Acta Scientific Ophthalmology (ISSN: 2582-3191)

Volume 6 Issue 10 October 2023

Research Article

Long-Term Follow-Up of the Effect of Accelerated CXL Protocol on Pellucid Marginal Degeneration

Hossein Jamali, Mohammad Hassan Jalalpour*, Mohammad Reza Badie and Maryam Nadi

Poostchi Ophthalmology Research Center, Department of Ophthalmology, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran

***Corresponding Author:** Mohammad Hassan Jalalpour, Poostchi Ophthalmology Research Center, Department of Ophthalmology, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran.

DOI: 10.31080/ASOP.2023.06.0687

Received: July 24, 2023

Published: September 28, 2023

Abstract

Purpose: Pellucid marginal degeneration (PMD) is a rare non-inflammatory corneal ectasia that progresses, making visual rehabilitation challenging. Since PMD is unique and different from keratoconus, the effect of collagen cross-linking might be different. This study aims to evaluate the efficacy of accelerated corneal collagen crosslinking (CXL) over a 5-year follow-up period in patients with PMD.

Methods: A retrospective interventional case series study was conducted on 43 eyes of 24 patients with PMD who underwent accelerated CXL. Visual acuity, refraction, topographic keratometry, pachymetry, and topometric indices were measured before and after the procedure.

Results: The study found an improvement in visual acuity from LogMAR 0.36 ± 0.22 before CXL to LogMAR 0.21 ± 0.12 after CXL ($P < 0.001$). The study also observed a reduction in the sphere from -2.46 ± 1.81 D before CXL to -1.7 ± 1.63 after CXL ($P < 0.001$). However, there was no significant difference in cylindrical value ($P = 0.83$). Flat keratometry decreased from 45.11 ± 1.75 D preoperatively to 44.30 ± 1.75 postoperatively ($P < 0.001$), but steep keratometry did not change significantly (preoperative 47.92 ± 1.74D, postoperative 47.53 ± 1.70, $P = 0.081$). Additionally, maximum keratometry reduced from 51.03 ± 3.21 D before CXL to 50.53 ± 3.42 after CXL ($P = 0.005$).

Conclusions: The results of this study suggest that accelerated CXL can be effective in treating PMD, as it was found to improve visual acuity and reduce spherical and maximum keratometry values.

Keywords: Collagen Cross-linking; Pellucid Marginal Degeneration; Keratoconus; Penetrating Keratoplasty; Deep Anterior Lamellar Keratoplasty

Abbreviations

BCVA: Best Corrected Visual Acuity; SE: Spherical Equivalent; ISV: Index of Surface Variance; IVA: Index of Vertical Asymmetry; IHD: Index of Height Decentration; IHA: Index of Height Asymmetry; R min: Minimum Cornea Curvature; D: Pentacam Belin-Ambrosio Total Deviation

Introduction

Pellucid marginal degeneration (PMD) is a rare, non-inflammatory corneal ectasia characterized by an inferiorly banded thin cornea with slight steepening superior to the thin zone [1-3]. Despite ectasia, Schlaeppi has described this as a "clear thin zone of the cornea named pellucid" to emphasize its clarity and lack of scarring, lipid accumulation, or vascularisation [4]. While some studies have reported the involvement of the superior, nasal, and even temporal zones, the thin zone is generally located inferiorly, extending from 4 to 8 o'clock [5-8].

As mentioned, PMD is characterized by inferior band corneal thinning 1-2 mm from the inferior limbus, causing vertical meridian flattening and generating against the rule astigmatism [9]. In PMD patients, protrusion of the cornea above the thin portion can

significantly reduce visual acuity [10]. The crab claw pattern seen on corneal topography is a hallmark of PMD, indicating inferior steepening with a much flatter vertical meridian [3,11]. However, since this pattern is also typical in eyes with inferiorly decentered keratoconus, it is inconclusive to diagnose PMD [12].

PMD patients usually seek treatment later in life, between the second and fifth decades [5,13,14]. Although there are several ways to distinguish PMD from keratoconus, telling the two apart can still be challenging [12,15]. PMD appears to be a unique entity based on its corneal characteristics [16,17].

PMD can be visually rehabilitated through surgical procedures such as intrastromal corneal ring segment, deep anterior lamellar keratoplasty, and penetrating keratoplasty. However, these procedures are associated with a higher risk of astigmatism and graft rejection [5,18,19]. Since PMD visual rehabilitation is complex [11], it is crucial to slow down its progression. In keratoconus, collagen crosslinking prevents corneal ectasia progression [20]. However, PMD is a unique entity from keratoconus, and the impact of CXL on PMD patients may vary.

To the best of our knowledge, there are only a few studies on the effect of CXL on PMD, and they have yet to investigate the long-term outcome of the pure accelerated CXL protocol [21-23]. Therefore, this study aims to assess the effect of the accelerated CXL protocol over an extended period.

Materials and Methods

This retrospective interventional case series study was approved by the institutional review board of Shiraz University of Medical Sciences and conducted by the Declaration of Helsinki and its subsequent revisions. Informed consent was obtained from all patients before their surgical intervention after explaining the procedure and potential risks in compliance with institutional and legal standards.

All PMD patients who underwent accelerated CXL from 2013 to 2020 were included in this study. PMD was diagnosed as a crab claw appearance in corneal topography, inferior displacement of the cone, and a band of corneal thinning under the cone. Patients underwent a comprehensive eye examination, including visual acuity, slit-lamp biomicroscopy, and indirect ophthalmoscopy. Scheimpflug imaging equipment (Pentacam HR, OCULUS) was used to collect data on steep and flat meridian keratometry values, average keratometry value (K mean), corneal thickness at the thinnest point, and topometric indexes such as index of surface variance (ISV), index of vertical asymmetry (IVA), keratoconus index (KI), center keratoconus index (CKI), index of height asymmetry (IHA), index of height decentration (IHD), and minimum radius of curvature (R min).

The inclusion criteria were mild to moderate PMD and a minimum corneal thickness of 400 µm or higher at the thinnest point with progression, defined as a 1D increase in K value after one year of follow-up. Patients with a history of herpetic keratitis, hard contact lens usage, autoimmune disease, and ocular surgery were excluded. Only one eye was treated with accelerated CXL per session, and the procedure was performed by a single surgeon using the accelerated CXL protocol.

Surgical technique

Topical 1% tetracaine hydrochloride anesthetized the patient's eye under sterile conditions. The middle 9.0 mm corneal epithelium was carefully removed using a Hocky knife. Next, 0.1% riboflavin with hydroxypropyl methylcellulose (HPMC; VibeX Rapid, Avedro, Waltham, MA) was administered every 3 minutes for 30 minutes in the accelerated protocol. The cornea was then exposed to 9 mW/cm^2 continuous irradiation for 10 minutes, resulting in a total irradiation dosage of 5.4 J/cm^2. After the procedure, the cornea was rinsed with a balanced salt solution, and a drop of 0.5% levofloxacin was administered. A silicone hydrogel bandage contact lens was used, and 0.5% levofloxacin combined with 0.1% betamethasone was administered four times daily. The bandage contact lens was removed after the epithelium healed, and postoperative drugs were gradually reduced over a month.

Statistical analysis

Statistical analysis was performed using SPSS software (version 26.0, SPSS Inc, Chicago, IL). Continuous variables were presented as mean and standard deviation. The Kolmogorov-Smirnov test was used to assess normal distribution. The paired t-test was used for parametric data, and the Wilcoxon signed-rank test was used for nonparametric data to compare preoperative vs postoperative measurements. A p-value of less than 0.05 was considered statistically significant.

Results

A total of 43 eyes from 24 patients (13 males and 11 females) were included in this study. The average age of the patients who received accelerated CXL was 36 ± 7 years, and the average follow-up time was 5.1 ± 0.6 years. Visual acuity significantly improved from

LogMAR 0.36 ± 0.22 to LogMAR 0.21 ± 0.12 (P < 0.001). In terms of refractive error, the sphere improved from -2.46 ± 1.81 to -1.7 ± 1.63 (P < 0.001), but there was no significant change in cylindrical value (p = 0.83). The spherical equivalent increased from -4.41 ± 1.61 to -3.20 ± 2.1 (P < 0.001).

Although the flat keratometry decreased from 45.11 ± 1.75 to 44.30 ± 1.75 (P < 0.001), there was no significant change in steep keratometry (preoperative: 47.92 ± 1.74; postoperative: 47.53 ± 1.70; P = 0.081). Maximum keratometry was significantly reduced from 51.03 ± 3.21 to 50.53 ± 3.42 (P = 0.005). Although the thinnest corneal thickness was decreased by about 12 micrometers, it was statistically insignificant (preoperative 470 ± 34 postoperative 458 ± 36 P = 0.057) (Figure 1). There was no significant change in corneal prolateness, as measured by the Q value (P = 0.11). The topometric indexes, including ISV, IVA, KI, CKI, IHA, IHD, and R min, did not change significantly (Table 1).

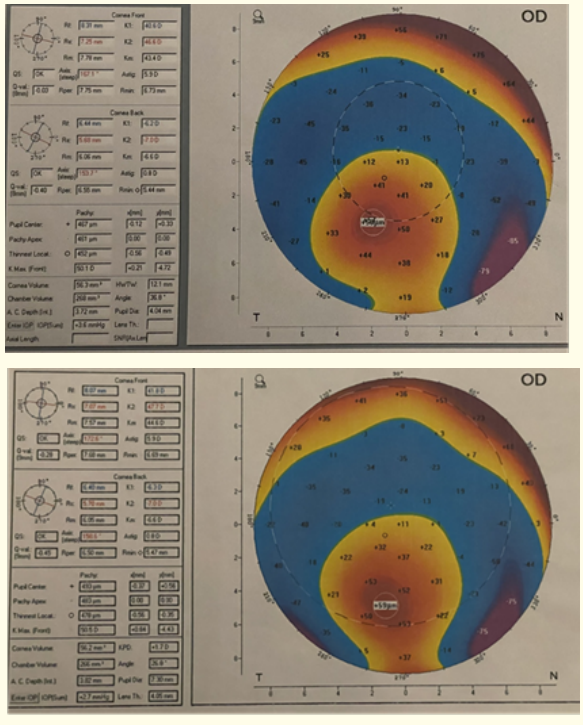

Figure 1: Pentacam on the left side shows a topographic date before collagen cross-linking. Pentacam on the right side shows topographic data after collagen cross-linking.

Variable	Before CXL	After CXL	P value
K1 flat meridian(diopter)	45.12 ± 1.75	44.30 ± 1.75	0.0001
K2 steep meeidian(diopter)	47.93 ± 1.74	47.53 ± 1.71	0.081
Kmax(diopter)	51.03 ± 3.21	50.53 ± 3.42	0.006
BCVA (log MAR)	0.36 ± 0.22	0.21 ± 0.12	0.0001
Thinnest point (micro meter)	470 ± 34	458 ± 36	0.059
Q value	-0.66 ± 0.24	-0.63 ± 0.23	0.114
Sphere (Diopter)	-2.46 ± 1.81	-1.7151 ± 1.63	0.0001
Cylinder (Diopter)	-3.40 ± 2.80	-3.38 ± 2.89	0.900
SE	-4.41 ± 1.61	-3.20 ± 2.1	0.0001
ISV	84. ± 31	85.37 ± 35	.976
IVA	0.92 ± 0.42	0.92 ± 0.51	0.571
IHD	0.50 ± 2.42	0.12 ± 0.06	0.562
IHA	29.2 ± 17.83	30.40 ± 18.81	0.789
Rmin	6.66 ± 0.41	6.63 ± 0.42	0.911
D	7.17 ± 5.77	7.04 ± 2.53	0.158

Table 1: Measured mean values for best corrected visual acuity, sphere, cylinder, spherical equivalent, ISV, IVA, IHD, Rmin, D, keratometry, Q value.

BCVA: Best corrected visual acuity, SE: Spherical Equivalent, ISV: Index of Surface Variance, IVA: Index of Vertical Asymmetry, IHD: Index of Height Decentration, IHA: Index of Height Asymmetry, R min: Minimum cornea curvature, D: Pentacam Belin-Ambrosio total deviation.

Discussion

Since corneal transplantation for PMD patients is invasive and does not guarantee a visual return, slowing its progression is vital. CXL has proven to delay or even prevent corneal transplantation in keratoconus while stabilizing the condition [24]. However, PMD is a type of ectasia that differs from keratoconus, and the effects of CXL on PMD may vary. Only a few studies have examined the effects of CXL on PMD. In this investigation, we used the Accelerated CXL technique instead of the conventional Dresden procedure and had a more extended follow-up period [21-23,25].

Although CXL is not a routine technique for visual rehabilitation, our data suggest a minor improvement in visual acuity. This finding contrasts Steppat., et al. and Irajpour., et al. [21,23], who

found no change in visual acuity, but our results are consistent with those of other investigations [22,25]. Our study found an improvement in flat keratometry (K1), which is similar to the findings of Bikove., et al. [25]. Similarly, like Irajpour., et al. study, we found no significant change in cylindrical value [21]. However, our investigation revealed an improvement in the spherical equivalent, contrary to Irajpour., et al. opinion [21].

In our study, we found no alterations in steep keratometry (K2), which is consistent with the findings of Irajpour., et al. [21], but in contrast to Steppat., et al. study, which detected no changes in corneal keratometry [23]. We also found reductions in maximum keratometry, contrary to previous studies that found no difference in maximal keratometry [21-23,25]. The thickness of the thinnest part of the cornea was also reduced in our study, which aligns with earlier investigations [21-23,25]. This transformation was likely due to corneal reepithelialization during CXL surgery, postoperative keratocyte apoptosis, and structural alterations in corneal collagen fibrils and the extracellular matrix in the anterior stroma [26].

At the 12-month follow-up, Pricher., et al. stated that the measurement of the cornea's thinnest point on the inferior vertical Scheimpflug image would increase. This might be related to the fact that CXL uses a different form of UV irradiation that is decentered [22]. Topometric indices, such as the ISV, IVA, KI, CKI, IHA, IHD, and R min, did not reveal any significant change, consistent with previous studies [21-23,25]. Several trials have combined CXL with laser vision correction to treat PMD, showing no ectasia progression [27,28]. According to Cagil., et al. [29], Transepithelial PTK and Accelerated CXL might be able to stop PMD progression. Cagil., et al. used the same Accelerated CXL protocol as in our investigation. They found that although the keratometry data was reduced, there was no change in best-corrected visual acuity.

To our knowledge, this is the first investigation to reveal the impact of the pure Accelerated CXL protocol on PMD, with a long-term (5-year) follow-up. Although this CXL procedure was unique, the results confirmed other studies' findings, indicating that this strategy can be beneficial. However, this study had some limitations due to its retrospective nature, non-comparative design, and lack of midterm follow-up due to the COVID-19 pandemic. Furthermore, the CXL method was not based on topographic aspects of the cornea.

It can be concluded that the Accelerated CXL protocol is a suitable therapy method for mild to moderate PMD, leading to stable corneal keratometry and topometric index over the next five years, as well as improved visual acuity.

Conflict of Interest

All authors declare that they do not have any conflict of interest.

Bibliography

1. Krachmer JHJAoO. "Pellucid marginal corneal degeneration". *Archives of Ophthalmology* 96.7 (1978): 1217-1221.

2. Belin MW., *et al*. "What's in a name: keratoconus, pellucid marginal degeneration, and related thinning disorders". *American Journal of Ophthalmology* 152.2 (2011): 157-162.e1.

3. Walker RN., *et al*. "Scheimpflug photographic diagnosis of pellucid marginal degeneration". *Cornea* 27.8 (2008): 963-966.

4. Schlaeppi VJPAO. "La dystrophie marginale inferieure pellucide della cornee". *Probl Actuels Ophthalmol* 1 (1957): 672-677.

5. Sridhar M., *et al*. "Pellucid marginal corneal degeneration". *Journal of Ophthalmology* 111.6 (2004): 1102-1107.

6. Dundar H., *et al*. "Unilateral superior pellucid marginal degeneration in a case with ichthyosis". *Contact Lens and Anterior Eye* 34.1 (2011): 45-48.

7. Puy P., *et al*. "Temporal pellucid marginal degeneration displaying high "with-the-rule" astigmatism". *Canadian Journal of Ophthalmology* 48.6 (2013): e142-e4.

8. Lee BW., *et al*. "Ecstatic disorders associated with a claw-shaped pattern on corneal topography". *American Journal of Ophthalmology* 144.1 (2007): 154-156.e3.

9. Karabatsas C and Cook SJE. "Topographic analysis in pellucid marginal corneal degeneration and keratoglobus". *Eye* 10.4 (1996): 451-455.

10. Tummanapalli SS., *et al*. "Evaluation of corneal elevation and thickness indices in pellucid marginal degeneration and keratoconus". *Journal of Cataract and Refractive Surgery* 39.1 (2013): 56-65.

11. Martínez-Abad A., *et al*. "Pellucid marginal degeneration: Detection, discrimination from other corneal ectatic disorders and progression". *Contact Lens and Anterior Eye* 42.4 (2019): 341-349.

12. Krachmer JH., *et al*. "Keratoconus and related noninflammatory corneal thinning disorders". *Survey of Ophthalmology* 28.4 (1984): 293-322.

13. Sridhar M., *et al*. "Superior pellucid marginal corneal degeneration". *Eye* 18.4 (2004): 393-399.

14. Imbornoni LM., *et al*. "Evolution of keratoconus: from diagnosis to therapeutics". *Klinische Monatsblätter für Augenheilkunde* 235.6 (2018): 680-688.

15. Klyce SDJIo and Science v. "Computer-assisted corneal topography. High-resolution graphic presentation and analysis of keratoscopy". *Investigative Ophthalmology* 25.12 (1984): 1426-1435.

16. Rabinowitz YS and McDonnell PJJJoRS. "Computer-assisted corneal topography in keratoconus". *Journal of Refractive Surgery* (1989): 400-408.

17. Rabinowitz YSJJoRS. "Videokeratographic indices to aid in screening for keratoconus". *Journal of Refractive Surgery* (1995): 371-406.

18. Al-Torbak AAJSJoO. "Deep anterior lamellar keratoplasty for pellucid marginal degeneration". *Saudi Journal of Ophthalmology* 27.1 (2013): 11-14.

19. Moshirfar M., *et al*. "Current options in the management of pellucid marginal degeneration". *Journal of Refractive Surgery* 30.7 (2014): 474-485.

20. Wittig-Silva C., *et al*. "A randomized controlled trial of corneal collagen cross-linking in progressive keratoconus: preliminary results". *Journal of Refractive Surgery* 24.7 (2008): S720.

21. Irajpour M., *et al*. "Corneal cross-linking in pellucid marginal degeneration: Evaluation after five years". *Journal of Current Ophthalmology* 34.2 (2022): 229.

22. Pircher N., *et al*. "Corneal crosslinking for pellucid marginal degeneration". *Journal of Cataract and Refractive Surgery* 45.8 (2019): 1163-1167.

23. Steppat M., *et al*. "Collagen cross-linking in patients with pellucid marginal corneal degeneration (PMD)". *Investigative Ophthalmology and Visual Science* 49.13 (2008): 4342.

24. Brittingham S., *et al*. "Corneal cross-linking in keratoconus using the standard and rapid treatment protocol: differences in demarcation line and 12-month outcomes". *Investigative Ophthalmology* 55.12 (2014): 8371-8376.

25. Bikbov M., *et al*. "Results of corneal crosslinking for pellucid marginal corneal degeneration". *Vestnik oftalmologii* 133.3 (2017): 58-66.

26. El-Massry AA-K., *et al*. "Evaluation of the effect of corneal collagen cross-linking for keratoconus on the ocular higher-order aberrations". *Clinical Ophthalmology* 11 (2017): 1461.

27. Stojanovic A., *et al*. "Topography-guided transepithelial surface ablation followed by corneal collagen cross-linking performed in a single combined procedure". *Journal of Refractive Surgery* 26.2 (2010): 145-152.

28. Kymionis GD., *et al*. "Management of pellucid marginal corneal degeneration with simultaneous customized photorefractive keratectomy and collagen crosslinking". *Journal of Cataract and Refractive Surgery* 35.7 (2009): 1298-1301.

29. Cagil N., *et al*. "Transepithelial phototherapeutic keratectomy followed by corneal collagen cross-linking for treating pellucid marginal degeneration: Long-term Results". *Cornea* 38.8 (2019): 980-985.