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Long Term Results of Collagen Cross Linking in Pellucid Marginal Degeneration

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Abstract: A retrospective interventional study involving 15 eyes of 10 patients with pellucid marginal degeneration (PMD) were treated with collagen cross linking (CXL) to evaluate itslong term effects on such patients. The eyes were divided as per riboflavin used namely hypo-osmolar, HPMC (hydroxy propyl methyl cellulose), iso-osmolar into group A, B and C respectively. Visual acuity, retinoscopic refraction, corneal topography, tomography and pachymetry were examined before and every six months after surgery for the first two years and then annually. logMAR UCVA (uncorrected visual acuity) and BCVA (best corrected visual acuity) with spectacles at 6 months and at final follow-up showed improvement in all groups, which were significant in group C. There was no significant difference in the pre and post-op spherical equivalent (P = 0.38) and the mean cylinder decreased by 0.53 ± 0.81 D (P = 0.19) which was not significant. Keratometric astigmatism decreased by 1.13 D (P = 0.2) measured by Scheimpflug imaging and by 1.4 D (P = 0.13) as measured by topography. Maximum keratometry (Kmax) showed a reduction from 50.62 ± 5.2 to 50.23 ± 4.9 (P = 0.07) at 6 months and 48.95 ± 4.7 (P = 0.09) at final follow-up. None of the treated eyes developed side effect of notable severity. Collagen cross linking is a safe and effective method to prevent progression in PMD. Stability of astigmatism, keratometric parameters and improvement in BCVA in our study indicates the efficacy of CXL to prevent progression in PMD.

Keywords: Pellucid Marginal Degeneration, Collagen Cross Linking, Pentacam

1. Introduction

Pellucid marginal degeneration (PMD) of the cornea is a progressive, rare, and non-inflammatory corneal disorder characterized by thinning in the peripheral portion of the inferior cornea with marked steepening just superior to the thinned zone [1, 2]. It occurs in both men and women and this thinning usually occurs 1–3 mm from the limbus in the 4–8 o'clock position [3]. There is usually high against the rule astigmatism. It is differentiated from peripheral corneal disorders associated with inflammation such as Terrien's marginal degeneration and Mooren's ulcer by the absence of vascularization. No known cause for the disease has been found. PMD has been postulated to be an abnormality of the connective tissue, but the exact pathogenesis is still unknown [1]. PMD is usually detectable between the third and fifth decade of life and is progressive in nature [3]. On corneal topography, marked steepening of the inferior corneal periphery can be seen, which also extends into mid-peripheral inferior corneal meridians [4]. Non-surgical approaches for the management for PMD include spectacle correction and rigid gas-permeable contact lenses [5, 6]. Surgical options for the management of pellucid marginal degeneration are intra-stromal corneal ring segments in case of mild to moderate cases intolerant to contact lenses and lamellar keratoplasty, crescentic lamellar keratoplasty or penetrating keratoplasty in advanced cases [7-9].

Corneal cross-linking was introduced by Wollensak et al in 2003 for the treatment of progressive keratoconus and related

disorders increasing the biomechanical strength of the cornea by about 300% [10]. Corneal collagen cross-linking (CXL) with riboflavin and ultraviolet-A (UVA) light is a corneal tissue strengthening technique, which uses riboflavin as a photosensitizer and UVA to increase the formation of intra and inter-fibrillar covalent bonds by photosensitized oxidation. Few studies have been reported in literature suggesting collagen cross linking as an effective option for the management of PMD [11]. However, most studies have a small sample size or a short duration of follow-up. Our study aims to prove the long term efficacy of collagen cross linking to prevent progression in PMD.

2. Materials and Methods

Our study was a retrospective interventional study which enrolled 15 eyes of 10 patients with pellucid marginal degeneration who were treated with CXL and adhered to the tenets of the Declaration of Helsinki. The eyes were divided as per riboflavin used namely hypo-osmolar, HPMC (hydroxy propyl methyl cellulose), iso-osmolar into group A, B and C respectively. These patients had documented progression of PMD on any one of the Scheimpflug imaging devices (Oculyzer II or Pentacam) and topography (TMS IV) or had borderline pachymetry in which any progression would have rendered them ineligible for treatment and underwent collagen cross linking for the same. Corneal topography was characteristic for PMD. The vertical axis images showed significant central irregular against-the-rule astigmatism, marked peripheral thinning within 2.0 mm of the limbus, and normal corneal thickness inferior to the band of thinning. Progression was defined as increase of at least 1.5 diopters (D) in maximum keratometry (Kmax) 6 months and/or reduction in corneal thickness of more than 15 μm at the thinnest point of the cornea in 6 months which is generally in the inferior periphery detected with the help of Scheimpflug imaging.

2.1. Inclusion Criteria

Diagnosis of PMD clinically and on topography and minimum thickness of 375 μm at the thinnest part of cornea.

2.2. Exclusion Criteria

Any signs of inflammation including vascularization or scarring, history of hydrops, history of eye surgery, history of trauma, one eyed patient, pre-treatment glaucoma and any other ocular disease.

2.3. Clinical Assessment

A detailed history of all patients was recorded and all patients underwent detailed ocular examination. Retinoscopic refraction and subjective acceptance were documented at each visit. Best spectacle corrected and contact lenses corrected visual acuity was measured on the logarithm of minimum angle of resolution (logMAR) scale using the ETDRS chart. The simulated keratometry (Ks and Kf), the average keratometry (Kavg) and astigmatism were noted from the sagittal map of corneal topography (Topo cyl). Maximum keratometry (Kmax) and its location, keratometric indices (Ks and Ks), and the thinnest pachymetry and its location were noted from Scheimpflug imaging. A minimum of three successive maps were recorded for each eye with each instrument. The one with the best centration and least extrapolated data was chosen among them.

2.4. Surgical Procedure

Informed consent was obtained from each patient. All surgeries were performed under topical anesthesia in a sterile environment. Patients with a minimum pachymetry of 400 μ underwent the standard "epithelium off" Dresden protocol of CXL using 0.1% isoosmolar riboflavin. Eyes with a minimum pachymetry between 375 and 400 μ underwent CXL using hypo-osmolar or HPMC riboflavin. An inferiorly decentered circular 8mm area of epithelium was removed using 20% alcohol solution. After 30 minutes of photosensitization with riboflavin, the cornea was exposed to ultraviolet A light (365 nm) with irradiance of $3mw/cm^2$ for 30 minutes from a distance of 50mm with limbal protection. The whole procedure was inferiorly decentered with limbal protection keeping in mind the anatomical involvement of PMD. Bandage contact lens was inserted till re-epithelization occurred. Topical antibiotics were prescribed for a week, topical steroids tapered over 8 weeks after epithelization was complete, and lubricants for 6 months. Patients with co-existing allergic conjunctivitis continued their previous treatment.

2.5. Clinical Assessment (Post-Operative)

2 eyes underwent hypotonic CXL (Group A); 2 eyes underwent HPMC CXL [12] (Group B) and 11 eyes underwent Isotonic CXL (Group C). 9 eyes underwent CXL after documentation of progression at subsequent visits. 6 eyes underwent CXL at the first visit based on low pachymetry values and any progression would have rendered the patients ineligible for CXL. Patients were seen every 6 months after surgery for the first 2 years and then annual follow-up. At each follow-up evaluation included visual acuity, manifest refraction, CDVA with glasses and contact lenses, slit lamp evaluation, complete ocular evaluation, specular microscopy, corneal topography and Scheimpflug imaging. Three patients (5 eyes) were not willing for contact lenses so did not undergo contact lens trial. SPSS 16 software was used for analysis of our data. We used non-parametric test (Wilcoxon signed rank test) because of low sample size (lower than 30).

3. Results

Fifteen eyes of ten patients were enrolled in our study. Mean age of patients was 32 ± 4 years (21 – 49). 8 of the patients were males and two of them were females. Mean follow-up was 43 ± 8 months. 4 eyes of 2 patients had a follow-up of 6 months while 11 eyes of 8 patients had a longer follow-up with a maximum follow up of 7 years. The 6 months follow-up results included 15 eyes and the final

follow-up results included 11 eyes.

3.1. Refraction and Visual Acuity

The UCVA and BCVA with spectacles and contact lenses pre-operatively, at 6 months follow-up and at final follow-up are given in Table 1. LogMar UCVA in Group A and Group B improved from 1.15 ± 0.21 to 0.85 ± 0.21 (P = 0.157) and from 1 ± 0.42 to 0.85 ± 0.21 (P = 0.317) at final follow-up respectively. In Group C logMar UCVA improved significantly from 0.95 ± 0.28 to 0.73 ± 0.24 (P = 0.007) at final follow-up. In Group A and Group B logMar BCVA with spectaclesimproved from 0.4 ± 0.28 to 0.35 ± 0.21 (P = 0.317) and from 0.25 ± 0.07 to 0.20 ± 0 (P = 0.317) at final follow-up respectively. In Group C logMar BCVA with spectacles improved significantly from 0.37 ± 0.29 to 0.20 ± 0.18 (P = 0.011) at final follow-up. There was no significant difference in the logMAR BCVA with contact lenses at 6 months or final follow-up. The astigmatism showed a reduction in Group A, C and increase of 0.25 ± 0.36 D (P = 0.317) in Group B which were statistically insignificant.

Table 1. *Comparison between pre-operative and post-collagen cross-linking variables.*

		HYPOTONIC		
		PRE-OP	**6 M F/U**	**FINAL F/U**
SCHIEMPFLUG (OCULYZER II/PENTACAM)	Ks	52.75 ± 1.06	51.25 ± 1.63 (P= 0.18)	48.9 ± 0.71 (P=0.18)
	Kf	50.1 ± 2.12	46.1 ± 0 (P= 0.18)	43.3 ± 0.28 (P= 0.18)
	Kavg	51.35 ± 0.64	48.68 ± 0.28 (P=0.18)	46.1 ± 0.49 (P=0.18)
	Kmax	53.05 ± 1.2	51.65 ± 1.48 (P=0.18)	49.5 ± 0.57 (P=0.18)
	Astigmatism	2.6 ± 3.25	5.13 ± 1.63 (P=0.18)	5.55 ± 0.35 (P=0.18)
	Pachy thinnest	428.5 ± 27.58	398 ±137.89 (P=0.65)	336 ± 83.44 (P=0.18)
	Pachy apex	466.5 ± 45.96	436.5± 103.94 (P=0.65)	392.5±137.89 (P=0.18)
	ISV	137± 73.54	139.5±105.36 (P=0.65)	139.5±101.12 (P =0.65)
	IVA	1.53 ± 0.87	1.57±1.36 (P=0.65)	1.57± 1.46 (P=0.65)
	IHD	0.16 ± 0.12	0.13± 0.1 (P=0.18)	0.15 ± 0.13 (P=0.65)
TOPO (D)	Ks	56.42 ± 4.69	55.38 ± 2.37 (P=0.65)	52.25 ± 0.49 (P=0.18)
	Kf	50.45 ± 2.34	50.02 ± 1.67 (P=0.65)	48.59 ± 4.26 (P=0.18)
	Kavg	53.48 ± 1.39	52.72 ± 0.31 (P=0.65)	50.42 ± 2.38 (P=0.18)
	Astigmatism	5.72 ± 6.82	5.31 ± 4.11 (P=0.65)	3.7 ± 3.71 (P=0.65)
VISION	LogMar UCVA	1.15±0.21	0.9± 0.14 (P=0.18)	0.85 ± 0.21 (P =0.157)
	LogMar BCVA glasses	0.4 ±0.28	0.35 ± 0.21 (P=0.317)	0.35 ± 0.21 (P=0.317)
	LogMar BCVA CL	….	…	…
REFRACTION (D)	Sphere	5.25 ± 2.47	4.5 ± 2.12 (P=0.18)	4.75 ± 2.47 (P=0.157)
	Cylinder	5.5 ± 0.71	6 ± 0 (P=0.317)	4.5 ± 1.41 (P=0.65)
INTRAOCULAR PRESSURE (mmHg)		12 ± 0	14 ± 0 (P=0.317)	13 ± 1.41 (P=0.317)
SPECULAR (cells/mm^2)		2552±141.42	2611.5 ± 98.29 (P=0.65)	2356.5 ± 157.68 (P=0.18)
MEAN FOLLOW-UP (Years)		4 ± 1.41		

		HPMC		
		PRE-OP	**6 M F/U**	**FINAL F/U**
SCHIEMPFLUG (OCULYZER II/PENTACAM)	Ks	50.8 ± 2.4	50.7 ± 2.69 (P=0.61)	50.5 ± 2.26 (P=0.33)
	Kf	44.05 ± 4.6	44.2 ± 5.52 (P=0.82)	43.2 ± 5.52 (P=0.138)
	Kavg	47.2 ± 3.68	47.25 ± 4.31 (P=0.76)	46.9 ± 3.82 (P=0.26)
	Kmax	50.85 ± 2.47	50.7 ± 2.55 (P=0.305)	50.6 ± 2.55 (P=0.247)
	Astigmatism	6.8 ± 2.26	6.45 ± 2.9 (P=0.655)	5.75 ± 0.35 (P=0.655)
	Pachy thinnest	470 ± 16.97	459.5 ± 19.09 (P=0.18)	459 ± 9.9 (P=0.18)
	Pachy apex	474.5 ± 17.68	462.5± 17.68 (P=0.157)	442.5 ± 4.95 (P=0.18)
	ISV	98.5 ± 0.71	94 ± 0 (P=0.18)	96 ± 0 (P=0.18)
	IVA	0.85 ± 0.37	0.88 ± 0.42 (P=0.65)	0.87 ± 0.41 (P=0.65)
	IHD	0.09 ± 0.01	0.1 ± 0.01 (P=0.65)	0.09 ± 0.01 (P=0.65)
TOPO (D)	Ks	50.92 ± 2.52	51.15 ± 2.05 (P=0.65)	50.87 ± 2.49 (P=0.18)
	Kf	43.05 ± 5.31	42.81 ± 4.94 (P=0.65)	42.82 ± 5.4 (P=0.18)
	Kavg	47 ± 3.96	46.95 ± 3.46 (P=0.65)	46.85 ± 3.94 (P=0.18)
	Astigmatism	7.85 ± 2.76	8.29 ± 2.96 (P=0.18)	8.05 ± 2.91 (P=0.18)
VISION	LogMar UCVA	1 ± 0.42	0.85 ± 0.21 (P=0.317)	0.85 ± 0.21 (P=0.317)
	LogMar BCVA glasses	0.25 ± 0.07	0.25 ± 0.07 (P=1.0)	0.2 ± 0 (P=0.317)
	LogMar BCVA CL	0 ± 0	0 ± 0 (P=1.0)	-0.1 ± 0 (P=1.0)
REFRACTION (D)	Sphere	1.5 ± 2.12	1.25 ± 1.77 (P=0.317)	1.5 ± 2.12 (P=1.0)
	Cylinder	5.5 ± 0.71	6 ± 0 (P=0.317)	5.75 ± 0.35 (P=0.655)
INTRAOCULAR PRESSURE (mmHg)		15 ± 1.41	14 ± 0 (P=0.317)	14 ± 0 (P=0.317)
SPECULAR (cells/mm^2)		2233 ± 66.47	2200.5 ± 45.96 (P=0.65)	2200.5 ± 45.96 (P=0.65)
MEAN FOLLOW-UP (Years)		3.25± 2.47		

		ISOTONIC		
		PRE-OP	**6 M F/U**	**FINAL F/U**
SCHIEMPFLUG (OCULYZER II/PENTACAM)	Ks	49.88±3.85	49.71±3.77 (P= 0.61)	49.39±4.3 (P=0.33)
	Kf	42.35±2.15	42.24 ± 2.54 (P=0.82)	43.35±3.01 (P=0.18)
	Kavg	45.89±2.29	45.86± 2.66 (P=0.76)	46.35±3.39 (P=0.26)
	Kmax	50.14 ± 3.75	49.88±3.65 (P=0.30)	49.57±4.23 (P=0.247)
	Astigmatism	7.51±3.86	7.48±3.53 (P=0.96)	6.04± 2.88 (P=0.037)
	Pachy thinnest	477.82±24.16	457.18±29.6 (P=0.005)	438.64±49.52 (P=0.005)
	Pachy apex	490.36±23.35	474.36±32.66 (P=0.041)	469± 46.42 (P=0.155)
	ISV	83.45±37.73	79.82±31.8 (P=0.89)	82± 39.22 (P=0.5)
	IVA	0.85±0.55	0.83±0.46 (P=0.6)	0.87± 0.57 (P=0.8)
	IHD	0.66±0.04	0.07±0.03 (P=0.37)	0.07± 0.05 (P=0.2)
TOPO (D)	Ks	50.46± 3.69	49.9± 3.83 (P=0.05)	50.66± 5.35 (P=0.15)
	Kf	42.38± 2.12	42.33± 1.99 (P=1.0)	43.36± 2.91 (P=0.59)
	Kavg	46.42± 2.24	46.11± 2.52 (P=0.59)	46.56± 2.92 (P=0.37)
	Astigmatism	8.1± 4.02	7.61± 3.5 (P=0.655)	7.39± 3.89 (P=0.655)
VISION	LogMar UCVA	0.95 ± 0.28	0.73 ± 0.24 (P=0.007)	0.73 ± 0.24 (P=0.07)
	LogMar BCVA glasses	0.37 ± 0.29	0.25 ± 0.15 (P=0.024)	0.2 ± 0.18 (P=0.01)
	LogMar BCVA CL	0.08 ± 0.1	0.03 ± 0.05 (P=1.0)	0.01 ± 0.04 (P=1.0)
REFRACTION (D)	Sphere	2.14 ± 2.13	2.75 ± 2.79 (P=0.48)	2.9 ± 3.06 (P=0.34)
	Cylinder	5.07 ± 1.92	4.55 ± 1.82 (P=0.26)	4.5 ± 1.87 (P=0.12)
INTRAOCULAR PRESSURE (mmHg)		16.09 ± 7.99	14.09 ± 2.21 (P=0.317)	13.45± 2.34 (P=0.317)
SPECULAR (cells/mm^2)		2495.27 ± 181.07	2378.55 ± 234.44 (P=0.04)	2250.18 ± 296.51 (P=0.01)
MEAN FOLLOW-UP (Years)		3.64 ± 2.19		

3.2. Tomographic Indices

Maximum keratometry (Kmax) showed a change from 50.14 ± 3.75 D to 49.88 ± 3.65 D (P = 0.31) at 6 months and 49.57 ± 4.23 D (P = 0.31) at final follow-up in Group C. However, the difference was not statistically significant. The astigmatism showed a reduction of 1.47 ± 0.98 D (P = 0.037) at final follow-up in Group C which was statistically significant, whereas in Group B astigmatism showed statistically insignificant reduction of 1.05 ± 1.91 D (P = 0.655). Other keratometric values i.e. Ksteep (Ks), Kflat (Kf) and Kaverage (Kavg) measured by Scheimpflug imaging were not statistically significant with P value > 0.05. Oculyzer image showing progression of PMD prior to CXL (Figure 1). Oculyzer image showing stabilization of parameters following CXL - 7 months follow-up in the same patient as Figure 1 (Figure 2). Pentacam image showing stabilization of parameters following CXL - 7 years follow up (Figure 3 A and B).

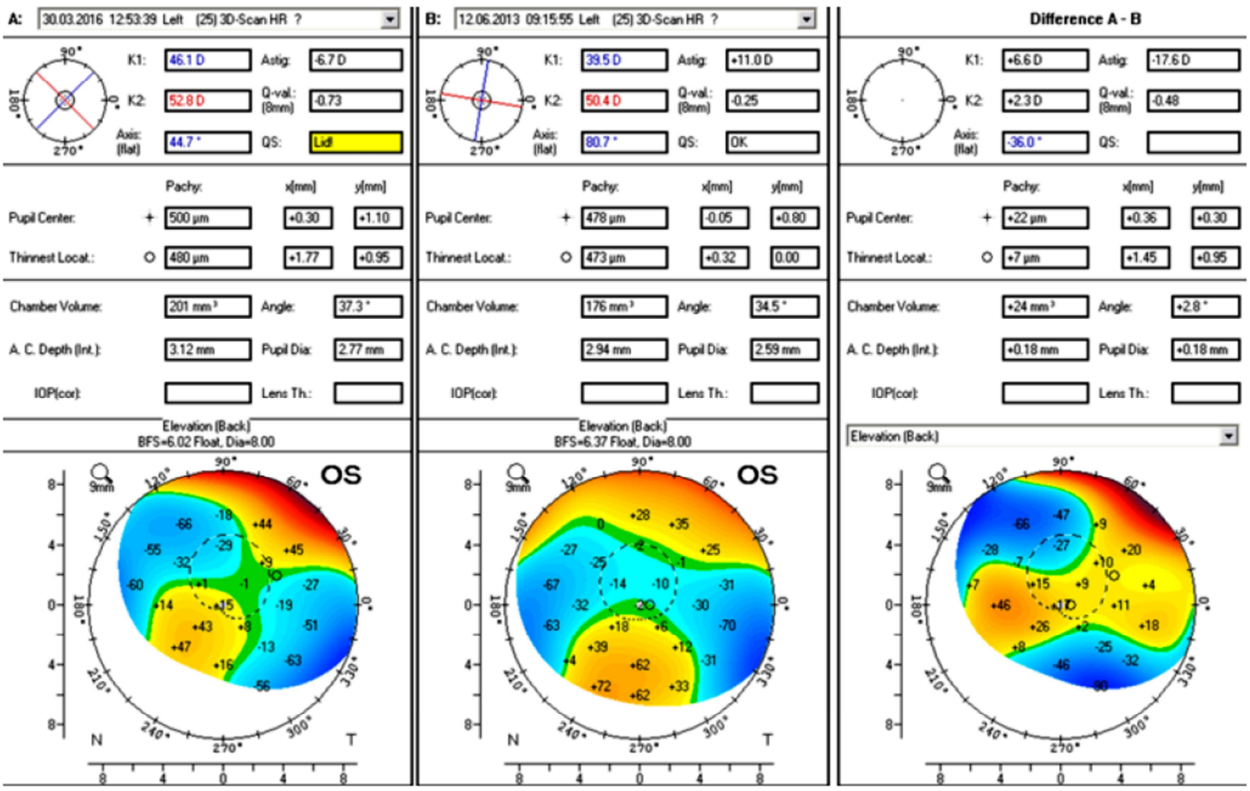


Figure 1. *Oculyzer image showing progression of PMD prior to CXL.*

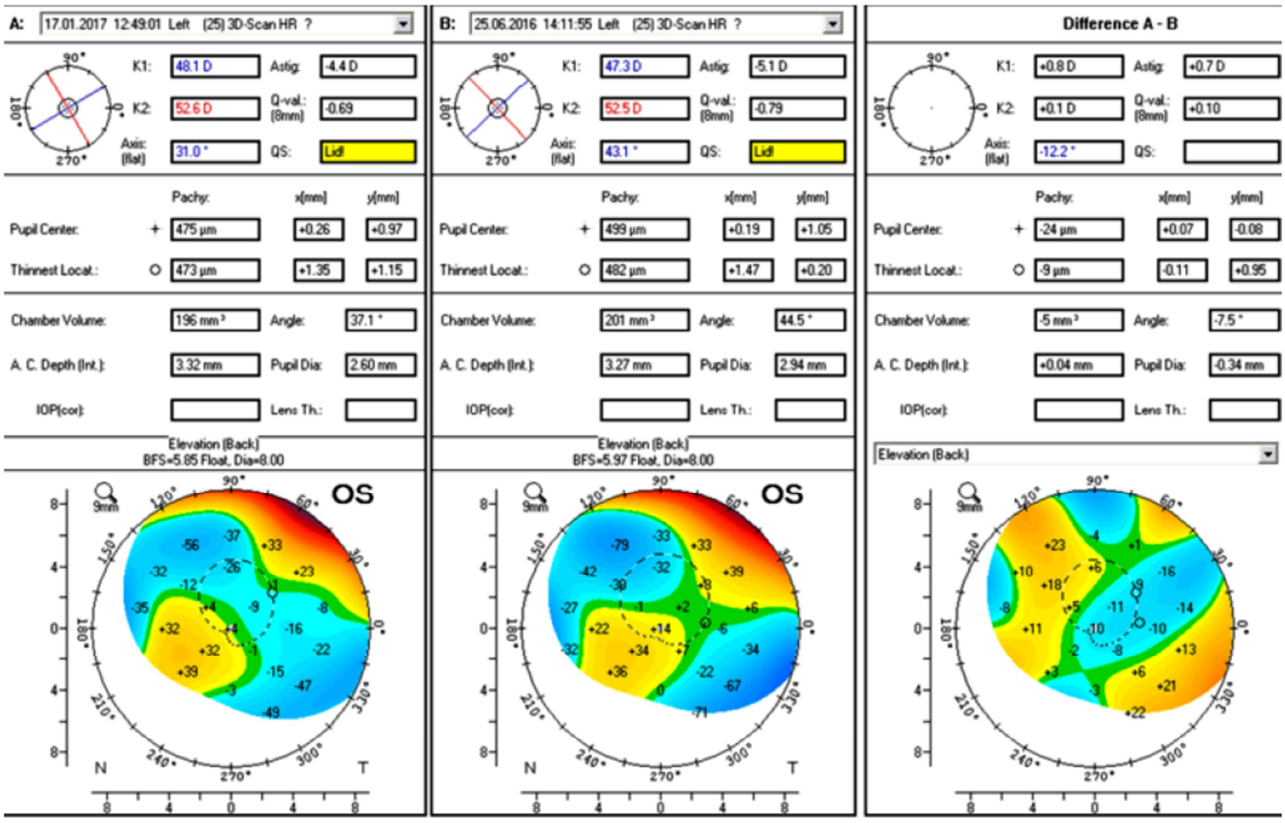
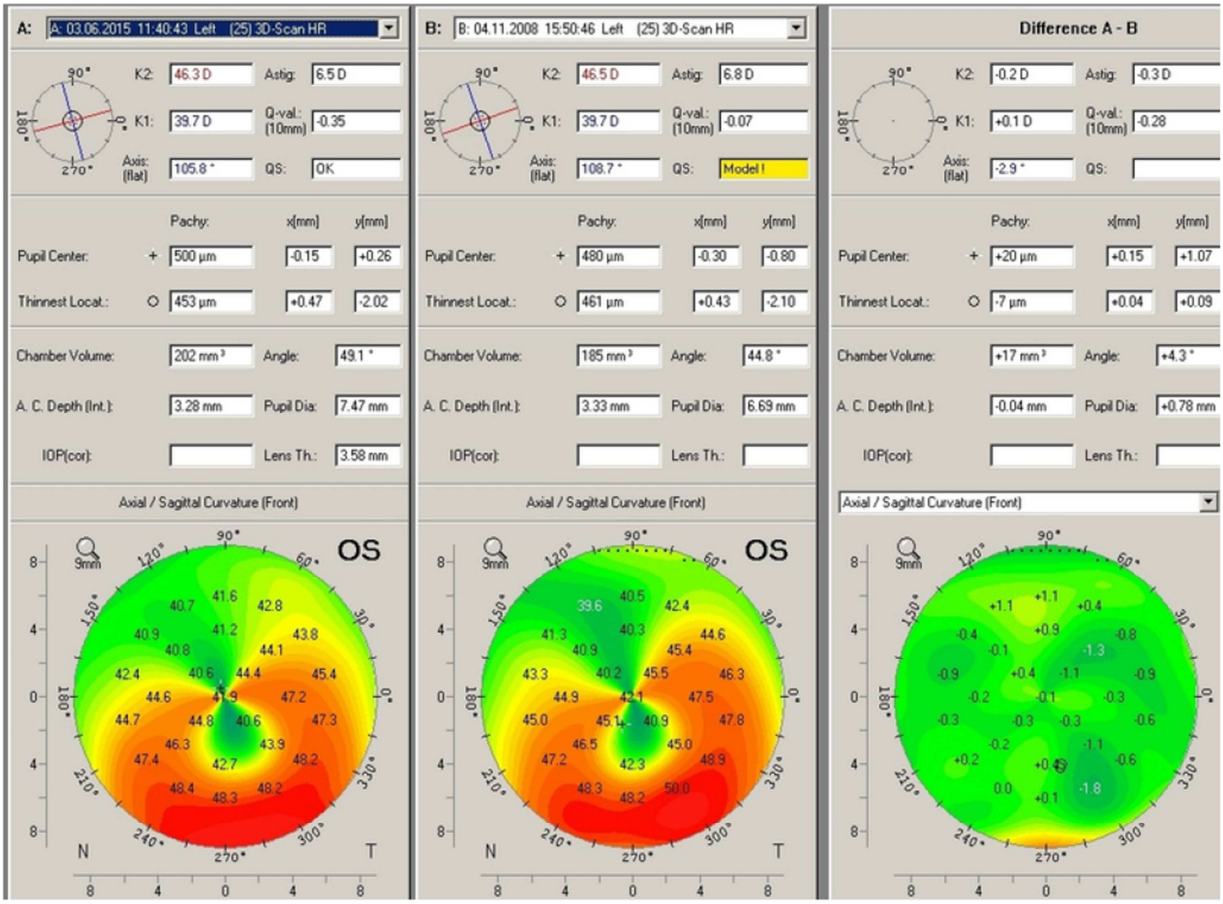
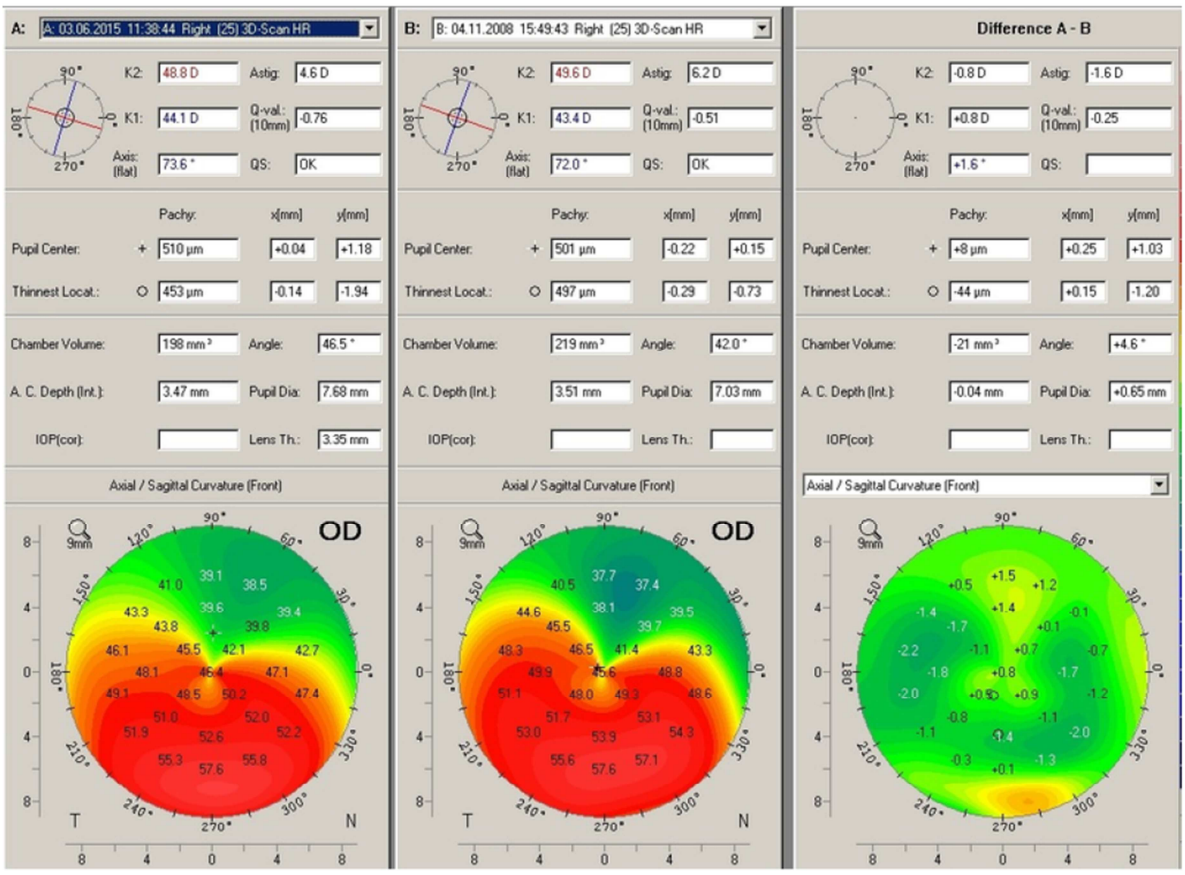


Figure 2. *Oculyzer image showing stabilization of parameters following CXL - 7 months follow-up inthe same patient as Figure.*



A



B

Figure 3. *A Pentacam image showing stabilization of parameters following CXL - 7 years follow-up, B Pentacam image showing stabilization of parameters following CXL - 7 years follow-up.*

3.3. Topographic Indices

Average keratometry (Kavg) showed flattening in Group A and B of 3.06 ± 0.99 D (P = 0.18) and 0.15 ± 0.02 D (P = 0.18) respectively and steeping of 0.14 ± 0.68 D (P = 0.79) in Group C at final follow-up; though the differences were not significant. Other keratometric values i.e. Ks, Kf and astigmatism measured by topography also did not show any statistical significance at 6 months and final follow-up with P value > 0.05. Topography showed stabilization following CXL at 3 years follow-up (Figure 4).

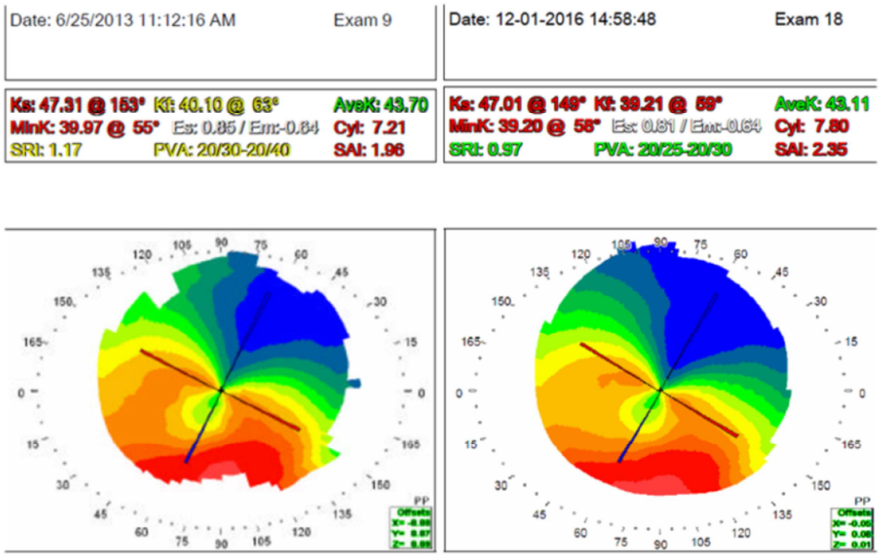


Figure 4. *Topography showing stabilization following CXL – 3 years follow-up.*

3.4. Pachymetry

Mean pachymetry at the thinnest point as measured by Scheimpflug imaging was reduced in all the groups from 428 ± 27.58 to 336.6 ± 83.44 μ (P = 0.180) in Group A, from 470 ± 16.97 μ to 459 ± 9.9 μ (P = 0.180) in Group B and from 477.82 ± 82 μ to 438.64 ± 49.52 μ (P= 0.005) in Group C at final follow-up. Changes in isotonic eyes were statistically significant.

3.5. Intra Ocular Pressure

Mean IOP pre-operatively was 12 mm of Hg, 15 ± 1.41 mm of Hg, 16.09 ± 7.99 mm of Hg and at final follow-up was 13 ± 1.41 mm of Hg (P = 0.317), 14 mm of Hg (P = 0.314), 13.45 ± 2.34 mm of Hg (P = 0.509) in Group A, B and C respectively. One patient showed increase in intra-ocular pressure post collagen cross linking but the pressure decreased after stopping steroids suggesting a steroid response. No other patients had an increase in intraocular pressure.

3.6. Specular Microscopy

The specular microscopy showed mean cell count of 2552 ± 141 cells/mm^2 (Group A), 2233 ± 66.47 cells/mm^2 (Group B), 2495 ± 181 cells/mm^2 (Group C) in pre-operative period and with count of 2356.5 ± 157 cells/mm^2 (P = 0.65), 2200 ± 45.9 (P = 0.65), 2250 ± 296 cells/mm^2 (P = 0.01) at final follow-up in Group A, B, C respectively. None of the patients had endothelial cell loss post collagen cross linking with no significant reduction in specular count.

Table 1 shows a comparison of the pre and post CXL variables. None of the patients in our study showed progression in the form of increase in astigmatism with decreased best corrected visual acuity, scarring or hydrops requiring surgical management.

4. Discussion

Pellucid marginal degeneration is a typically bilateral, inferior and peripheral corneal thinning disorder. The surgical management of these cases is a difficult procedure with a long and uncertain visual recovery [8]. Corneal collagen CXL has been used to treat progressive keratoconus since it was first introduced [10]. Nevertheless, new applications are under investigation and have shown promising results, such as the treatment of postoperative LASIK ectasia [13], the strengthening of recalcitrant corneal ulcerations and bullous keratopathy [14]. Histologically and clinically, CXL is a well-published therapeutic possibility for corneal ectasias [15]. Usefulness of CXL in ectatic disorders especially like keratoconus has been proved in many studies and we know CXL makes the cornea rigid with increased formation of intra and inter fibrillar covalent bonds [9, 16]. Based on this, collagen cross linking as a new and less invasive therapeutic method was adopted to arrest the progression of ectasia, characteristic of PMD [10, 17]. However, there have been no long term studies till date on patients of PMD who have underwent CXL for arresting progression.

Ziadhasan et al presented a case report in which progression of PMD was stopped by CXL, and the UCVA and BCVA increased during the observation period [18]. UCVA improved from 0.8 to 0.55 logMAR and BCVA improved from 0.7 to 0.25 logMAR. The mean keratometry (Kavg) by topography decreased from 45 D to 42.22 D, similar to our study. Bayraktar et al presented a case report with 2 patient and 4 eyes in which significant improvement in UDVA and CDVA with decrease in keratometric readings including Kf, Ks and Kmax post CXL was noted. The follow-up in these cases was only for 22 months [19]. Steppat et al reported CXL 13 eyes of 8 patients of PMD in whom CXL was done and showed stability of Kmax (47.04 ± 1.46 to 47.24 ± 1.54) and visual acuity (0.57 ± 0.22 to 0.64 ± 0.18) with a follow-up of 18 months [20]. However, one patient showed deterioration in BCVA inspite of treatment. Our study in comparison showed stability in Kmax with significant improvement (P = 0.01) in BCVA in largest group (Group C) and had a long follow-up with a maximum of 7 years. Bashir et al enrolled 22 eyes of 16 patients with PMD who underwent CXL. Their study showed a stabilisation in simulated keratometric values with decrease in Kmax by 0.4 D as compared to 3.45 D, 0.25 D, 0.57 D decrease in Kmax in groups A, B and C in our study. Stability of other values and absence of detectable change after study period implied halting of the progression of the disease [20]. However, the follow-up period in this study was only for 6 months as compared to 43 ± 8 months in our study. In current study, none of the patients developed acute hydrops or scarring or increased irregular astigmatism leading to decrease in BCVA. Also, none of the eyes showed steepening of the Kmax. There was reduction in thinnest pachymetry post CXL treatment in all the groups. Similar post-operative corneal thinning has been noted in previous keratoconus studies too [21-23]. Reasons like post CXL epithelial remodeling, complex structural and physiologic wound healing corneal changes have been anticipated, but exact cause still remains to be elucidated [24]. An apprehension about CXL especially pertinent to PMD is that of limbal stem cell damage following CXL treatment, due to the location of corneal thinning and the corresponding site of CXL treatment. In accordance with previous studies, hereit was prevented with the usage of metallic limbal ring [25, 26].

5. Conclusion

CXL has been proven to be a safe method to prevent progression among PMD patients. This is minimally invasive technique and in early stages saves the need of invasive procedures like corneal transplantation. This study is unique as it reports the longest follow up of PMD patients post CXL. Most of the parameters measured in our study showed stabilization with no evidence of progression and significant improvement in UCVA over a long follow-up. Limitations included a retrospective design, small sample size and non –

involvement of any statistical test in bilaterally treated patients.

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