Simultaneous Photorefractive keratectomy (PRK) with Corneal Cross Linking (CXL) For Treatment of Early Keratoconus.

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Abstract: Purpose: To study the efficacy and safety of PRK and corneal cross linking (CXL) For treatment of early Keratoconus. **Methods:** Twenty two eyes of fifteen patients with early progressive keratoconus were included**.** all patient underwent Simultaneous PRK and corneal cross linking (CXL) The outcomes were evaluated at 12 months in all eyes. **Result:** ninety five percent of UNCVA postoperatively are equal to preoperatively BCVA or gained 1 or more lines 5% only Lost 1 or more lines, 64% of the eyes are within 1.0D. of emmetropia. Non of the eyes had > 2.0 D and 59% of the eyes had Astigmatism by K-Reading within 1.0D. Non of the eyes had > 2.0D. **Conclusion:** Simultaneous PRK + CXL is a very effective way to stop progression of early KC and it improves patient visual acuity and quality of vision provided that we adhere to the selection criteria of that we recommend**.**
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Keywords: safety; keratoconus; corneal cross linking; emmetropia; eye

1. Introduction

Keratoconus is a degenerative, non inflammatory disease of the cornea with onset generally at puberty. It is progressive in 20% of cases and can be treated by lamellar or perforating keratoplasty. Its incidence in the general population is reported to be about 1/2000. It is characterized by stromal thinning and cone shaped steepening of the cornea that result in irregular astigmatism and refractive myopia[1] Incidences of 1/600-1/420 seem more reasonable in keeping with current diagnostic capacity. Changes in corneal collagen structure[2], organisation and intercellular matrix[3], as well as apoptosis [4] and necrosis of keratinocytes prevalently or exclusively involving the central anterior stroma and the Bowmann lamina, are documented in the literature [5].

The available options to treat keratoconus are; spectacle correction in early stages. Since keratoconus tend to progress, hard contact lenses are major treatment modality for keratoconus. Intracorneal rings can be considered in early keratoconus to improve the refractive error with no definite role in halting the progression of the disease. 21% of keratoconus patients eventually need penetrating or lamellar keratoplasty[6-7].

Recently, a new technique, corneal collagen cross linking, has been introduced by wollensak *et al.* to stabilize progressive keratoconus[8]. There are number of studies reported that CXL is safe and effective in halting the progression of keratoconus[9-10] and post-refractive surgery corneal ectasia[11].

The technique of corneal collagen cross-linking consists in photopolymerisation of stromal fibres by the combined action of a photosensitising substance (riboflavin or vitamin B2) and ultraviolet light from a solid state UVA source Photopolymerisation increases the rigidity of corneal collagen and its resistance to keratectasia. Corneal cross linking (CXL) minimally alter refractive error particularly when applied to cornea at an early stage[12].

A study was done in the literature which looked at the long-term results of photorefractive keratectomy (PRK) in keratoconus detected by videokeratography , the conclusions of this study indicate that PRK seems to be a safe procedure for reducing or eliminating myopia or astigmatism in keratoconus suspect eyes-most probably forme fruste keratoconus with a stable refraction [13].

PRK has been used as a treatment for the visual rehabilitation of keratoconic patients for several years; however, its main drawback is that it is a tissue removal technique. The stromal thinning introduced by ablation most likely triggers further destabilization of corneal biomechanics, progression of keratoconus, and astigmatism. In cases of stable or forme fruste keratoconus, surface ablation techniques have promising results, with several studies reporting the use of laser ablation to correct astigmatism in patients with stable keratoconus[14]. There is a consensus among many Ophthalmologists that light PRK (<= 50um) is reasonably safe[15-16].

Considering that CXL is capable of stiffening the cornea and halting progression of keratoconus, the combination of laser ablation and CXL provides a promising treatment for keratoconus.

The objective of our study was to evaluate the visual outcome, refraction, topography pattern, and keratoconus progression following simultaneous PRK and CXL in keratoconus patient.

2. Patients and Methods:

This prospective interventional case series comprised twenty eyes of fifteen patients. Inclusion criteria were early keratoconic eyes by topography with clear central cornea, , a BSCVA of 20/25 or better, minimum central corneal thickness of 450 µm and steepest keratometry ≤ 51 D. All eyes must have refractive error that can be corrected with 60 µm ablation depth or less.

Preoperative examinations included UCVA, BSCVA, manifest refraction, slit lamp biomicroscopy, dilated fundus examination, topography and ultrasonic pachymetry.

Surgical technique

All patients had uneventful PRK with mitomycine C (MMC) followed by CXL. Thirty minutes before surgery, an Proparacaine 2% eye drops were used to anesthetize the ocular surface. The patients face was prepped with povidone-iodine 10%. The eyelashes were isolated using sterile drape. A 9.0 mm trephine, centered on the pupil was used to mark corneal epithelium. Corneal epithelium was removed either by using blunt scraper after application of 20% alcohol or by using Amoil's brush in some cases PTK was used. Stromal ablation was done using Schwind Amaris excimer laser system (Schwind Inc, Germany) with 6 mm optical zone, 1.25 mm transition zone and 8.5 mm ablation zone. MMC 0.02% was applied for 20 seconds using mirocel sponge then vigorous irrigation with BSS was done. We used ultrasound pachymetry to locate the central and thinnest point. For CXL, riboflavin 0.1% drops were applied every 5 minutes for 30 minutes. we performed slit-lamp inspection, using blue light for riboflavin shielding, followed by irradiation with the UV-X Corneal Crosslinking System (Iroc Medical, Zurich, Switzerland; distributed by Peschke GmbH, Nuremberg, Germany). For the 30-minute treatment, the parameters were: 370 nm, 3mW/cm2, 5.4 j/cm2, balanced saline solution was applied, along with ofloxacin 0.3% and one drop of diclofenac ophthalmic eye drop and a bandage contact lens. Postoperative medications include oflaxacin0.3% four times/day, fluorometholone four times/day and lubricating eye drops every two hours.

Patients were reviewed on the first and seventh postoperative days, and subsequently at 3 weeks, 6 weeks, 3 months 6 months and one year. At each examination, unaided visual acuity was determined, and the cornea was examined by the slit lamp. Autorefractometry as well as manifest subjective refraction were performed, and best corrected visual acuity (BCVA) was determined at the three weeks, six weeks and three months examinations. Post operative corneal topography was performed at the 3 months 6 month and one year.

3. Results

This study comprised 22 eyes of fifteen patients 27% patients were male and 73 % of patients were female the mean age of study patients was 26 years old operated on between February 2007 and June 2007 that had simultaneous customized PRK and CXL for keratoconus correction. All patients finished 12 months follow up. Figure 1 shows the patients gender and table 1 shows the patients age

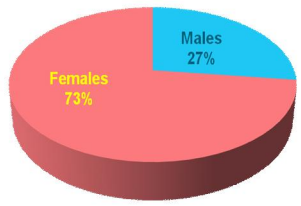


Fig1.sex

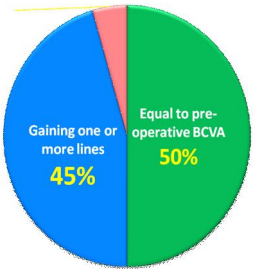
Mean	**26 y**
Minimum	**19 y**
Maximum	**40 y**

Table 1.Age

The mean UCVA improved from 0.3 ± 0.14 preoperatively to 0.93 ± 0.12 and 0.92 ± 0.1 at 3 months (P=0.055) and 12 months (*P*=0.094) respectively. The improvement was statistically significant.

The mean BSCVA improved from 0.95 ± 0.14 preoperatively to 1.1 ± 0.11 and 1.2 ± 0.13 at 3 months (P=1) and 12 months (*P* =0.005) respectively. The improvement was statistically significant at 12 months.

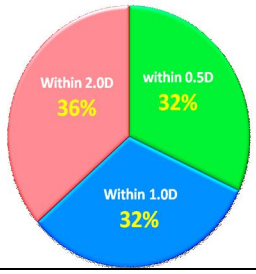
Ninety five percent of UNCVA are equal to pre-op BCVA or gained 1 or more lines 5% only Lost 1 or more lines figure(2) 64% of the eyes are within 1.0D. of Emmetropia Non of the eyes had > 2.0 D figure(3). 59% of the eyes had Astigmatism by K-Reading within 1.0D. Non of the eyes had > 2.0D (Figure4).



11	10	1
50%	45%	5%

* Equal to pre-op BCVA + Gaining 1 or more lines = **95%**
* Losing 1 or more lines = **5%**

Fig. (2)

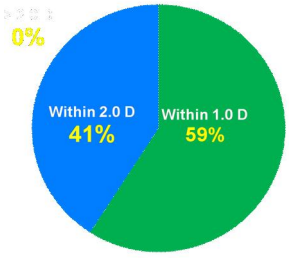


7	7	8
32%	32%	36%

* **64%** Within 1.0D.

* **100%** are within 2.0D.

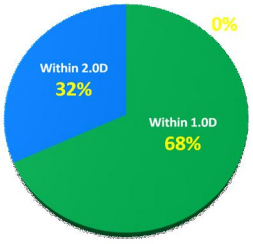
Fig. (3)



13	9	0
59%	41%	0%

* **100%** are within 2.0D.

Fig. (4)



15	7	0
68%	32%	0%

* **100%** are within 2.0D.

Fig (5)

Manifest refraction spherical equivalent

The mean spherical equivalent (SE) refraction decreased significantly from -3.42 ± 2.91 D preoperatively to -1.72 ± 1.54 D and -1.55 ± 1.38 D at 3months (*P*=0.013) and 12 months (*P*=0.010) respectively (Table 2). The changes in spherical equivalent (SE) were statistically significant at 3 and 12 months.

Manifest refraction cylinder

The mean manifest refraction cylinder decreased from -1.49 ± 1.67 D preoperatively to -1.00 ± 1.5 and -1.01 ± 1.45 D at 3 months (*P*=0.015) and 12 months (*P*=0.141) respectively (Table 2). The changes in manifest refraction cylinder were significant at 3 months but not at 12 months.

Keratometry

The mean average K-value decreased from45.04 ±3.29 D preoperatively to 43.14 ± 2.72 D and 43.01 ± 2.25 D at 3 months (*P*= 0.052) and 12 months (*P*=0.055) respectively (Figure 5). The changes in k-value were not significant.

The following table represent K.reading as regard the mean K, the maximum K and astigmatism by K in dioptre(D) Table(3).

Table (2)	*UNCVA	*BCVA	*Sph. Eq	*Astigma.	*CCT(um)
Preoperative					
Mean	0.3	.95	- 3.42D	-1.49D	500
Minimum	0.05	0.84	- 0.75D	0.00D	445
Maximum	0.9	1.2	-6.38D	-4.40D	536
Postoperative	*UNCVA	*BCVA	*Sph. Eq	*Astigma	*CCT(um)
Mean	0.93	1.1	- 1.55D	-1.01D	436
Minimum	0.25	0.4	- 0.35D	0.00D	389
Maximum	0.98	1.2	-2.88D	-2.20D	494

*UNCVA=Uncorrected visual acuity *BCVA=Best corrected visual acuity *Sph. Eq=Spherical equivalent. *Astigma=Astigmatism *CCT(um)=Central corneal thickens

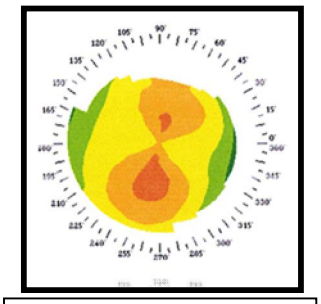
Table (3)	K .READING		
Preoperative	Mean k (D)	Max.k (D)	Astigm.K (D)
Mean	45.04	46.15	2.22
Median	45.26	42.97	0.82
Maximum	48.91	50.36	3.95
Postoperative	Mean k (D)	Max.k (D)	Astigm.K (D)
Mean	43.14	45.31	2.09
Median	44.06	41.86	0.77
Maximum	**47.21**	**48.44**	**3.01**

Table(4) types of topography of keratoconus in study patients.

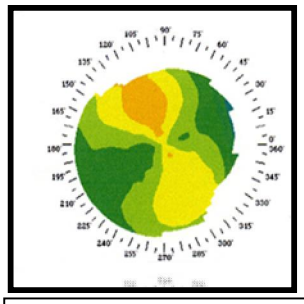
Table(4).Types of topography	No.	%
Asymmetric Bowtie (skew deviation)	4	18%
Asymmetric Bowtie	4	18%
Represent Inferior steepening	8	36%
PMD (pellucid marginal degeneration)	2	9%
Symmetric Bowtie	4	18%

Inferior-superior asymmetry

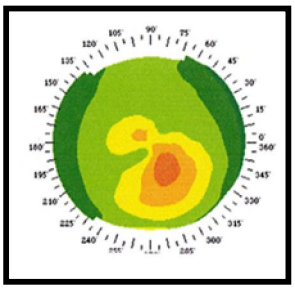
The mean inferior-superior asymmetry decreased from 4.92 ± 2.38 D preoperatively to 3.68 ± 1.83 D and 3.61 ± 1.76 D at 3 months (P= 0.928) and 12 months (*P*=0.731) respectively (Figure 6). The changes were not significant.



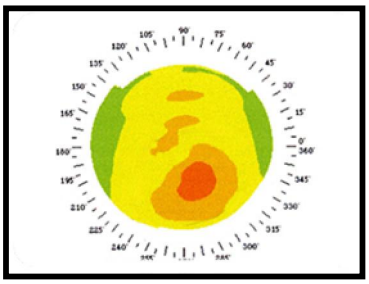
Symmetric Bowtie

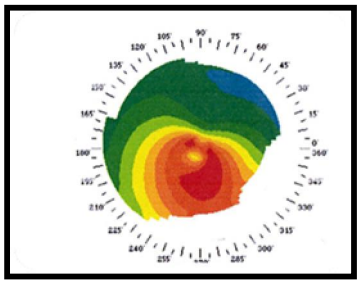


Asymmetric Bowtie



Asymmetric Bowtie

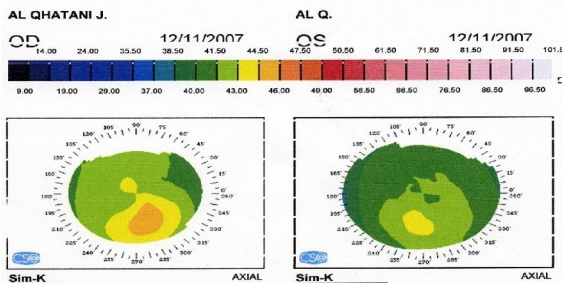


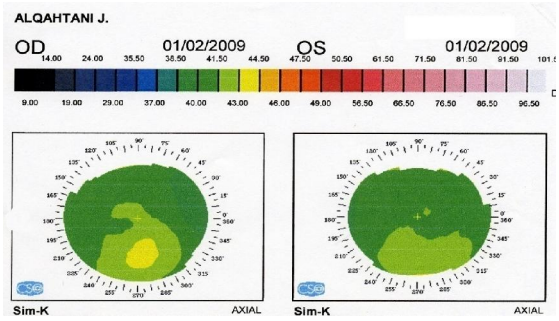


Inferior Steepening

PMD (Pellucid Marginal Degeneration)

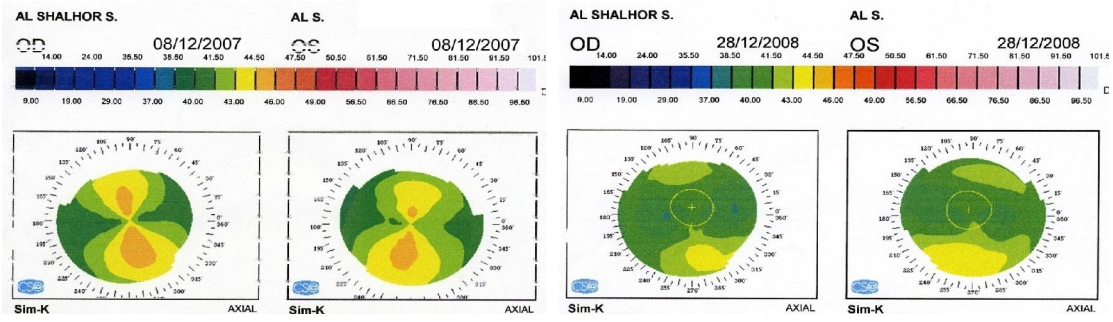
Preoperative Postoperative



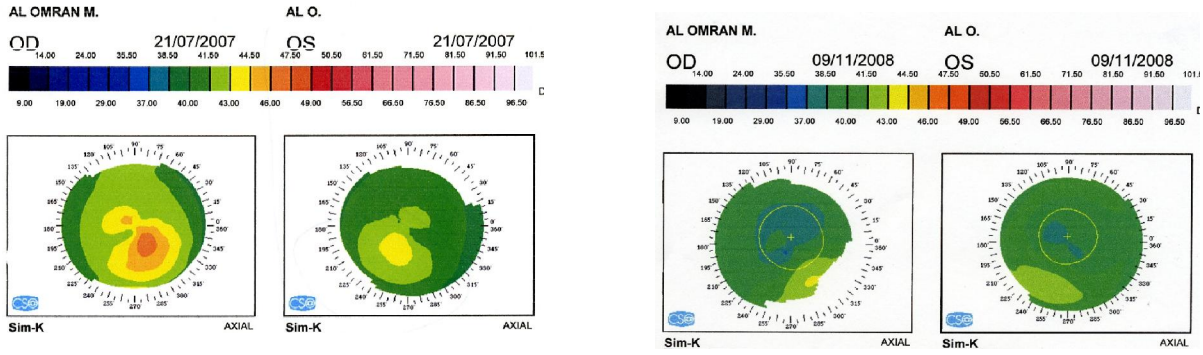


Rt.	Lt.		Rt.	Lt.
20/150	20/200	UNCVA	20/16	20/16
20/16	20/16	BCVA	20/16	20/16

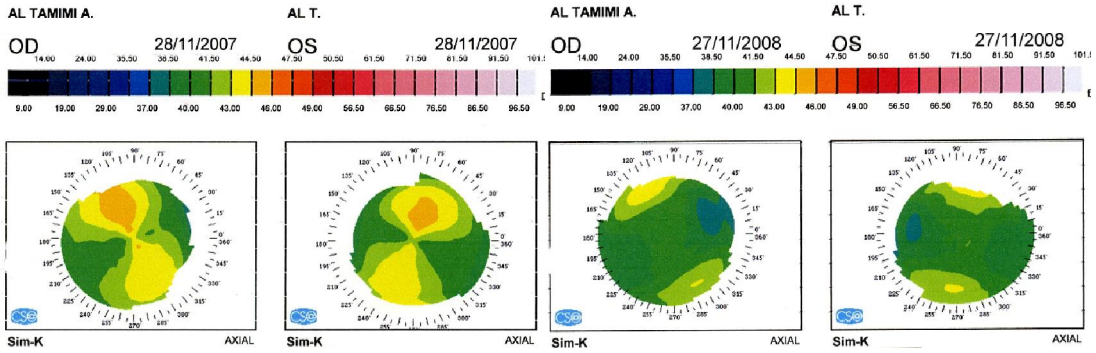
Fig (6) :Types of corneal topography of keratoconus in study patients.



Rt.	Lt.		Rt.	Lt.
20/200	20/400	UNCVA	20/16	20/16
20/16	20/16	BCVA	20/16	20/16



Rt.	Lt.		Rt.	Lt.
20/100	20/400	UNCVA	20/16	20/16
20/16	20/16	BCVA	20/16	20/16



Rt.	Lt.		Rt.	Lt.
20/60	20/60	UNCVA	20/22.5	20/22.5
20/28.5	20/25	BCVA	20/22.5	20/22.5

Fig(7) :Corneal topography pre and post operative.

4. Discussion:

The goal of simultaneous custom PRK and CXL is to offer keratoconus patients corneal stability as well as functional vision. Reaching functional vision involves improving UCVA, BCVA, and corneal irregularity so that patients are less dependent on contact lenses to achieve better quality of vision. Custom PRK is a predictable and effective technique to achieve remodeling of the corneal surface and rehabilitation of refractive impairment. CXL is capable of stabilizing the corrected cornea and inhibiting keratoconic progression.

In 2007 a study was done by Kanellopoulos and Binder on patient with bilateral, progressive Keratoconus underwent UVA irradiation (3 mW/cm for 30 minutes) after topical 0.1% riboflavin drops over a deepithelialized cornea. Twelve months later, a topography-guided photorefractive keratoectomy (PRK) was performed in 1 eye for a refractive error of -3.50 -4.00 x 155 by using an attempted treatment of -2.50 -3.00 x 155. the results was In the treated left eye, the UCVA after the UVA CCL improved from 20/100 to 20/80, and the BSCVA improved from 20/50 to 20/40. Eighteen months after the topography-guided PRK, the UCVA was 20/20, and the BSCVA was 20/15, with a refractive error of Plano -0.50 x 150. The cornea was clear, and the endothelial cell count remained unchanged. The untreated right eye continued to progress during the same period[17].

However, a two-step procedure with CXL followed by PRK after a 1-year interval has three major limitations. First, the stiffened, crosslinked corneal tissue is removed by PRK in an additional step, potentially decreasing the possible benefits of CXL. Second, the efficacy of this approach is limited because the corneal ablation rate could be different in crosslinked versus virgin corneas. The response of cross linking stromal corneal tissue to excimer laser ablation not will known (This could lead to unpredictable refractive results). Third, there is an increased possibility of post-PRK haze formation because 6 months after CXL, the anterior stroma is

repopulated by new keratocytes. Due to these aspects, we consider custom PRK immediately followed by CXL as the best option for treating keratoconus. The main advantage of this technique is that the ablation does not interfere with the already crosslinked part of the cornea. On the contrary, crosslinking of the ablated stroma offers the advantage of depopulating keratocytes and reducing the possibility of haze formation. The ablation is capable of reshaping the corneal surface, and CXL then halts progression of the disorder[18].

In this study PRK treatment was planned based on the patient's corneal thickness. Limited treatments of up to 50 µm were performed; the ablation depth was mapped out by modifying the target correction. CXL treatment was performed immediately following the ablation we demonstrated a rapid and significant improvement in UCVA and BCVA. we found that 95% of UNCVA are equal to pre-op BCVA or gained 1 or more lines and only 5% Lost 1 or more lines there was no keratoconic progression in all patients. Topographic picture got improved in 55% of the eyes, 36% of the eyes had significant change and 9% of the eyes had minor change.

Topographic evaluation showed marked improvement of irregularity (Figure 5), including significant reduction of corneal coma-like aberrations. As regard astigmatism about 59% of the eyes had Astigmatism by K-Reading within 1.0D and 68% of the eyes had Astigmatism by Refraction within 1.0D. Non of the eyes had > 2.0D. A reduction in topographic astigmatism was observed after 12 months' follow-up, with no significant improvement in visual outcomes.

Corresponding to the positive change of UCVA and BCVA, we found a reduction of myopia. Probably due to regularization of the cornea, subjectively accepted cylinder was higher after CXL+PRK in many cases. The underlying reason for the positive changes in visual acuity and refraction is the observed corneal flatting, as shown by the reduction of maximum and minimum keratometry values. Complications were found in one of 22 eyes. This eye lost one line of BCVA due to prolonged central Descemet's folds and stromal edema up to 10 weeks.

Conclusion

Based upon our 1-year follow-up of 22 eyes we can conclude that Simultaneous PRK + CXL is a very effective way to stop progression of early KC, it improves patient visual acuity and quality of vision provided that we adhere to the selection criteria of that we recommend the corneal thickness not les than 450 micron, the ablation depth not more than 50 micron, K reading not more than 51,sepherical equivalent can be corrected by ablation of 50 micron,

Topographic picture correlated with early keratoconus and the BCVA not less than 20/25.

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