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Original Research Article

Corneal Cross Linking With Riboflavin on Initial Diagnosis of Keratoconus in Patients Less Than 18 Years of Age

Mallikarjun M Heralgi[1*], Kavitha V[2**], Hariprasad Vokuda[3*], Ajay Badami[3*]

[1]Consultant (Cataract), [2]Consultant, [3]Resident,
[*]Cornea and Refractive Surgery, Sankara Eye Hospital, Thirthahalli Road, Harakere, Shimoga, Karnataka, India.
[**]Sankara Eye Hospital, Thirthahalli Road, Harakere, Shimoga, Karnataka, India.

Corresponding Author: Mallikarjun M Heralgi

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ABSTRACT

Purpose: To evaluate the efficacy and safety of Corneal Cross Linking (CXL) with Riboflavin on initial diagnosis of Keratoconus in Patients less than 18 years of age.
Materials and Methods: In this retrospective interventional study, we enrolled 10 eyes of 7 patients, who underwent corneal UVA-riboflavin induced cross linking at initial diagnosis of keratoconus at our institute. They were followed up for 1 year. Evaluated parameters were, uncorrected visual acuity (UCVA), best corrected visual acuity (BCVA), keratometry and manifest refraction.
Results: Mean age of the patients was 15.5 years, with four male and three female patients. We found improvement in uncorrected visual acuity (from 0.67±0.37 to 0.62±0.31), best corrected visual acuity (from 0.40±0.16 to 0.32±0.18), keratometry minimum (from 47.8±3.9 to 46.5±3.87), keratometry maximum (from 53.6±6.85 to 51.5±7.07), mean spherical refraction (from 1.46 DS±1.43 to 1.28 DS±1.48), mean cylinder (from 2.75 DC±1.42 to 2.28 DC±1.40). There was no intra- or postoperative complications.
Conclusions: We conclude that CXL therapy in patients with keratoconus younger than 18 years seems to be a reasonable procedure considering its aggressive and rapid progression in children.

Keywords: Keratoconus, UVA, collagen crosslinking, pediatric.

INTRODUCTION

Keratoconus is characterized by progressive corneal protrusion and thinning with secondary changes in the structure and organization of corneal collagen. [1-3] Worldwide, younger patients at diagnosis are frequently from Middle Eastern or Asian backgrounds, and they tend to present with severe keratoconus. [4,5]

Treating patients with CXL for keratoconus at an earlier age could be of greater benefit than waiting for progression and have more advanced disease requiring corneal transplantation. [6] CXL is effective in halting the progression of keratoconus with an excellent safety profile. Hence we undertook this study and offered the patient the benefit of CXL at the initial diagnosis of keratoconus.

MATERIALS AND METHODS

This was a retrospective interventional study of ten eyes of seven patients. The inclusion criteria for the study were eyes with keratoconus documented by slit lamp examination, topography, corneal thickness>400 microns at the thinnest location, and children of less than 18 years.

Eyes with corneal thickness less than 400 microns at the thinnest point, concurrent corneal infections, central or Para central scarring, and those who had a

history of herpetic keratitis were excluded.

Collagen cross linking was immediately offered to the patient at the time of initial diagnosis of keratoconus.

Written informed consent was obtained from parents of all patients undergoing the procedure, and the study protocol was approved by the hospital's ethics committee. All patients underwent a detailed ophthalmic examination including assessment of the uncorrected distant visual acuity (UDVA) and corrected distant visual acuity (CDVA), subjective acceptance, slit lamp and dilated fundus examination. Both UDVA and CDVA were recorded using Snellen's chart and later converted to log MAR values. All patients underwent corneal topography using the placido based videokeratography (Keratron, Optikon, Rome). Keratometric values (K1 and K2) were derived from automated keratometry and confirmed with the topography and the pachymetry was derived from an ultrasound pachymetry (Tomey 2000, Japan). All patients underwent the above tests at baseline and at all subsequent visits.

Surgical Technique: The surgical procedure of corneal cross-linking induced by riboflavin and UVA was performed in all patients according to a modification of the Siena protocol.

Under topical anesthesia with 0.5% proparacaine and after applying a lid speculum, the cornea was de-epithelized over 8 mm diameter with a blunt spatula. Photosensitizing riboflavin 0.1% + 20% dextran (Linker, India), was applied every 5 minutes for 30 minutes to achieve adequate penetration of the solution. Limbus was shielded. The eye was then irradiated for 30 minutes with UVA of 370 nm wavelength at a working distance of 30 mm with an irradiance of $3mW/cm^2$ (CL-UVR, Appasamy associates, India). Riboflavin solution was applied once every 5 minutes during irradiation. At the end of the procedure, saline wash was given to cornea and conjunctiva to remove excess riboflavin and antibiotics drops were instilled. A soft bandage contact lens (Bausch & Lomb, Haryana, India) was applied and was removed on the 3rd postoperative day or once the epithelium healed.

Postoperative treatment included nepafenac 0.1% eye drops (Nevanac, Alcon, India), three times a day for five days, a combination of topical tobramycin 0.3% + fluorometholone 0.1% (FML-T, Allergan, India) three times a day for 4 weeks, and topical artificial tears supplements (Refresh liquigel, Allergan, India) for two months.

Subsequent examinations were at 1, 3, 6 and 12 months. At each examination, refraction, best corrected visual acuity (BCVA) with glasses, corneal topography, keratometry readings and central corneal thickness (CCT) were recorded.

Statistical analysis

The raw data was entered on excel sheets (Microsoft Corp.) and imported to the Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, version 17.0) for analysis. The significance level was set at <0.05.

RESULTS

Table 1: Table showing patient details regarding their, age, sex and the eye which has undergone CXL

Patient	Age in years	Sex	Right eye	Left eye
1	17	Female	CXL	CXL
2	18	Female	CXL	Patient was not willing for CXL
3	13	Female	Lamellar keratoplasty, DALK	CXL
4	18	Male	CXL	CXL
5	15	Male	CXL	CXL
6	12	Male	CXL	Lamellar keratoplasty, DALK
7	17	Male	Lamellar keratoplasty, DALK	CXL

Ten eyes of seven patients were included in the study with four males and three females; mean age of the patients was 15.5 ± 2.59 years (range: 12-18 years). Three patients underwent CXL in eyes, two patients in right eye and two patients in left

eye. In three patients, the other eye had advanced keratoconus at diagnosis and they underwent deep anterior lamellar keratoplasty (DALK). One patient was not willing for CXL therapy in the other eye. (Table 1)

UDVA and CDVA (in Log MAR): The mean preoperative UDVA was 0.67 [±0.37] and CDVA was 0.40 [±0.16]. At the end of one year, the mean UDVA was 0.62 [±0.31] and mean CDVA was 0.32 [±0.18]. The values at the end of one year did show slight improvement.

Spherical, Cylinder: At the end of one year, there was a slight improvement in the mean preoperative sphere and cylinder, from -1.46 DS [±1.43] and -2.75 DC [±1.42] to -1.28 DS [±1.48] and -2.28 DC [±1.40] respectively.

Keratometry: There was a flattening of 1.3 D in the mean K1 and 2.1 D in mean K2 at the end of the 1-year follow-up.

(Table 2) (Figure 1, figure 2, figure 3)

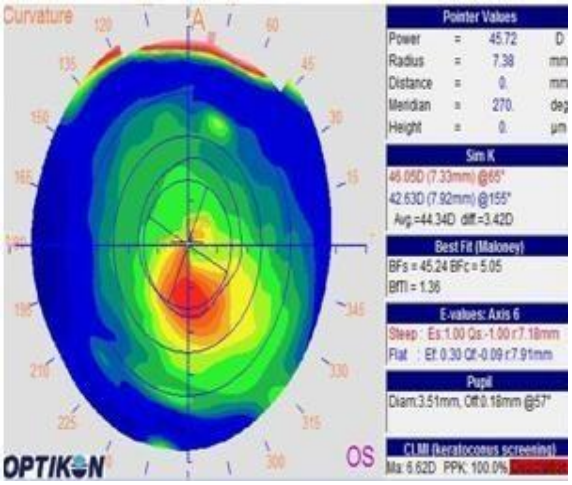

Figure 1 - preoperative corneal topography

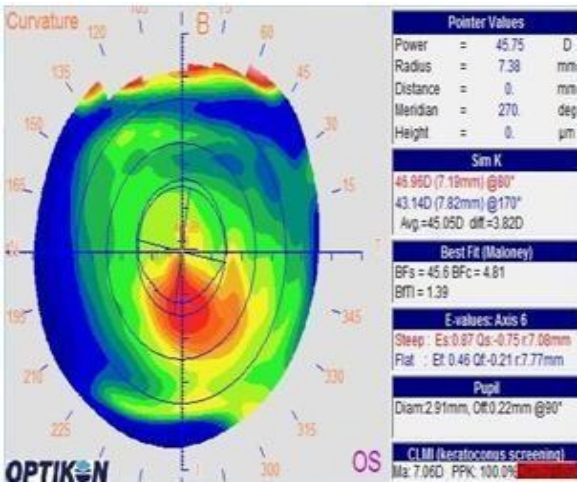

Figure 2 - post operative 1 year

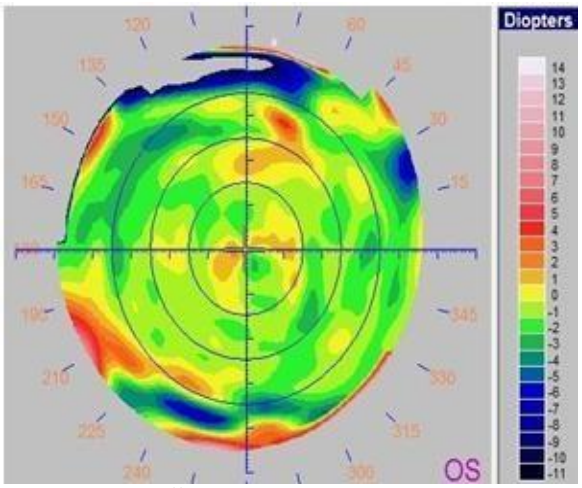

Figure 3- difference map showing no progression.

Table 2: Table showing the mean UDVA (uncorrected distant visual acuity), CDVA (best corrected visual acuity), K1/K2 (flatkeratometry/steep keratometry), spherical and cylindrical refraction,preoperatively and at 1-year postoperative period.

Variables	Pre-op	Post-op	p value*
UCVA	0.67±0.37	0.62±0.31	0.276
BCVA	0.40±0.16	0.32±0.18	0.102
Kmin	47.8±3.9	46.5±3.87	0.138
Kmax	53.6±6.85	51.5±7.07	0.176
Spherical	1.46±1.43	1.28±1.48	0.276
Cylinder	2.75±1.42	2.28±1.40	0.104

*non significant by Wilcoxon sign rank test

Table 3: Table showing pachymetry values at pre-operatively and postoperatively at 1, 3, 6 and 1 year

patient	Eye	Pre-op	Post op 1month	Post-op 3 month	Post-op 6month	Post-op 1 year
1	Left	436	396	423	434	434
	Right	432	399	429	430	430
2	Right	421	390	420	420	420
3	Left	445	425	436	446	446
4	Right	437	402	436	438	438
	Left	424	398	420	421	421
5	Right	433	404	423	430	430
	Left	422	396	419	419	419
6	Right	437	410	424	435	435
7	Left	438	409	429	436	436

Pachymetry: after initial decrease in central corneal thickness in the first follow up month, the value then increased to near preoperative state at the end of the follow up period. (Table 3)

There were no complications noted after CXL in any of the patients. Postoperatively, the mean time for epithelial healing was 3.32 ± 1.15 days. Mild haze was noticed in a majority of subjects on slit-lamp examination but did not have any effect on the visual acuity and subsided completely by four weeks after surgery.

There was no evidence of delayed wound healing, ocular surface damage, or uveitis after CXL in any of the patients.

DISCUSSION

Young age appears to be associated with more severe forms of keratoconus and faster disease progression, with an inverse correlation between age and severity. [7,8] Progression of keratoconus is "explosive" in children, with a short time between the onset of functional symptoms and the development of a severe form of keratoconus. This may lead to progressive visual impairment in pediatric patients and affect the social as well as educational development of the child and thus, negatively affecting their quality of life. [9-11] Corneal collagen cross-linking is an emerging treatment option for pediatric patients with keratoconus. [12,13] The Siena CXL Pediatrics trial, the largest prospective study report involving 152 eyes of 77 patients (from 10 to 18 years) with the longest follow-up of 3 years demonstrated that, after CXL, keratoconus stabilized and demonstrated rapid and significant visual function improvement in pediatric patients. They found an improvement in both UDVA and CDVA in patients under 18 years of age when compared to those in the 19-26 years age group. [14]

Very few studies have been published about the effectiveness of CXL in the younger age group who have undergone cross linking immediately on diagnosis of keratoconus, without waiting for progression to occur. [15]

This study compares the short term results of corneal collagen cross linking with riboflavin for keratoconus in pediatric corneas. In this retrospective interventional study, collagen cross linking was immediately offered to the patient without waiting for the progression to occur. We then analyzed and compared visual acuity, refractive, topographic and pachymetric outcomes at the end of one year, with no procedure related complications.

Even though, we did not observe statistically significant improvement (because of small sample size), in the CDVA and topographic indices, a trend towards improvement in CDVA and stabilization of topographic indices were noted at the end of one year follow up.

Thus, we propose that awaiting documentation of progression is not mandatory and CXL in children and adolescents can be offered soon as the diagnosis has been made.

The weakness of this study is, it being a retrospective and an uncontrolled one and also with a small number of study cases and shorter duration of follow up period.

CONCLUSION

We conclude that CXL therapy at initial diagnosis of keratoconus younger than 18 years seems to be a reasonable procedure considering its aggressive and rapid progression in children.

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