RESEARCH

TO EVALUATE THE EFFICACY OF CORNEAL COLLAGEN CROSS- LINKING WITH RIBOFLAVIN IN KERATOCONUS

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Received : 08/06/2022
Received in revised form : 20/08/2022
Accepted : 31/08/2022

Keywords:
Uncorrected Visual Acuity (UCVA), Best corrected visual acuity (BCVA), Astigmatism, Pachymetry, Tonometry.

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DOI: 10.47009/jamp.2022.4.4.50

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2022; 4 (4); 255-263

Abstract

Background: To evaluate the efficacy of corneal collagen cross-linking with riboflavin in keratoconus. **Materials and Methods:** This was a Prospective interventional study done at sarojinidevi eye hospital Hyderabad. The study group included 35 eyes of 30 consecutive patients with Keratoconus. Cross-linking was done using riboflavin 0.1% with dextran 20% as photosensitizer and Ultraviolet-A radiation. The pre-operative and post-operative corneal topography and tomography with pentacam, pachymetry, tonometry, un-corrected and best-corrected visual acuity were done. **Result:** In our study 35 eyes of 30 patients underwent corneal collagen cross linking with riboflavin and ultraviolet-A light. The age of the patient ranged from 13 to 30 years with a mean of 20.47 yrs. Out of 30 patients, 14 were males (46.67%)& 16 (53.3%) were females. Right eye was operated in 17(56.66%), Left eye in 08(26.67%), and 5(16.67%) patients underwent surgery in both eyes. The mean follow-up period was 13.17 months. Post-operative uncorrected visual acuity increased by a mean of LogMAR 0.08286(P-Value <0.0001). Post-operative best corrected visual acuity increased by a mean of LogMAR 0.0794(P-Value< 0.0001). Post-operative astigmatism decreased by a mean of 0.68D(P-Value 0.0001). Post-operative K-max decreased by a mean of 1.47D(P<0.0001). Post-operative Central Pachymetry decreased by a mean of 26.71 microns(p<0.0001). Post-operative intraocular pressure remained in normal range. Transient post-operative haze was seen in a few cases in our study which resolved with no sequelae on topical steroids. **Conclusion:** Corneal Collagen cross-linking is a safe and effective procedure showing statistically significant improvement in post-operative UCVA, BCVA and a reduction in astigmatism, K readings and central corneal thickness.

INTRODUCTION

Keratoconus is the most common form of corneal dystrophy typically affecting adolescents and young adults. It is characterized by non-inflammatory progressive thinning of corneal stroma leading to conical ectasia of the cornea inducing irregular astigmatism, high myopia and in advanced cases scarring resulting in visual loss and mild to marked impairment in the quality of vision. Because of the younger age of the patients, keratoconus often has a significant negative effect in the quality of life. Initial management is based on refractive correction with spectacles and contact lenses and intrastromal corneal ring segments, but further ectatic progression may lead to corneal transplantation.[1]

Corneal collagen cross-linking with riboflavin and Ultraviolet-A is relatively a newer modality of treatment which is minimally invasive that addresses primarily the pathophysiology of keratoconus to halt the progression of the disease. It is a technique of corneal tissue strengthening using riboflavin as a photosensitizer and Ultraviolet-A to increase the formation of intra and interfibrillar covalent bonds of corneal collagen by photo-polymerization. We have made an attempt to evaluate the effectiveness of riboflavin, Ultraviolet-A light induced cross-linking of collagen in improving the visual acuity and in stabilizing the progression of keratoconic eyes during a study period between November 2013 to November 2015 at sarojinidevi eye hospital.

To evaluate the efficacy of corneal collagen cross-linking with riboflavin in keratoconus.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

MATERIALS AND METHODS

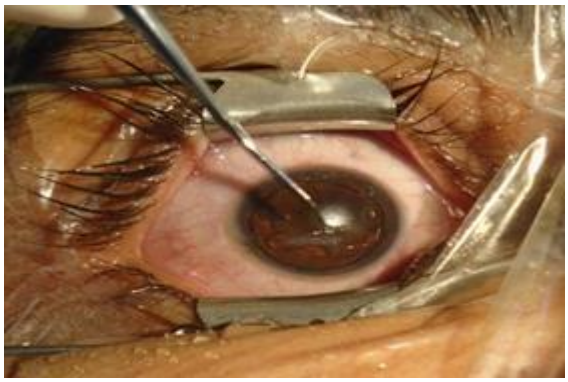
Prospective Interventional study, Sarojini eye hospital, Hyderabad November 2013 to November 2015 in Patients with Keratoconus. 35 eyes with Keratoconus and willing for Corneal Collagen Cross-linking with Riboflavin and UVA Radiation during the study period of November2013 to November 2015 were included in the study. The last case enrolled was on 3rd March 2015. Informed consent was taken from all patients.

Ethical committee approval was taken from institute's ethical committee board.

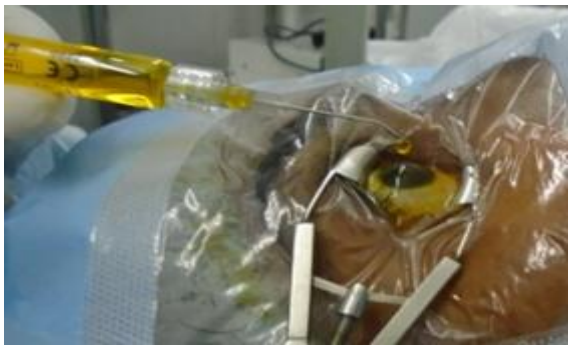
Inclusion criteria: Be at least 13 years of age, male or female, of any race, minimum Corneal pachymetry of 400 microns, have a maximum corneal curvature, as measured by Kmax of ≥ 47.00 D; for contact lens wearers removal of contact lenses is required for a 2-week period prior to the screening visit(s), for contact lens wearers manifest refraction must be stable between two visits which occur at least 7 days apart. A stable refraction is one in which the manifest refraction spherical equivalent and the average K (Km) on the Pentacam taken at the first visit do not differ by more than 0.75 D from the respective measurements taken at the second exam.

Exclusion criteria: If a female is pregnant or nursing, history of previous corneal surgery or the insertion of Intacs in the eye to be treated, history of previous Limbal Relaxing Incision (LRI) procedure in the eye to be treated, corneal pachymetry< 400 microns prior to epithelial debridement at the thinnest point measured by Pentacam in the eye to be treated, eyes which are aphakic, eyes which are pseudophakic and do not have a UV blocking lens implanted, eyes that have the maximum corneal curvature (K-max) outside of the central 5mm zone as measured by the Pentacam, previous ocular condition (other than refractive error) in the eye to be treated that may predispose the eye for future complications like history of corneal disease , clinically significant corneal scarring in the cross-linking treatment zone that is not related to keratoconus or, in the investigator's opinion, will interfere with the cross-linking procedure, history of delayed epithelial healing in the eye to be treated, patients with nystagmus or any other condition that would prevent a steady gaze during the treatment or other diagnostic tests, patients with a current condition that, in the investigator's opinion, would interfere with or prolong epithelial healing, history of previous corneal crosslinking treatment in the eye to be treated, have used an investigational drug or device within 30 days of the study or be concurrently enrolled in another investigational drug or device trial within 30 days of the study and sensitivity or known allergy to the use of the test article(s) or their components;

Patients selected for surgery underwent a complete ophthalmic examination as Preoperative evaluation including visual acuity, slit lamp examination, tonometry, gonioscopy, dilated fundus evaluation, corneal topography and Tomography and pachymetry



Epithelium removal



Soaking of Riboflavin

Ultraviolet-A Exposure

Figure 1: Surgical steps followed in study

Patients who were diagnosed with Keratoconus thorough preoperative evaluation were taken up for surgery. Preoperatively Pilocarpine (2% w/v) eye drops were instilled for making the pupil miotic. Surgeries were carried out under Topical anaesthesia (Proparacaine HCl 0.5%) All surgeries were done by a single experienced surgeon. The operation was performed with the help of an operating microscope with co axial illumination. Lids, eyebrows and forehead were painted with betadine solution. The surgical field was draped with sterile disposable drape. Self-retracting lid speculum was used to

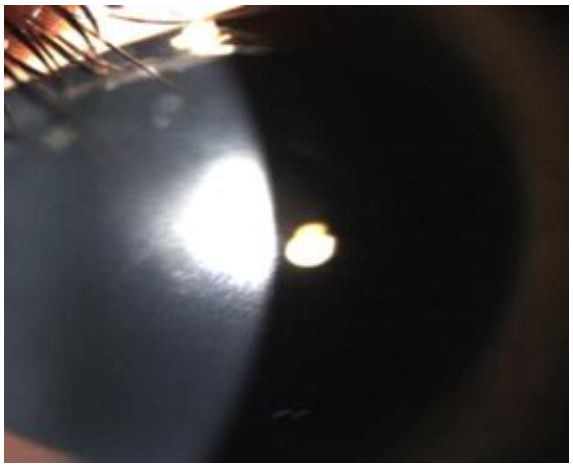
ISSN (O): 2687-5365; ISSN (P): 2753-6556

separate the lids. The fornices were thoroughly washed with saline.

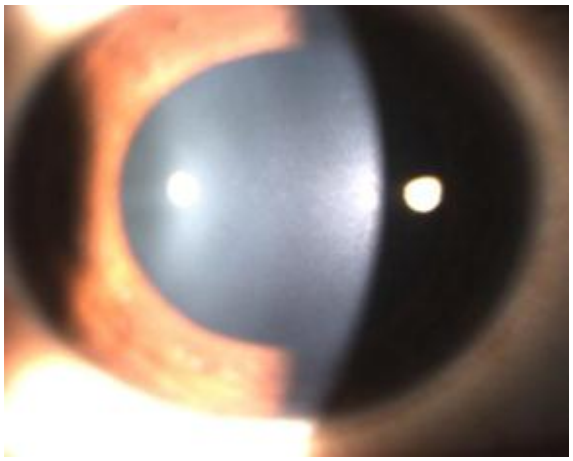
Surgical Steps:

The central 8.5mm of the corneal epithelium was removed using a blunt knife under topical anaesthesia. Riboflavin 0.1% with Dextran 20% was used as photosensitizer. Riboflavin drops were applied every 3 minutes for 30 minutes. Followed by ultraviolet - A light of 370nm was applied for 30 minutes using 3 mW/cm2 irradiance. Even during the period of Ultraviolet-A exposure Riboflavin drops were applied every 5 minutes. After 30 minutes of irradiation, the ultraviolet source was removed. The eye was washed with saline.

A bandage contact lens was fitted to the corneal surface until re-epithelialisation.



1 month Post-operatively



6 months post-operatively

Figure 2: post-operative photos in study

Post-operatively patients were started on Gatifloxacin eye drops 0.3% 4 times a day for 3 weeks & Prednisolone acetate eye drops 1% in tapering manner for 6 weeks, preservative free tear substitute 4 times a day for 2 months and oral analgesics. The patients were seen again on the first and third postoperative days. The bandage contact lens was removed on the third postoperative day once the epithelium was healed. Further follow up visits were done at 1week to rule out infection if any, 1month and at 3, 6 ,12 and 18 months post-operatively. Uncorrected Visual acuity, Best corrected visual acuity, Slit lamp examination, Pachymetry, tonometry, corneal topography and Tomography using Pentacam were performed at each visit.

Statistical Analysis

Descriptive data was presented as mean and frequency (percentage). Students Paired t-test was used to assess difference between continuous variables. Differences were considered statistically significant when P value was < 0.05.

RESULTS

35 eyes of 30 patients who underwent Corneal Collagen Cross-linking with Riboflavin at sarojinidevi eye hospital during the period of November 2013 to November 2015 were taken into our study. The mean follow-up period was 13.17 months (range 7-21months).

Out of 30 patients, 14 were males & 16 were females. The age of the patient ranged from 13 to 30 years with a mean of 20.47 yrs. The youngest patient operated was 13yrs. Majority (36.67%) of the patients were between 13 to 15yrs of age. Out of 35 eyes of 30 patients, Right eye was operated in 17, Left eye in 08, and 5 patients underwent surgery in both eyes.

Total number of eyes operated were 35 out of which 22 were Right and 13 were Left eyes.

Visual acuity testing was done by Snellen's chart and converted to LogMAR for statistical analysis. 33 eyes (94.29%) had pre-operative uncorrected visual acuity of 6/12 or less. Only 2(5.71%) eyes had Pre-operative Uncorrected Visual Acuity better than 6/12. Mean Pre-operative Uncorrected visual Acuity was LogMAR 0.808.

21 eyes (60%) had Pre-operative Best corrected visual acuity of 6/12 or less. 14 eyes (40%) had Pre-operative Best Corrected Visual Acuity better than 6/12. Mean Pre-operative Best corrected visual Acuity was LogMAR 0.3668.

The Pre-operative K1 values ranged from 41.1D to 54.8D with a Mean K1 value of 47.89D. 23 eyes (65.72%) had K1 value of more than 46D.

The Pre-operative K2 values ranged from 45.4D to 62.2D with a Mean K1 value of 52.85D. 22 eyes (62.85%) had K2 value of more than 51D.

The Pre-operative K-max values ranged from 48.8D to 69.8D with a Mean K-max value of 58.39D. 25 eyes (71.43%) had K-max value of more than 55D.

The Pre-operative Astigmatism values ranged from 0.9D to 12.4D with a Mean value of 4.96D. 19 eyes (54.29%) had Astigmatism of more than 4D.

In one Patient where the pre-operative Astigmatism was 0.9D Collagen Cross-linking was done as her K-max value was 48.8D with Central corneal thickness of 476 microns with typical keratoconus finding in other eye.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

The Pre-operative Central Pachymetry ranged from 410 microns to 543 microns with a Mean of 466.57 microns. 22 eyes (62.86%) had Central pachymetry of less than 475 micons.

The Pre-operative values Intraocular pressure ranged from 11 to 18.7mm of Hg with a Mean value of 15.41mm of Hg. Majority of the eyes (33-94.29%) had their intraocular pressure below 18mm of Hg.

Mean Pre-operative Uncorrected visual Acuity was LogMAR 0.808 and mean Post-operative Uncorrected Visual Acuity was LogMAR 0.7251. Post-operative Uncorrected visual Acuity increased by a mean of LogMAR 0.08286.

This increase was statistically significant.

Paired t- test: $p<0.0001$

32 eyes (91.42%) had post-operative uncorrected visual acuity of 6/12 or less. 3 eyes (8.58%) had Uncorrected Visual Acuity better than 6/12. Mean Post-operative Uncorrected visual Acuity was LogMAR 0.725.

Post-operative Uncorrected visual acuity remained stable in 22 (62.86%). It improved by 1 or more line in 13 eyes (37.14%).

14 eyes (40%) had Post-operative Best corrected visual acuity of 6/12 or less. 21 eyes (60%) had Best Corrected Visual Acuity better than 6/12. Mean Post-operative Best corrected visual Acuity was LogMAR 0.287.

Post-operative Best corrected visual acuity remained stable in 22 (62.86%). It improved by 1 or more line in 13 eyes (37.14%). The Post-operative K1 values ranged from 40.8D to 55.5D with a Mean K1 value of 46.82D. 19 eyes (54.28%) had K1 value of more than 46D. Post-operative K1 decreased by a mean of 1.07D.

The Post-operative K2 values ranged from 44.6D to 59.0D with a Mean K2 value of 51.32D. 18 eyes (51.43%) had K2 value of more than 51D. Post-operative K2 decreased by a mean of 1.53D

The Post-operative Astigmatism values ranged from 0.8D to 12.17D with a Mean value of 4.506D. 17 eyes (48.57%) had Astigmatism of more than 4D.

Post-operative astigmatism remained stable in 7 eyes (20%). It decreased by upto 1D in 23 eyes (65.71%) and by >1 to 2D in 5 eyes (14.29%)

The Post-operative K-max values ranged from 47.6D to 67D with a Mean K-max value of 56.84D. 23 eyes (65.71%) had K-max value of more than 55D.

Post-operative K-max remained stable in 1 eye (2.86%). It decreased by upto 2D in 25 eyes (71.43%) and by more than 2D in 9 eyes (25.71%). The Post-operative Central Pachymetry values ranged from 378 microns to 519 microns with a Mean value of 439.86 microns. 29 eyes (82.86%) had Central pachymetry of less than 475 microns. The Post-operative Intraocular pressure ranged from 11 to 18.3mm of Hg with a Mean value of 14.79mm of Hg. Majority of the eyes (34) (97.14%) had their intraocular pressure below 18mm of Hg.

Mean Pre-operative Best corrected visual Acuity was LogMAR 0.3668 and Post-operative Best corrected Visual Acuity was LogMAR 0.287. Post-operative Best Corrected visual Acuity increased by a mean of LogMAR 0.0794

This increase was statistically significant.

Paired t- test: $p<0.0001$

The Pre-operative Mean Astigmatism was 4.96D and the Post-operative Mean Astigmatism was 4.50D. Post-operative mean Astigmatism value decreased by 0.46D

This decrease was statistically significant.

Paired t- test: $p<0.0001$

The Pre-operative Mean K-max value was 58.39D and the Post-operative Mean K-max value was 56.84D. Post-operative mean Kmax value decreased by 1.55D.

This decrease was statistically significant.

Paired t- test: $p<0.0001$

The Pre-operative Mean Central Pachymetry value was 466.57 microns and the Post-operative Mean Central Pachymetry value was 439.86 microns. Post-operative mean Central Pachymetry value decreased by 26.71 microns. This decrease was statistically significant.

Table 1: Demographic characteristics of study patients.

Sex	No of patients	Percentage
Male	14	46.67%
Female	16	53.33%
Total	30	100%
Age interval (yrs)		
13-15	11	36.67%
16-19	4	13.33%
20-23	4	13.33%
24-27	7	23.34%
28-30	4	13.33%
Eye operated		
Right	17	56.66%
Left	08	26.67%
Both	05	16.67%
Laterality		
Right	22	62.86%
Left	13	37.14%
Total Eyes	35	100%

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Table 2: Pre-operative parameters

Pre-operative Uncorrected Visual Acuity (UCVA)	No of eyes	Percentage
6/60 or less	14	40%
>6/60 – 6/24	11	31.43%
>6/24 – 6/12	8	22.86%
>6/12 - 6/6	2	5.71%
Pre-operative Best Corrected Visual Acuity (BCVA)		
6/60 or less	3	8.57%
>6/60 – 6/24	5	14.29%
>6/24 – 6/12	13	37.14%
>6/12 - 6/6	14	40%
Pre- operative K1 (Flat axis)		
40 - 43	4	11.42%
>43 – 46	8	22.86%
>46 - 49	11	31.43%
>49 -52	6	17.14%
>52	6	17.14%
Pre-op K2 in Diopters		
<45	0	0
>45 - 48	5	14.29%
>48 – 51	8	22.86%
>51 - 54	7	20%
>54 -57	10	28.57%
>57 – 60	3	8.57%
> 60	2	5.71%
Pre-operative K-max (Keratoconus Apex)		
45 – 50	3	8.57%
>50– 55	7	20%
>55 - 60	15	42.85%
>60 -65	5	14.29%
>65 – 70	5	14.29%
Pre-op Astigmatism in Diopters		
0–2	3	8.57%
>2– 4	13	37.14%
>4 - 6	10	28.57%
>6 -8	6	17.14%
>8 – 10	2	5.72%
>10	1	2.86%
Pre-op CCT in Microns	No of eyes	Percentage
401-425	7	20%
426 – 450	5	14.29%
451 - 475	10	28.57%
476 -500	6	17.14%
501 -525	3	8.57%
>525	4	11.43%
Pre-op IOP in mm of Hg		
10-12	5	14.29%
12-14	8	22.86%
>14-16	2	5.71%
>16-18	18	51.43%
>18-20	2	5.71%

Table 3: Comparison between Pre-operative and Post-operative Uncorrected visual Acuity

	Paired differences					t	P-Value
PreOp UCVA-PostOp Ucva	Mean	SD	SE	95% confidence interval of the difference			
				Lower	Upper		
	0.08286	0.11873	0.2007	0.4207	0.12364	4.129	<0.01

Table 4: Post-operative parameters

Post-op UCVA	No of eyes	Percentage
6/60 or less	12	34.28%
>6/60 – 6/24	10	28.57%
>6/24 – 6/12	10	28.57%
>6/12 - 6/6	3	8.58%
Post-operative Uncorrected Visual Acuity		
Improved by >2 lines	3	8.57%
Improved by 2 lines	2	5.71%
Improved by 1 line	8	22.86%
Stable	22	62.86%

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Post-op BCVA		
6/60 or less	1	2.86%
>6/60 – 6/24	6	17.14%
>6/24 – 6/12	7	20%
>6/12 - 6/6	21	60%
Post-operative Best Corrected Visual Acuity		
Improved by >2 lines	1	2.86%
Improved by 2 lines	3	8.57%
Improved by 1 line	9	25.71%
Stable	22	62.86%
Post-op K1 in Diopters		
40 - 43	7	20%
>43 – 46	9	25.72%
>46 - 49	10	28.57%
>49 -52	6	17.14%
>52	3	8.57%
Post-operative K2 (Steep axis)		
<45	2	5.71%
>45 - 48	5	14.29%
>48 – 51	10	28.57%
>51 - 54	10	28.57%
>54 -57	4	11.43%
>57 – 60	4	11.43%
> 60	0	0%
Post- operative Astigmatism		
0–2	3	8.57%
>2– 4	15	42.86%
>4 - 6	9	25.71%
>6 -8	6	17.14%
>8 – 10	1	2.86%
>10	1	2.86%
TOTAL	35	100%
Change in Astigmatism in Diopters		
>1.5-2	1	2.86%
>1-1.5	4	11.43%
>0.5-1	8	22.85%
>0-0.5	15	42.86%
Stable	7	20%
Post-op Kmax in Diopters		
45 – 50	4	11.43%
>50– 55	8	22.86%
>55 - 60	15	42.86%
>60 -65	6	17.14%
>65 – 70	2	5.71%
Post-operative Change in K-max (Keratoconus Apex)		
>6-8	2	5.71%
>4-6	1	2.86%
>2-4	6	17.14%
>0-2	25	71.43%
Stable	1	2.86%
Post-op CCT in Microns		
376-400	5	14.29%
401-425	9	25.71%
426 – 450	12	34.29%
451 - 475	3	8.57%
476 -500	2	5.71%
501 -525	4	11.43%
>525	0	0%
Post-op IOP in mm of Hg		
10-12	7	20%
>12-14	7	20%
>14-16	7	20%
>16-18	13	37.14%
>18-20	1	2.86%

Table 5: Comparison between Pre-operative and Post-operative Best corrected visual Acuity

	Paired differences					**t**	**P-Value**
PreOp UCVA-PostOp Ucva	Mean	SD	SE	95% confidence interval of the difference			
				Lower	Upper		
	0.7943	0.12513	0.2115	0.3844	0.12241	3.755	<0.01

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Table 6: Comparison between Pre-operative and Post-operative Astigmatism

Paired Samples Test									
.	Paired Differences					T	df	Sig. (2-tailed)	p-value
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference					
				Lower	Upper				
PreOp Astigmatism-PostOp Astigmatism	0.45114	0.47601	0.08046	.28763	.61466	5.607	34	.000	<0.01

Table 7: Comparison between Pre-operative and Post-operative K-max value

Paired Samples Test									
	Paired Differences					T	df	Sig. (2-tailed)	p-value
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference					
				Lower	Upper				
PreOp Astigmatism-PostOp Astigmatism	1.54571	1.73228	0.29281	.95006	2.14077	5.279	34	.000	<0.01

Table 8: Comparison between Pre-operative and Post-operative Central Pachymetry

Paired t- test: p<0.0001 Paired Samples Test									
	Paired Differences					T	Df	Sig. (2-tailed)	p-value
Pre Op Centr Pach – Post Op Centr Pa	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference					
				Lower	Upper				
	26.71429	11.80870	1.99603	22.65786	30.77072	13.384	34	0.000	<0.05

DISCUSSION

The aim of our study was to evaluate the results of corneal collagen cross-linking with riboflavin and ultraviolet light. Several studies from Europe have shown that corneal collagen cross linking with riboflavin and ultraviolet light is effective in stopping progression of keratoconus. A good safety profile has also been documented. But there are very few reports from India. In keratoconus a significant increase in corneal rigidity has been measured in eyes treated with collagen cross linking with riboflavin (IJO). This helps in various ways. In addition to arresting progression of keratoconus, it improves UCVA, BCVA, reduces K reading, astigmatism and higher order aberrations, as well as improve keratoconus indices.[2]

In our study 35 eyes of 30 patients underwent corneal collagen cross-linking with riboflavin and ultraviolet light. The mean follow-up period was 13.17 months. The follow-up period ranged from 7-21 months.

Out of 30 patients, 14 were males & 16 were females. The age of the patient ranged from 13 to 30 years with a mean of 20.47 yrs. The youngest patient operated was 13yrs. Majority (36.67%) of the patients were between 13 to 15yrs of age. Out of 35 eyes of 30 patients, Right eye was operated in 17, Left eye in 08, and 5 patients underwent surgery in both eyes. 33 eyes (94.29%) had pre-operative uncorrected visual acuity of 6/12 or less. 2 eyes (5.71%) have Pre-operative Uncorrected Visual Acuity better than 6/12. 32 eyes (91.42%) had post-operative uncorrected visual acuity of 6/12 or less. 3 eyes (8.58%) have Post-operative Uncorrected Visual Acuity better than 6/12.

On comparing post-operative uncorrected visual acuity with pre-operative uncorrected visual acuity the post-operative uncorrected visual acuity increased by a mean of LogMAR 0.08286. This increase was statistically significant (P-Value <0.0001). 21 eyes (60%) had Pre-operative Best corrected visual acuity of 6/12 or less. 14 eyes (40%) had Pre-operative best corrected visual acuity better than 6/12. 14 eyes (40%) had Post-operative Best corrected visual acuity of 6/12 or less. 21 eyes (60%) had Post-operative best corrected visual acuity better than 6/12. On comparing post-operative best corrected visual acuity with pre-operative best corrected visual acuity the post-operative best corrected visual acuity increased by a mean of LogMAR 0.0794. This increase was statistically significant (P-Value< 0.0001). The post-operative best corrected visual acuity remained stable in 21 eyes (62.86%). It improved by 1 line in 9 eyes (25.71%) and by 2 lines or more in 4 eyes (11.43%). Our results compared well with other studies. In the study conducted by Efekan coskunseven et al,[3] the UCVA increased by a mean of LogMAR 0.06±0.05. BCVA increased by a mean of LogMAR 0.10±0.14 at a mean follow-up of 9 months. In the study conducted by Ramez Barbara et al.[2] the UCVA increased by a mean of LogMAR 0.22. BCVA increased by a mean of LogMAR 0.2 at a mean follow-up of 25.5 months. In the study conducted by Laden Saffarian et al. 4the UCVA increased by a

ISSN (O): 2687-5365; ISSN (P): 2753-6556

mean of LogMAR 0.31. BCVA increased by a mean of LogMAR 0.11 at 12 months follow-up.

In the study conducted by Maddolena De Benardoet al,[4] the BCVA increased by a mean of LogMAR 0.1 at 12 months follow-up and by a mean of LogMAR 0.2 at 24 months. In the study conducted by Vinay B Agarwal,[5] the best corrected visual acuity improved by at least 1 line in 54% of eyes and remained stable in 28% of eyes at 1 year follow-up. The Pre-operative Astigmatism ranged from 0.9D to 12.4D with a Mean of 4.96D. 19 eyes (54.29%) had Astigmatism of more than 4D. The Post-operative Astigmatism ranged from 0.8D to 12.17D with a Mean of 4.28D. 18 eyes (51.43%) had Astigmatism of more than 4D.

On comparing post-operative astigmatism with pre-operative astigmatism the post-operative astigmatism decreased by a mean of 0.68D. This decrease was statistically significant (P-Value 0.0001). The results in our study were similar to other studies in the study conducted by Efekon coskunseven et al,[3] the astigmatism decreased by a mean of 1.04D after a mean follow-up of 9months. In the study conducted by Ramez Barbara et al,[2] the astigmatism decreased by a mean of 0.86D (P=0.002) after a mean follow-up of 9 months. In the study conducted by Laden Saffarian et al,[6] the astigmatism decreased by a mean of 0.78D after 12months follow-up. In the study conducted by Maddolena De Benardo et al,[4] the astigmatism decreased by a mean of 0.38D after 24 months follow-up. The Pre-operative K-max (keratoconus apex) values ranged from 48.8D to 69.8D with a Mean K-max value of 58.39D. 25 eyes (71.43%) had K-max value of more than 55D.

The Post-operative K-max values ranged from 47.6D to 67D with a Mean K-max value of 56.92D. 23 eyes (65.71%) had K-max value of more than 55D. On comparing post-operative K-max with pre-operative K-max the Post-operative K-max decreased by a mean of 1.47D. This decrease was statistically significant (P<0.0001). The results in our study were similar to other studies. In the study conducted by Wittig-Silva C et al.[7] The K-max decreased by a mean of 1.45D at 12 months. In the study conducted by Efekon coskunseven et al.[3] the K-max decreased by a mean of 1.57D after a mean follow-up of 9 months. In the study conducted by Ramez Barbara et al,[2] the K-max decreased by a mean of 0.1D after a mean follow-up of 25.5 months. In the study conducted by Maddolena De Benardoet al,[4] the K-max decreased by a mean of 2.22D after a follow-up of 24 months. The Pre-operative Central Pachymetry (central corneal thickness) ranged from 410 microns to 543 microns with a Mean of 466.57 microns. 22 eyes (62.86%) had Central pachymetry of less than 475 microns. The Post-operative Central Pachymetry ranged from 378 microns to 519 microns with a Mean of 439.86 microns. 29 eyes (82.86%) had Central pachymetry of less than 475 microns.

On comparing post-operative central pachymetry with pre-operative central pachymetry the Post-operative Central Pachymetry decreased by a mean of 26.71 microns. This decrease was statistically significant (p < 0.0001). In the study conducted by Efekon coskunseven et al,[3] no statistically significant change was found in post-operative pachymetry at a mean follow-up of 9 months. In the study conducted by Maddolena De Benardoet al,[4] the post-operative central pachymetry decreased by a statistically significant mean of 22.2 microns (P<0.01) at 24 months follow-up.

The Pre-operative Intraocular pressure ranged from 11 to 18.7mm of Hg with a Mean value of 15.41mm of Hg. The Post-operative Intraocular pressure ranged from 11 to 18.3mm of Hg with a Mean value of 14.79mm of Hg. On comparing the post-operative intraocular pressure with pre-operative intraocular pressure the Post-operative Intraocular pressure decreased by a mean of 0.62mm of Hg. This decrease was statistically significant (P-Value<0.0001). In the study conducted by Ramez Barbara et al,[2] the post-operative intraocular pressure increased by a mean of 0.47mm of Hg(P=0.532) at a mean follow-up of 25.5 months. In the study conducted by Efekon coskunseven et al,[3] the post-operative intraocular pressure increased by a mean of 2mm of Hg(range 7 -15mm)(P=0.01)at a mean follow-up of 9months. The authors state that this finding was not a safety concern but rather demonstrated the efficacy of cross linking. A stiffer cornea measures at a higher IOP that is similar to the observed IOP measurement differences between the thicker and thinner corneas. The results of our study showed a statistically significant improvement in post-operative UCVA, BCVA and a reduction in astigmatism. There is also a significant improvement in K readings. The central corneal thickness decreased significantly. This is probably because of the expected significant increase of corneal rigidity with collagen cross linking.

Transient post-operative haze was seen in a few cases in our study which resolved with no sequelae on topical steroids. Significant haze was seen in 3.57% of cases in the study by Soeters et al,[8] and in 14.28% of cases in the study by Kodavoor et al,[9] Delayed epithelialization of up to 10 days and transient glare and corneal oedema were also reported (Hala el Rami et al.).[10] Transient glare was reported in a few cases but delayed epithelization and corneal oedema was not seen in our study.

Limitations of Our Study

Lack of data on endothelial cell counts- Endothelial cell counts were not done in our study. But other studies (Maddolena De Benardo et al) showed no significant difference in endothelial cell counts in the follow-up period. Spherical and higher order aberrations were not studied. But other studies (Vinay Agarwal),[3] did not show significant variations. Sample size was 35 and follow-up period was a mean of 13.17 months. Larger sample size and longer follow-up would help better determine the safety and efficacy of the procedure. Longer follow-up would have made sure that endothelial function does not suffer from any delayed side effects. Longer

ISSN (O): 2687-5365; ISSN (P): 2753-6556

follow-up also helps to determine if the stabilization is long lasting especially in children.

CONCLUSION

In our study Corneal collagen cross-linking with riboflavin and Ultraviolet-A light was effective during the study period in halting the progression of keratoconus as evidenced by an improvement in Uncorrected visual acuity, Best corrected visual acuity, decrease in the corneal curvature and astigmatism demonstrated by topography. There is significant decrease in corneal pachymetry. The intraocular pressure remained within normal range. No major or sight threatening complications were noted. In the early post-operative period corneal haze was noted but was transient. By early diagnosing and treating the keratoconus with cross-linking the need for future corneal transplant may be decreased. As there is stabilization in keratoconus with corneal collagen cross-linking this procedure may be extended to other corneal ectatic conditions like Pellucid Marginal Corneal Degeneration and Iatrogenic ectasia. The cross-linked corneas may also be subjected to other refractive procedures like Intrastromal corneal rings and Phakic Intraocular lens for improving the quality of vision. It is a safe and effective procedure. However a larger series and long-term follow-up is necessary to draw definitive conclusions.

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ISSN (O): 2687-5365; ISSN (P): 2753-6556