Original Article

Preliminary Results of UV-A Riboflavin Crosslinking in Progressive Cases of Keratoconus, in Pakistani Population

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Purpose: Keratoconus is a progressive non-inflammatory thinning disorder of the cornea which being a disease of young, has a significant psychosocial value. Corneal crosslinking with Riboflavin stops progression by increasing the strength of the cornea and has revolutionized the treatment of corneal ectasias at an early stage.

Materials and Methods: This is an ongoing prospective interventional single site study conducted in Armed Forces Institute of Ophthalmology, Rawalpindi, Pakistan.35 cases of more than 12 years with progressive keratoconus or any other corneal ectasia were included in the study after March 2006.

Results: The mean age was 17.71±4.6 years. 41.9% of the cases were males while 58.1% of them were females with a frequency of 13 and 18 respectively. Right eye was treated in 54.8% of the cases whereas left eye was treated in 45.2% of the cases with a frequency of 17 and 14 respectively. Mean pre-operative BCVA was 0.53+/-0.36 which improved by at least one line in 61.29% of the cases, remained stable in 35.48% cases and deteriorated in 3.23% cases. Mean post-operative BCVA was 0.39+/-0.24.Pre-operative mean of steepest K reading (K steep) was 50.60+/-5.41D,which reduced to 48.85+/-6.11D ($p< 0.001$). The steepest K reading improved in 67.74% cases, remained stable in 25.81% cases and deteriorated in 6.45% cases. Two cases (6.45%) developed keratitis leading to corneal scarring.

Conclusion: Our study shows that CXL is a safe and effective procedure in stopping progression of corneal ectasias.

Keratoconus is a progressive noninflammatory thinning disorder of the cornea which leads to mixed myopic and irregular astigmatism[1]. It is derived from the Greek words Keratosmeaning "cornea" and Konos meaning "cone". Eberhard Spoesi and Theo Seiler developed corneal cross-linkage (CXL) procedure in late 1990's[2,3]. Wollensak et al introduced the procedure as an alternative to penetrating keratoplasty in treating progressive keratoconus in 2003[4]. Owing to the latest diagnostic modalities the incidence of keratoconus is reported to be about 1 in 600 to 1 in 420[5]. Moreover, being a disease of young, keratoconus has a significant psychosocial value causing loss of productivity and disproportionate impact on quality of life[6].

CXL strengthens the cornea by increasing the numbers of covalent bonds between collagen fibers. Once the Riboflavin is activated by ultraviolet-A light, it promotes a free radical pathway that causes cross-linkage of corneal collagen and increases its strength by more than 300%[7]. CXL was approved in Europe for clinical use in January 2007 and is still undergoing FDA trials in United States.

Apart from treating corneal ectasias, CXL with Riboflavin is being studied in treatment of corneal

infections where in vitro trials have shown elimination of methicillin resistant Staph Aureus and Pseudomonas[8]. CXL is also being tried for the treatment of pseudophakic corneal edema where the corneal tissue was thinned by[9].

MATERIALS AND METHODS

This ongoing prospective interventional single site study was conducted in Armed Forces Institute of Ophthalmology, Rawalpindi, Pakistan. 35 cases of more than 12 years with progressive keratoconus or any other corneal ectasia and who could complete follow up of 6 months were included in the study after March 2006. Any patient having corneal scarring, uncontrolled VKC or glaucoma, corneal thickness less than 400µm or prior history of corneal surgery were excluded from the study.

Informed written consent was obtained from the participants and the study was reviewed and approved by ethics committee.

Pre-operative complete ocular examination was performed including LogMAR BCVA, keratometery (Canon RK-F1), videokeratography (Haag-StreitCTK 922) and pachymetry (Reichert IOPac Advanced). Relevant information was documented on a follow-up proforma. The CXL was performed under sterile conditions as a day-care procedure. After anaesthetizing with proparacaine hydrochloride 0.5% (Alcain) eye drops, Central 8 mm of corneal epithelium was removed. A drop of 0.1% riboflavin solution was applied to the cornea every 2 minutes for thirty minutes before the irradiation. Aqueous flare in anterior chamber was checked on a slit-lamp. The ultraviolet lamp (IROC AG, Zurich, Switzerland) was checked on meter to confirm that UV-A light with a wavelength of 365+/-10 nm and an irradiance of 3+/-0.3mW/cm2 was being emitted. Then central cornea was irradiated with this source for 30 minutes during which riboflavin instillation was continued every 2 minutes.

Post-operative care included application of bandage contact lens, topical Moxifloxacin (Vigamox) and Prednisolone (Predforte) eye drops till complete re-epithelialization of the cornea. Follow-up examination was performed at 6 months for record of BCVA and K-readings.

Data had been analyzed using SPSS version 15. Mean and standard deviation (SD) were used to describe the variables. Frequency and percentage was used to describe variables such as gender and eye involved. Paired sample t-test was applied to check the significance of change in numeric variables. P-value <0.05 was considered as significant.

RESULTS

Out of 35 cases enrolled for this study 4 cases were lost for follow-up. Results of 31 cases who completed the follow-up were analyzed. All cases were having progressive keratoconus, other ectasias being very rare. Pre and post operative keratometry readings were taken as criteria for corneal stabilization. However pre and post operative BCVA was taken as additional criterion. The mean age was 17.71+4.6 years. 41.9% of the cases were males while 58.1% of them were females with a frequency of 13 and 18 respectively. Right eye was treated in 54.8% of the cases whereas left eye was treated in 45.2% of the cases with a frequency of 17 and 14 respectively.

Mean pre-operative BCVA on LogMAR was 0.53+/-0.36.BCVAimproved by at least one line in 61.29% of the cases, remained stable in 35.48% cases and deteriorated in 3.23% cases. Mean post-operative BCVA on LogMAR was 0.39+/-0.24. This was a statistically significant improvement ($p<0.001$).

Pre-operative mean of steepest K reading (K steep) was 50.60+/-5.41D. After treatment with CXL, mean K steep reduced to 48.85+/-6.11D ($p< 0.001$). The steepest K reading improved in 67.74% cases, remained stable in 25.81% cases and deteriorated in 6.45% cases.

Two cases (6.45%) developed keratitis leading to corneal scarring.

DISCUSSION

Raiskup-Wolf F et al in their study concluded that the improvement in vision after CXL is due to decrease in astigmatism and corneal curvature as well as topographical homogenization secondary to increase corneal rigidity. They followed up patients for up to six years. At 1 year post op 53% (127/241) of eyes had gained one line BCVA from baseline and decreased astigmatism by a mean of 0.93D in 50% (120/241). Keratometry and astigmatism remained unchanged in 17% (41/241) and 36% (86/241) eyes respectively[10]. Mean improvement in our study is comparable to this study in which there is improvement in BCVA by one line though after one year.

Grewel et al also concluded in his study halt of progression in keratoconus[11]. By 1 year post op he did

Table-1: Demogarphic description of patients (n = 31)

Variables	Frequency n (%)
Gender	
Male	13 (41.9)
Female	18 (58
Eye Involved	
Left	14
Right	17

Table 2: Pre & Post-operative description of different variables (n = 31)

Variables	Pre Operative		Post Operative		p-value
	Mean	SD	Mean	SD	
BCVA(Log MAR)	0.53	0.36	0.319	0.24	< 0.001
K Steep	50.60	5.41	48.85	6.11	< 0.001
K Flat	46.83	4.42	46.40	5.27	0.393

Age	Sex	Eye	Pre-op BCVA (LogMAR)	Post-op BCVA (LogMAR)	Pre-op K Steep (DS)	Pre-op K Flat (DS)	Post-op K Steep (DS)	Post-op K Flat (DS)	Difference K Steep	Result K Steep	Result BCVA Lines
15	F	R	1.00	0.60	65.25	60.00	64.00	60.25	-1.25	Better	-2
15	F	L	1.00	0.60	63.00	57.50	61.25	56.25	-1.75	Better	-2
13	F	R	0.18	0.18	42.00	40.25	41.25	43.25	-0.75	Better	0
13	F	L	0.18	0.18	52.50	50.50	51.75	50.25	-0.75	Better	0
13	M	R	0.78	1.00	55.25	50.25	61.50	54.75	6.25	Worse	+1
13	M	L	0.78	0.48	49.50	47.50	49.25	47.25	-0.25	Same	-2
18	M	R	0.60	0.60	52.75	48.75	49.75	48.75	-3.00	Better	0
18	M	L	0.48	0.48	51.25	48.75	50.25	47.25	-1.00	Better	0
14	F	R	0.78	0.48	45.25	44.00	46.00	43.00	0.75	Worse	-2
14	F	L	1.00	0.60	47.50	45.00	46.25	43.25	-1.25	Better	-2
16	M	R	1.00	0.60	56.25	48.50	55.75	48.00	-0.50	Same	-2
16	M	L	1.00	0.48	57.00	48.25	56.00	47.50	-1.00	Better	-3
19	M	R	0.78	0.18	53.25	49.00	51.25	47.50	-2.00	Better	-4
16	M	R	0.30	0.18	47.75	46.75	45.75	46.25	-2.00	Better	-1
12	F	R	0.18	0.18	49.75	44.75	44.25	51.50	-5.50	Better	0
16	F	R	0.00	0.00	42.00	40.25	41.50	43.50	-0.50	Same	0
12	F	L	0.30	0.18	51.50	46.50	45.50	51.75	-6.00	Better	-1
16	F	L	0.00	0.00	52.50	50.50	53.00	51.75	0.50	Same	0
16	F	R	0.18	0.00	47.75	46.00	47.25	45.75	-0.50	Same	-1
19	M	R	0.18	0.18	52.75	48.75	49.75	48.75	-3.00	Better	0
19	M	L	0.18	0.18	51.25	48.75	50.25	47.25	-1.00	Better	0
21	F	L	0.60	0.18	53.50	45.50	50.25	45.25	-3.25	Better	-3
23	M	L	1.00	0.30	51.00	45.25	50.75	44.75	-0.25	Same	-4
20	F	R	0.30	0.30	44.50	42.00	45.00	42.00	0.50	Same	0
30	F	R	0.18	0.18	48.00	44.75	47.50	43.25	-0.50	Same	0
24	F	R	0.48	0.18	45.00	43.25	40.75	39.25	-4.25	Better	-2
24	F	L	0.30	0.00	44.75	43.50	40.50	39.25	-4.25	Better	-1
16	F	R	0.78	0.30	47.75	42.25	43.25	38.00	-4.50	Better	-3
16	F	L	1.00	0.30	47.50	41.75	43.50	38.50	-4.00	Better	-4
26	M	R	0.78	0.60	55.25	50.25	49.75	45.00	-5.50	Better	-1
26	M	L	0.30	0.18	45.25	42.75	41.75	39.50	-3.50	Better	-1

Fig. 1: Age description of patients (n = 31)

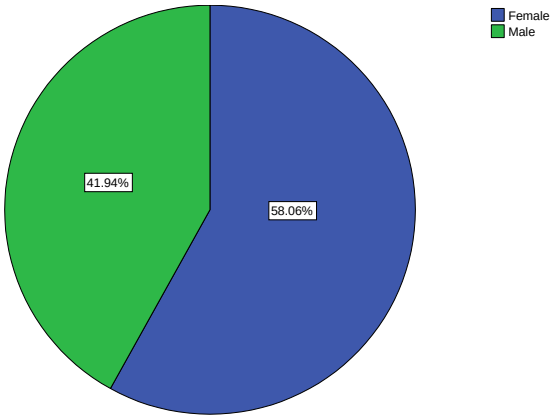


Fig. 2: Gender description of patients (n = 31)

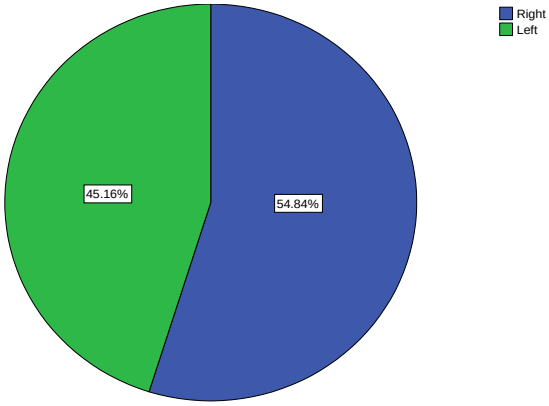


Fig. 3: Eye involved or damage (n = 31)

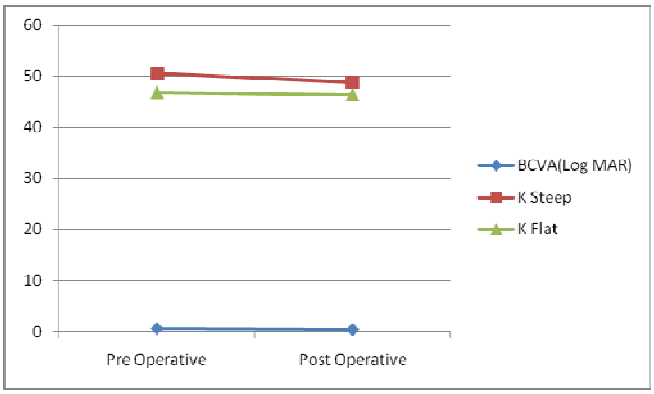
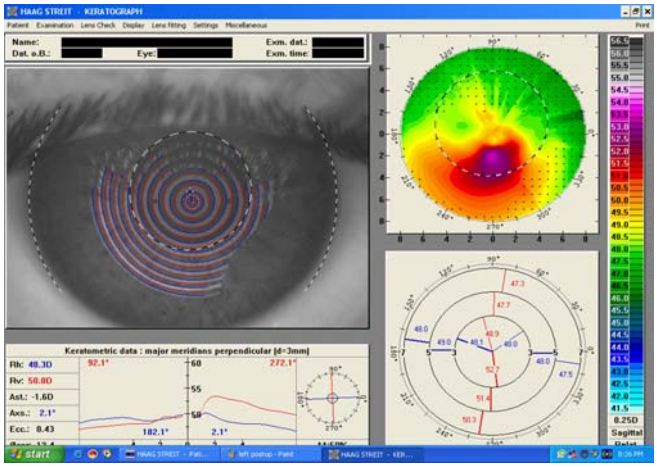
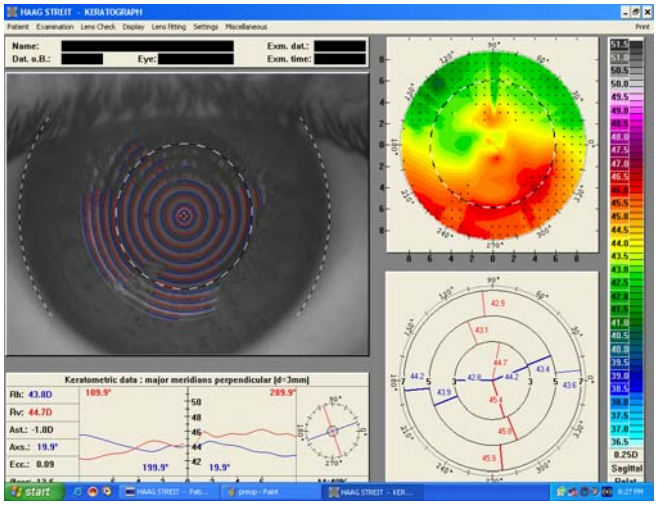


Fig. 4: Change in variables before and after the operation (n = 31)



Pre-Operative Picture



Post-Operative Picture

not observe any statistically significant changes from baseline mean BCVA (p=0.89) whereas our study showed statistically significant improvement after only 6 months of follow up.

In a study conducted by Agarwal in India, BCVA improved at least one line in 54% of eyes and remained stable in 28% of eyes after follow up of 12 months[5].This study carries high significance being conducted in South Asia. Research cases were comparable with each other considering similar social and environmental factors. Our study showed slightly better visual results which are comparable with this study.

Hoyer and colleagues found that visual acuity improved significantly in at least one line or remained stable in the first year in 48.9% and 23.8% respectively; in the second year in 50.7% and 29.6% respectively, and in the third year in 60.6% and 36.4%respectively. Keratectasia significantly decreased in the 1st year by 2.29 D, in the 2nd year by 3.27 D, and in the 3rd year by 4.34 D[12].Conforming with this study we also found improvement of about 2 D within 6 months only. Improvement in keratectasia is directly related to post op duration which is encouraging for our ongoing study because we may expect progressive improvement in BCVA as well as K readings in our cases with longer follow-up. BCVA improves by virtue of decreased astigmatism resulting from increased corneal rigidity[13-15].

Carina and colleagues conducted study on 117 cases and found to have keratitis and corneal scarring in 4 cases. Amount of visual loss was determined by the location of scarring. In our study we had only two cases who developed the complication which gives us the confidence to say that CXL is a safe procedure[16,17].

CONCLUSION

Our study shows that CXL is a safe and effective procedure in stopping progression of corneal ectasias. It is recommended that more studies with longer follow up and larger sample size be conducted to see long term effects of this procedure.

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