55 to 2.80 g/mm^2) ($p = 0.0001$). Three and six months after CXL, the mean values for corneal sensation were 0.48 ± 0.06 g/mm^2 (range: 0.40 to 0.55 g/mm^2) and 0.44 ± 0.05 g/mm^2 (range: 0.40 to 0.55 g/mm^2), respectively. There were no statistical differences comparing the corneal sensation values at three and six months after CXL with the preoperative values ($p = 0.66$, $p = 0.9$, respectively) (Figure 1).

Wearing time and subjective performance

The mean lens wearing time preoperative and at the third and sixth months after

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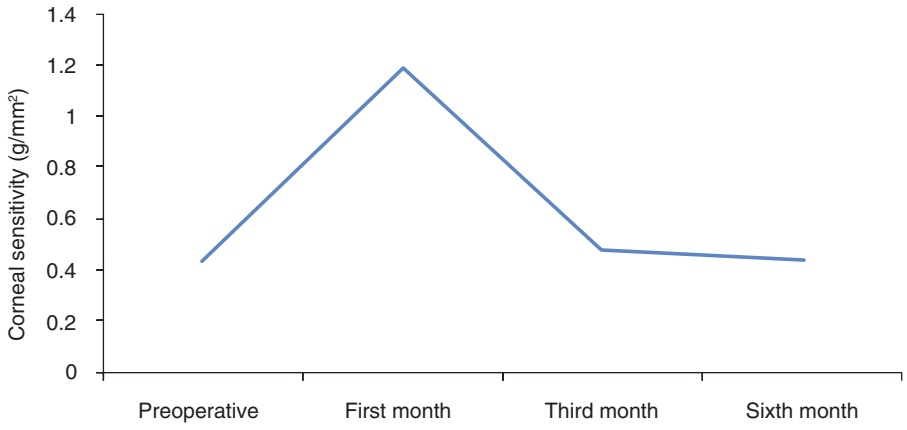


Figure 1. Corneal sensitivity changes before corneal cross-linking and after one, three and six months

CXL were 6.4 ± 2.5 hours per day (range: 3 to 8 hours per day), 12.6 ± 1.4 hours per day (range: 10 to 14 hours per day) and 13.2 ± 1.7 hours per day (9 to 15 hours per day), respectively ($p < 0.001$, preoperative versus third month; $p < 0.001$, preoperative versus sixth month) (Figure 2).

The number of patients who needed a break from their RGP contact lens during the day was one (3.3 per cent) at three months and two (6.6 per cent) at six months.

Comparing foreign body sensation, comfort and overall satisfaction, the differences between preoperative and at three and six months after CXL scores were significant ($p = 0.001$, $p = 0.001$, respectively), with significantly lower scores preoperatively as shown in Table 1. There was no significant difference in subscale scores between the third month and sixth month ($p > 0.05$). Likert scale scores correlated significantly with corneal sensitivity at preoperative and three and six months after CXL ($p = 0.02$, $p = 0.03$, $p = 0.03$, respectively and Spearman correlation coefficients, $r = -0.752$, $r = 0.644$, $r = 0.656$, respectively).

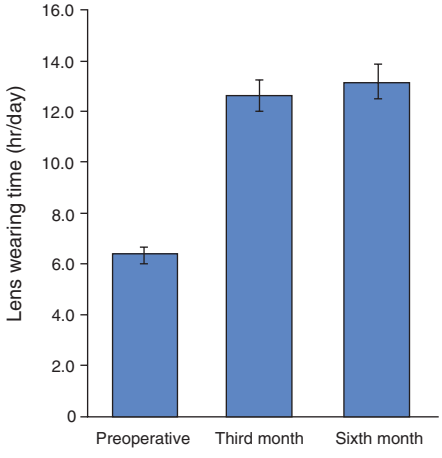


Figure 2. Comparisons of mean rigid gas-permeable (RGP) contact lens wearing time at preoperative and third and sixth months after corneal cross-linking

In vivo confocal microscopy

Preoperatively, the sub-basal nerve plexus displayed the extremely tortuous and branched nerve fibre pattern typical of keratoconus. Characteristic hyperreflective keratocyte nuclei were visualised in the anterior, middle and posterior stroma.

At one month post-operatively, no sub-basal nerve plexus could be visualised in the central cornea in 90 per cent of patients. Confocal microscopic examination revealed a reticular hyperreflective stromal architecture, without visualisation of the typical hyperreflective keratocyte nuclei (Figure 3). It was not until the third post-operative month that the first sub-basal nerve fibres again became visible on confocal microscopy in the central cornea of 90 per cent of patients. Gradual restoration of corneal innervation with almost similar preoperative levels at post-operative month six was remarkable (Figure 3).

Over the six-month period of the investigation, no adverse effects or endothelial cell damage were noted in any of the patients treated.

DISCUSSION

Rigid contact lenses offer significant improvements in optical performance over spectacle and hydrogel lenses in keratoconic patients; however, fitting RGP contact lenses in irregular astigmatism is difficult because of lens instability due to the superior flat and inferior step profile of the cornea with a significant decentration tendency of the contact lenses.[17] Although RGP lenses provide good visual acuity, discomfort and problems with stability cause discontinuation of these lenses in many patients during the adaptation period. The present study showed increased RGP tolerance and wearing time after CXL with the positive impact of reduced sensitivity in RGP-intolerant patients. Additionally, we documented that CXL with de-epithelialisation causes an initial reduction in corneal sensitivity post-operatively, as expected, because of the transient denervation. In our group of patients, we detected a prominent reduction in corneal sensitivity at one month post-operatively and then a progressive recovery during the next five months. All patients had their corneal sensation restored to the preoperative level at six months. Wasilewski, Mello and Moreira[10] and Kontadakis and colleagues[11] also reported a similar range of corneal sensitivity to our study patients after the CXL procedure for keratoconus.

Dogru and colleagues[18] analysed corneal sensitivity in keratoconic patients and found that 48 per cent of the patients with keratoconus had low corneal sensitivity. The corneal sensitivity was significantly lower in patients with severe keratoconus compared with patients with mild or moderate disease. In our group of patients, corneal sensitivity seemed to be within normal values, although it was not compared with a control group of normal corneas. This is expected because most of the patients in the current study group were in the early stages of keratoconus.

In our study, we included patients who were not able to tolerate RGP lenses because of their irregular corneal astigmatism. Wearing time of RGP lenses for most of the patients was limited (mean 6.4 hours, range: 3 to 8 hours) before CXL procedure. Wearing time increased to 12.6 hours per day and 13.2 hours per day at post-operative third and sixth months, respectively. We think that the reduced

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	Preoperative (n = 30) (Mean ± SD)	Third month (n = 30) (Mean ± SD)	Sixth month (n = 30) (Mean ± SD)	p†	p‡
FB sensation	1.9 ± 1.2 (4.0–5.0)	4.3 ± 1.1 (3.0–5.0)	4.1 ± 1.4 (2.0–5.0)	<0.001	<0.001
Comfort	2.2 ± 1.5 (1.0–3.0)	4.6 ± 0.8 (4.0–5.0)	4.6 ± 0.6 (4.0–5.0)	<0.001	<0.001
Overall satisfaction	2.1 ± 1.7 (1.0–3.0)	4.6 ± 0.7 (4.0–5.0)	4.7 ± 0.9 (4.0–5.0)	<0.001	<0.001

Wilcoxon test:
† Preoperative versus third month
‡ Preoperative versus sixth month
FB: foreign body

Table 1. Comparison of foreign body sensation, comfort and overall satisfaction preoperatively and three and six months after corneal cross-linking

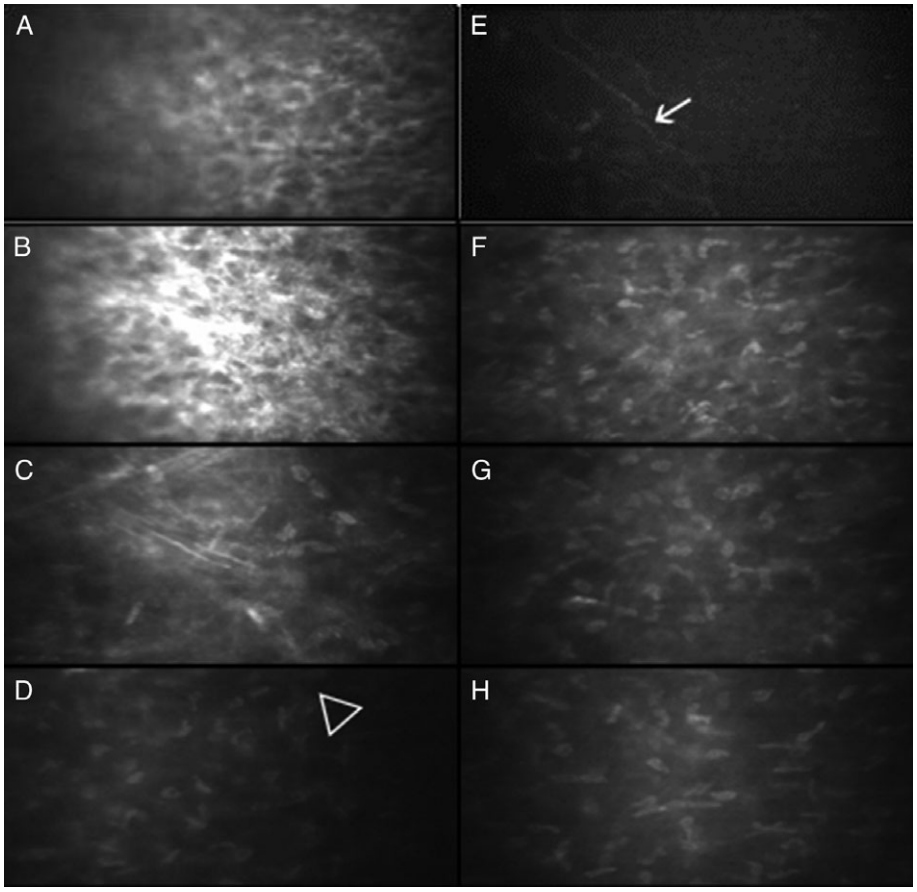


Figure 3. At one month post-operatively (A–D), confocal microscopic examination revealed a reticular hyperreflective stromal architecture (C), without visualisation of the typical hyperreflective keratocyte nuclei (arrow head) (D) and sub-basal nerve plexus (A). Gradual restoration of corneal architecture almost at preoperative levels at post-operative month six (E–H) was remarkable. The corneal sub-basal nerve plexus became visible (arrow) (E). Hyperreflective keratocyte nuclei were visualised in the anterior, middle stroma without reticular hyperreflective stromal architecture.

corneal sensitivity after CXL was attributable to the improvement in RGP lens tolerance occurring between one and three months. The cornea becomes more optically regular after the CXL treatment[19,20] and this can also contribute to an improvement in RGP lens fitting and lens tolerance; however, reduced corneal sensitivity did not seem to explain why comfort wearing RGP lenses persisted three and six months after corneal sensitivity returned to the preoperative level. Kranitz and colleagues[19] and Toprak and Yildirim[20] demonstrated that after CXL treatment, the cornea significantly flattens and becomes more optically regular, resulting in regression of the severity of keratoconus. Improvements in topographic indices might be important indicators of normalisation of the keratoconic cornea. Shalchi, Wang and Nanavaty[21] stated in their article in which they analysed the studies investigating epithelium-off corneal CXL for keratoconus that 27 of 29 (93 per cent) of the studies showed a reduction in Kmax (median: 1.01 D, range: 0.14 to 6.16 D). In our study, a decrease of –0.86 D was observed six months after epithelium-off CXL. This flattening effect of CXL impacts on RGP contact lens fitting and tolerance, suggesting the necessity of a patient-specific approach and a better understanding regarding the actual mechanism behind its potent flattening effect.

Wu and colleagues[15] investigated RGP contact lens-related life quality in keratoconic patients with different grades of severity. They showed that patients with mild and moderate keratoconus were able to achieve a sufficient lens wearing time (mean: 10.4 hours per day; 9.6 hours per

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day, respectively), whereas the severe keratoconic patients showed a significantly reduced wearing time (mean: 4.8 hours per day).

Analysis concerning Likert scale scores revealed that there were significant differences among preoperative and postoperative findings at three and six months. The continued subjective excellent tolerance of RGP lenses after CXL was demonstrated by comparable daily wearing times. Visser, Soeters and Tahzib[22] reported scleral lens tolerance after CXL for keratoconus. The continued good subjective tolerance of scleral lenses after CXL was demonstrated by comparable daily wearing times and the number of breaks during the day, as well as very small differences in comfort, lens dryness, lens handling and overall satisfaction after one year.

In this study, sub-basal nerve plexus confocal images after CXL revealed that corneal innervation is significantly reduced at one month post-operatively and is gradually restored almost to preoperative levels at post-operative month six. Our results correlate with those of previous qualitative studies on corneal confocal microscopic analysis of the sub-basal nerve plexus in post-CXL patients. Mazzotta and colleagues[6] reported a more rapid regeneration of subepithelial nerve fibres that begins at the first month and is almost complete six months after the procedure but does not return to the preoperative structure until two years after the procedure. Kymionis and colleagues[9] reported that reinnervation begins during the third month after CXL. They reported that the nerves are visible after three months but are not yet restored to the preoperative density. Kontadakis and colleagues[11] indicated that corneal innervation is significantly reduced at post-operative month one and is gradually restored almost to preoperative levels nine months post-operatively.

Recently, Xia and colleagues[7] investigated the damage to corneal nerves and subsequent corneal nerve regeneration in response to UVA with de-epithelialisation treatment in rabbits. The appearance of injured nerve fibres in the treatment area coincided with the reduction of corneal sensitivity, suggesting that the reduced corneal sensitivity following UVA with de-epithelialisation is strongly associated with the destruction of corneal nerve architecture. They noticed that the recovery of corneal sensitivity appeared to be faster than the regeneration of injured nerve fibres. Al-Aqaba and colleagues[26] indicated that the immediate disappearance of sub-basal nerves by confocal microscopy was noted only in corneas that were treated with a epithelium-off CXL. In contrast, they were able to detect these nerves in corneas that were treated with the transepithelial (epithelium-on) approach. Therefore, it is likely that early disappearance of sub-basal nerves is attributable to mechanical scraping of both the epithelium and the sub-basal nerves.[26] Furthermore, the corneal epithelium might protect the deeper corneal nerves from the damaging effects of UVA exposure.[27] Epithelium-on CXL techniques have been shown in numerous studies to be less effective than epithelium-off CXL, with a decreased depth of treatment, so decreased exposure to UV/riboflavin may also account for less effect on the nerve plexus.[21,28]

Our study had limitations in terms of a small sample and the lack of a control group. We used only the contact aesthesiometer to monitor corneal sensitivity. Our study could not evaluate the corneal sensitivity's recovery to chemical and temperature stimuli. We started fitting RGP lenses one month post-CXL, while previous authors have fitted RGP lenses as soon as the epithelial defect has healed, as early as one week after CXL.[29] Given the fact that RGP lenses affect the corneal healing process after CXL,[29] the ideal time for fitting RGP lenses post-CXL remains uncertain.

In conclusion, increased RGP contact lens tolerance after CXL may be associated with the potential role of decreased corneal sensitivity and corneal flattening after CXL.

REFERENCES

1. Zadnik K, Steger-May K, Fink BA et al. Between-eye asymmetry in keratoconus. *Cornea* 2002; 21: 671–679.
2. Krachmer JH, Feder RS, Belin MW. Keratoconus and related noninflammatory corneal thinning disorders. *Surv Ophthalmol* 1984; 28: 293–322.
3. Zadnik K, Barr JT, Gordon MO et al. Biomicroscopic signs and disease severity in keratoconus. Collaborative Longitudinal Evaluation of Keratoconus (CLEK) Study Group. *Cornea* 1996; 15: 139–146.
4. Spoerl E, Seiler T. Techniques for stiffening the cornea. *J Refract Surg* 1999; 15: 711–713.
5. Wollensak G, Spoerl E, Seiler T. Riboflavin/ultraviolet-a-induced collagen crosslinking for the treatment of keratoconus. *Am J Ophthalmol* 2003; 135: 620–627.
6. Mazzotta C, Traversi C, Baiocchi S et al. Corneal healing after riboflavin ultraviolet-A collagen cross-linking determined by confocal laser scanning microscopy in vivo: early and late modifications. *Am J Ophthalmol* 2008; 146: 527–533.
7. Xia Y, Chai X, Zhou C et al. Corneal nerve morphology and sensitivity changes after ultraviolet A/riboflavin treatment. *Exp Eye Res* 2011; 93: 541–547.
8. Filippello M, Stagni E, Buccoliero D et al. Transepithelial cross-linking in keratoconus patients: confocal analysis. *Optom Vis Sci* 2012; 89: e1-7.
9. Kymionis GD, Diakonis VF, Kalyvianaki M et al. One-year follow-up of corneal confocal microscopy after corneal cross-linking in patients with post laser in situ keratosmileusis ectasia and keratoconus. *Am J Ophthalmol* 2009; 147: 774–748.
10. Wasilewski D, Mello GH, Moreira H. Impact of collagen crosslinking on corneal sensitivity in keratoconus patients. *Cornea* 2013; 32: 899–902.
11. Kontadakis GA, Kymionis GD, Kankariya VP et al. Effect of corneal collagen cross-linking on corneal innervation, corneal sensitivity and tear function of patients with keratoconus. *Ophthalmology* 2013; 120: 917–922.
12. Marfurt CF, Cox J, Deek S et al. Anatomy of the human corneal innervation. *Exp Eye Res* 2010; 90: 478–492.
13. Krumeich JH, Daniel J, Knulle A. Live-epikeratophakia for keratoconus. *J Cataract Refract Surg* 1998; 24: 456–463.
14. Pesudovs K, Garamendi E, Elliott DB. The Contact Lens Impact on Quality of Life (CLIQ) Questionnaire: development and validation. *Invest Ophthalmol Vis Sci* 2006; 47: 2789–2796.
15. Wu Y, Tan Q, Zhang W et al. Rigid gas-permeable contact lens related life quality in keratoconic patients with different grades of severity. *Clin Exp Optom* 2015; 98: 150–154.
16. Lass JH, Lembach RG, Park SB et al. Clinical management of keratoconus. A multicenter analysis. *Ophthalmology* 1990; 97: 433–445.
17. Lim N, Vogt U. Characteristics and functional outcomes of 130 patients with keratoconus attending a specialist contact lens clinic. *Eye (Lond)* 2002; 16: 54–59.
18. Dogru M, Karakaya H, Ozcetin H et al. Tear function and ocular surface changes in keratoconus. *Ophthalmology* 2003; 110: 1110–1118.
19. Kranitz K, Kovacs I, Mihaltz K et al. Changes of corneal topography indices after CXL in progressive keratoconus assessed by Scheimpflug camera. *J Refract Surg* 2014; 30: 374–378.
20. Toprak I, Yildirim C. Effects of corneal collagen crosslinking on corneal topographic indices in patients with keratoconus. *Eye Contact Lens* 2013; 39: 385–387.
21. Shalchi Z, Wang X, Nanavaty MA. Safety and efficacy of epithelium removal and transepithelial corneal collagen crosslinking for keratoconus. *Eye (Lond)* 2015; 29: 15–29.
22. Visser ES, Soeters N, Tahzib NG. Scleral lens tolerance after corneal cross-linking for keratoconus. *Optom Vis Sci* 2015; 92: 318–323.
23. Macsai MS, Varley GA, Krachmer JH. Development of keratoconus after contact lens wear. *Patient characteristics. Arch Ophthalmol* 1990; 108: 534–538.
24. Segal O, Barkana Y, Hourovitz D et al. Scleral contact lenses may help where other modalities fail. *Cornea* 2003; 22: 308–310.
25. Romero-Rangel T, Stavrou P, Cotter J et al. Gas-permeable scleral contact lens therapy in ocular surface disease. *Am J Ophthalmol* 2000; 130: 25–32.

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26. Al-Aqaba M, Calienno R, Fares U et al. The effect of standard and transepithelial ultraviolet collagen cross-linking on human corneal nerves: an ex vivo study. *Am J Ophthalmol* 2012; 153: 258–266.
27. Spadea L, Salvatore S, Paroli MP et al. Recovery of corneal sensitivity after collagen crosslinking with and without epithelial debridement in eyes with keratoconus. *J Cataract Refract Surg* 2015; 41: 527–532.
28. Cerman E, Toker E, Ozarslan Ozcan D. Transepithelial versus epithelium-off crosslinking in adults with progressive keratoconus. *J Cataract Refract Surg* 2015; 41: 1416–1425.
29. Sehra SV, Titiyal JS, Sharma N et al. Change in corneal microstructure with rigid gas permeable contact lens use following collagen cross-linking: an in vivo confocal microscopy study. *Br J Ophthalmol* 2014; 98: 442–447.

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