Corneal crosslinking with riboflavin and ultraviolet light before or after subepithelial keratectomy laser-assisted (LASEK) in patients with thin corneas.

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Purpose: To report the results obtained performing Corneal Crosslinking with ultraviolet light A and riboflavin before or after subepithelial keratectomy laser-assisted (LASEK) in patients with thin corneas.
Location: Vejarano Laser Vision Center, Metepec, Estado de México, México.
Method: Retrospective study observational of a series of cases, 33 eyes (17 patients) preoperative studies are performed for performing refractive surgery who underwent LASEK treatment and later Crosslinking or Crosslinking an later LASEK. It is reported the results and experience obtained with the combination of both valuing sphere, cylinder, spherical equivalent, corneal hysteresis, corneal relaxing factor and intraoperative or postoperative complications.
Results: The monitoring period between the first and the second procedure was of 4 months and after the second procedure was of six months. The mean corneal hysteresis (CH) and the mean corneal resistance factor (CRF) were significantly higher than the post-operative values after LASEK regardless of the order of carrying out the crosslinking. The corneal crosslinking increases the CH and CRF but not in a meaningful way. The realization of crosslinking posterior to LASEK is associated with increased incidence of corneal haze. The crosslinking does not affect corneal cylinder values but it does affect in the field in a range of average increase of +0.43 Dioptres.
Conclusions: Changes are confirmed in CH and CRF and after the procedure of LASEK there is a disturbance in the biomechanical corneal, which improves but not significantly with the yield of crosslinking. In case of combining both techniques is advisable to initiate with the crosslinking in order to avoid haze.

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INTRODUCTION:

The subepithelial keratectomy Laser-Assisted (LASEK) is a procedure more safer with less incidence of haze, than the photorefractive keratectomy (PRK),it has no problems related with flap and is the technique of choice for mild to moderate corrections in cases of thin corneas,recurrent erosions or predisposition to trauma, (martial arts, military activities, sports ...), curved or flat corneas. [1,2].

Ectasia post-refractive surgery is one of the most feared complications of refractive surgery. The biggest risk factors for corneal ectasia are large ablations, low residual stromal thickness, retreats and presurgical abnormal corneal topography [2,5,6]. reducing the strength of corneal biomechanics is an essential element in the chain of events that lead to iatrogenic corneal ectasia post-refractive surgery [2,3,4]. Biomechanically surface procedures are less invasive for corneal, in case of ablation because of myopia[9].

The corneal crosslinking with riboflavin and ultraviolet A (UVA) is a method that increases the biomechanical stability of the cornea, inducing reinforcements between and within the corneal fibers, using riboflavin and UVA light as photo mediators [3.4], so that stops and returns partially the progress of iatrogenic keratectasia refractive surgery, increasing the biomechanical stability of the cornea [2.3]. After performing the crosslinking, is shown an increase in the corneal rigidity and the values of corneal hysteresis values and resistance factor remain stable over time.[10].

The Ocular Response Analyzer (ORA) is an instrument capable of measuring the viscoelastic properties of the cornea [7.8]. According to the factory corneal hysteresis (CH) is the viscous damping corneal tissue or the capacity of energy absorption. The parameter corneal resistance factor (CRF) is a measure of the cumulative effects of viscous damping and elastic resistance of the cornea [8].Refractive surgery alters biomechanical properties of the cornea, which apparently have an important role in treatment results,being the values of CH and CRF which is significantly lower with a refractive procedure suggesting that the creation of the flap,ablation or both, alter the ability of the cornea to absorb or dissipate energy [7, 8]. Keratoconic corneas have low values of CH and CRF, with a high tendency to develop an ectasia-post LASIK[7].

This study aims to show the results obtained in patients with thin corneas, CH and CRF low, no medical history of keratoconus who are submitted to refractive surgery and combined with the realization of crosslinking to increase the biomechanical properties of the cornea and prevent thus the occurrence of post-surgical ectasia, ensuring good long-term results.

PATIENTS AND METHODS:

Medical records of all patients who underwent between January 2008 and June 2009 the LASEK procedures and Crosslinking or Crosslinking corneal and LASEK, in Laser Vision Center Vejarano Institute for having a history of of thin corneas, high defect for corneal thickness (considering minimum residual stromal bed 280 microns) and low values of CH and CRF.

Pre and post operative examinations.

All patients, prior to any of the two procedures were performed automated and subjective refraction, corneal topography and pachymetry (Pentacam HR ®, OCULUS Optikgeraete GmbH), CH and CRF by ORA,which was taken to verifying the readings showing symmetrical peaks in height and width. With these results was examined under slit lamp and fundus under dilation. In patients with a medical history of contact lens wear, patients had a minimum rest period of 15 calendar days before taking measurements.

These same measures are taken after the third month of the first procedure and before a second procedure (LASEK or Crosslinking), which are also repeated after the second procedure between the sixth month of the last procedure.

Surgical Technique

All procedures LASEK were performed by any of the authors, operating room temperature between 18 and 21 ° C, humidity between 30 and 40%. It uses the same excimer laser (Esiris Schwind) nomogram propre is used to program the laser, always with optical zones of 6.5 mm, 5 and 6.5 in case of ablations in multizone.

LASEK technique, was used 20% alcohol solution for 20 seconds, was performed complete removal of the epithelium in all cases, placing contact lens. In any type of ablation was used mitomycin-C 0.02% for 20 seconds for ablations up to 50 microns , 40 seconds for ablations between 51 and 99 microns. To greater ablations than 100 microns the time of Mitomycin-C was one minute, with subsequent washing with balanced salt solution and placement of therapeutic contact lens.

Crosslinking corneal procedure is used, vitamin riboflavin 5 phosphate 0.1%, which is protected against light during the entire procedure. The corneal epithelium is removed completely in an optical zone of 9 mm, then 20% of application of alcohol for 20 seconds. It starts to apply the isoosmolar solution every 3 minutes during the first 30 minutes. After the eye is irradiated for 30 minutes with ultraviolet light, at a working distance of 5 cm with an irradiance of 3 mW/cm2, corresponding to a dose of 5.4J/cm2 surface. During irradiation is instilled isotonic 0.1% riboflavin every five minutes. After treatment is placed therapeutic contact lens.
Patients are reviewed at three and six months after the treatments.

RESULTS.

It brings together a total of 33 eyes (17 patients) that were divided into two groups: 22 eyes (12 patients) Group No. 1, patients who underwent LASEK and at the third month corneal crosslinking. 5 patients (9 eyes) Group No. 2, patients who underwent corneal crosslinking and the third month LASEK.

In Group # 1, 31.81% of the eyes had an equivalent spherical error to -2.0 diopters (D), 36.36% between -2.0 and -4.0 D, between -4.0 and 22.72% and 9.11%-6.0d D - 6.0 over, pachymetry half 498 ± 18 microns. In Group No. 2, 22.22% of eyes had a spherical equivalent error to -2.0 D, 33.33% between -2.0 and -4.0 D, 33.33% between -4.0 and -6.0 D and 11.12% higher than -6.0 D, half pachymetry 500 ± 20 microns.

Table No. 1 shows the average sphere, cylinder, equivalent spherical, CH and CRF preoperative and postoperative prior to performing a second procedure, ie (it means) Crosslinking in Group No. 1 and No. LASEK in Group 2.

Table No. 1. Refraction Pre and post surgical				
	Group 1		Group2	
Presurgical				
Refraction (D)	Media ± DE	Rank	Media ± DE	Rank
sphere	-2.19 ± 3.3	-9.0 a +1.75	-3.20 ± 1.5	-7.75 a +0.25
cylinder	-3.2 ± 1.98	-7.0 a -0.7	-1.1 ± 0.86	-3.25 a 0
EE	-3.83 ± 2.96	-9.87 a -0.125	-3.67 ± 1.46	-7.87 a -1.12
CH	7.3 ± 1.98	4.8 – 10.1	7.5 ± 1.86	4.7 – 9.9
CRF	11.07 ± 1.92	8.1 – 13.4	10.9 ± 1.84	7.9 – 12.1
post Surgical				
sphere	-0.22 ± 0.8	-1.25 a +1	-2.80 ± 1.3	-7.25 a +0.25
cylinder	-1.2 ± 1.01	-3.0 a 0	-1.21 ± 0.7	-3.0 a 0
EE	-0.86 ± 1.2	-2.5 a + 2.5	-3.28 ± 1.5	-7.3 a -0.75
CH	5.3 ± 1.04	4 – 6.5	8.0 ± 1.52	5 – 10.1
CRF	7.5 ± 1.38	6 – 9.1	11.5 ± 1.74	7.9 – 12.5
DE = Standard deviation.EE = Spherical equivalent.CH = Corneal hysteresisCRF. Corneal resistance factor				

In group No.1

There were no intraoperative complications, the 9.11% menor hypocorrection or equal to-1.25D, there is a significant decrease in CH and CRF ($p < 0.001$) after LASEK. In group # 2, after crosslinking, there is an average improvement of sphere of +0.43 D ($p < 0.04$),there is no significant changes in the value of the cylinder relative to preoperative value. The values of CH and CRF, have improved in all patients evaluated but not significant ($p < 0.3$) the difference respect the values prior to the execution of Crosslinking. In group No. 2 are not recorded intraoperative or postoperative complications.

Between 3 and 6 months (on average the 4th month), the patients in each group underwent a second procedure, the results are shown in Table No. 2.

Table No. 2. Refraction Pre and post surgical 2° Procedure				
	Group 1		Group 2	
Presurgical				
Refraction (D)	Media ± DE	Rank	Media ± DE	Rank
sphere	-0.22 ± 0.8	-1.25 a +1	-2.80 ± 1.3	-7.25 a +0.25
cylinder	-1.2 ± 1.01	-3.0 a 0	-1.21 ± 0.7	-3.0 a 0
EE	-0.86 ± 1.2	-2.5 a + 2.5	-3.28 ± 1.5	-7.3 a -0.75
CH	5.3 ± 1.04	4 – 6.5	8.0 ± 1.52	5 – 10.1
CRF	7.5 ± 1.38	6 – 9.1	11.5 ± 1.74	7.9 – 12.5
Post surgical				
sphere	0.20 ± 0.97	-1.25 a +1.75	-0.35 ± 0.9	-1.50 a +1.0
cylinder	-1.42 ± 0.89	-3.0 a -0.5	1.05 ± 1.12	-2.75 a 0
EE	-0.53 ± 0.86	-1.5 a +0.87	-0.76 ± 1.3	-2.0 a +0.75
CH	5.68 ± 0.61	4.9 – 6.3	5.6 ± 1.2	4 – 6.8
CRF	8.1 ± 1.3	3.7 – 6.9	5.2 ± 1.42	4.5 - 7
DE = Standard deviation.EE = Spherical equivalent.CH = Corneal hysteresisCRF. Corneal resistance factor				

Once the second procedure, the sixth month clinical records were reviewed and it is shown that for Group No. 1, it is observed that the values of CH and CRF increased but not significantly (p> 0.06), also observed as the constant one hipermetropización reflected in an increase in mean sphere D +0.42 (p <0.06), with deterioration of visual acuity in 13.62% (3 eyes) at the expense of the sphere situation observed in the first procedure for group No. 2. Turn on the group No. 1, is presented in the postoperative haze in 7 patients (31.81%) with deteriorating visual acuity and glare feeling symptomatic. In group No. 2, not recorded complications, only one case of undercorrection. There were no cases with haze. The CH and CRF values after LASEK, show variations similar to those presented in the pre-and post-surgical first procedure for the first group. In both groups at 6 months, CH and CRF values show no significant changes in both groups.

DISCUSSION

In the long term, post-surgical corneal ectasia remains the most feared complication of refractive surgery. Because the incidence of this complication after LASIK procedures, along with the understanding of the biomechanics of the cornea, have made that many refractive surgeons came back to techniques of surface ablation [11].

In order to prevent this complication in this study is added to the surface method embodiment, the application of corneal crosslinking with riboflavin and UVA with the purpose to exploit the benefits of this process and to increase corneal rigidity and maintain values of CH and CRF stable over time.[10].

As the previous studies (7,8,9,13,14,) the values of CH and CRF decreased significantly after refractive surgery, but is remain stable over time, once the cross linking [10, 12,] also decreased of hysteresis are not correlated with the quantity of tissue with ablation [13],at least six months after surgical refractive procedure. The decrease of CH and CRF after LASEK procedure, is the same whether or not the patient has a procedure of cross linking.

By comparing the order in performing both procedures there is no significant difference in outcome in refraction, but it is noteworthy that there is a constant after the completion of crosslinking, there is an increase in the value of the mean sphere of +0.43 D (p <0.04) in which there is a variation in the good refractive result when this procedure is done after LASEK. Additionally, the rate of complications such as haze was higher in the group who underwent LASEK first and then crosslinking in the group that performed the same procedures in reverse order, although in the amount of the sample is not possible to establish statistically significant difference, it is well known that the incidence of haze in this case was 31.81%, and there is a significant increases when the crosslinking is performed after LASEK.

In conclusion: prevention of ectasia post surgical induced, is the best strategy and is neccesary to do an special emphasis on recognizing corneas at risk before

surgery [5,6]. The combination of crosslinking and LASEK in thin corneas and / or lower CH and CRF, is one of such strategies that combines the benefits of crosslinking on corneal biomechanics with good refractive results of LASEK. For the notorious frequency of haze, presented in combination LASEK - Crosslinking, in corneas suspicious is always recommended perform LASEK before crosslinking. Other prospective and comparative studies is neccesary performed to determine whether these findings have clinical relevance.

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