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The effect of Iso-osmolar riboflavin 0.1% on corneal thickness in corneal collagen cross-linking combined ultraviolet A irradiation

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ABSTRACT

Purpose: To monitor central thickness changes prior to corneal collagen cross-linking combined ultraviolet A irradiation, using iso-osmolar riboflavin 0.1%. *Method:* Corneal thickness was measured pre-operatively before epithelial removal. Corneal thickness following epithelial debridement was calculated via subtracting 50 µm. Iso-osmolar riboflavin 0.1% was instilled into the eye every two minutes for ten minutes. Corneal thickness before and after instillation of iso-osmolar riboflavin was compared using Wilcoxon

SPSS test. *Results:* 34 eyes of 17 patients were included in this study. The mean spherical refractive error for all participants was -2.14 ± 1.95 D and the mean astigmatism was -1.35 ± 1.04 D. Measured pachymetry was found significantly higher than calculated pachymetry for all participants. In female subjects, the difference between calculated and measured pachymetry was not statistically significant, when bed hydration was and was not performed, *p*-values were 0.508 and 0.93 respectively. In male subjects, the difference between calculated and measured pachymetry was statistically significant for all the eyes. *Conclusion:* Iso-osmolar riboflavin can cause a temporary increase in corneal thickness. However, when corneal swelling is desired in thin corneas, use of hypo-osmolar riboflavin may be more effective in preventing any subsequent damage.

Keywords: Corneal collagen cross-linking (CXL), Corneal thickness, Pachymetry, Iso-osmolar riboflavin.

1. INTRODUCTION

Corneal cross-linking has been developed to be the therapeutic option which changes the course of keratoconus by stopping its progression (Alkharashi et al., 2014, & Onofrey et al., 2005). However, the use of this procedure is guarded by many factors, most importantly is a corneal pachymetric reading of more than 400 µm at its thinnest point. Photochemical CXL was developed at the University of Dresden in 1998. It induces cross-linking of corneal collagen through combining riboflavin (vitamin B_2) and ultraviolet A irradiation. Corneal collagen cross-linking (CXL) significantly increases corneal stiffness. This effect occurs immediately after treatment (Hafezi, 2011, Koller et al., 2009). A major concern in CXL is the photochemical damage caused by UV exposure. Photochemical damage consists of damage to the endothelial cells, epithelial stems cells and corneal nerves. To prevent endothelial cell damage, the preoperative corneal thickness should be 400 µm or more at the thinnest location. Corneal nerves are damaged following CXL however, complete regeneration occurs within six months after CXL (Nasrollahi K et al., 2015; Mrochen M et al., 2007; Soeters N, Tahzib NG, 2015).

Caporossi et al., 2010 reported long-term stability of keratoconus after CXL without relevant side effects. Improvement in uncorrected and best-spectacle corrected visual acuity was also noted.

Caca et al., 2013 also conducted a study on eleven eyes of eleven patients with progressive keratoconus and corneal ectasia. This study concluded that the use of isotonic riboflavin solution without dextran yielded stability in corneal thickness with mild swelling during the procedure.

On the other hand, Wu H et al., 2014 reviewed fifteen eyes with progressive keratoconus. Corneal thickness was monitored during corneal collagen cross-linking with dextran-free hypo-osmolar riboflavin solution. Wu concluded that using hypo-osmolar riboflavin solution results in stability of keratoconus twelve months after surgery. The same findings were also observed by Nassaralla et al., 2013 and Kaya et al. 2012. Nassaralla also reported that the effects of hypo-osmolar riboflavin solution are transient and short acting.

Previous studies suggest that CXL is a safe and effective option in the treatment of progressive keratoconus. Also all studies agreed that the effects of both solutions are temporary and short acting.

2. MATERIALS AND METHOD

Seventeen participants with any degree of keratoconus who underwent Photorefractive keratectomy (PRK) combined CXL were included in this prospective study. Those with incomplete data, severe dryness, ocular infections, collagen vascular disorders, or any systemic disease that has ocular manifestations were excluded. Participants whose corneal thickness is less than 400 µm were excluded. Pregnant and nursing female participants were also excluded. Patients with advanced keratoconus, in which Vogt striae were present are not fit for CXL and hence excluded. All the procedures were approved by the Research Ethics committee of the university by this code CAMS 86-36/37.

Pachymetry was performed before epithelial removal and after instillation of iso-osmolar riboflavin 0.1%. Central corneal thickness was measured by the same examiner using Pacscan^{TM} 300P ultrasound pachymeter. Three pachymetric readings were taken for each eye and the average reading was calculated. 50 µm of the corneal epithelium was removed through trans-epithelial Photorefractive keratectomy (PRK) using Schwind Amaris 750S laser system. Bed hydration was performed on the left eye only for all the participants. After epithelial debridement, the patient was moved for CXL. Iso-osmolar riboflavin 0.1% was instilled into the eye every two minutes for ten minutes. Corneal thickness was measured after riboflavin instillation and before UV exposure. Three readings were taken and average was calculated for each eye. Ultraviolet A irradiations were projected into the eye for six or three minutes depending on the degree of keratoconus. Corneal thickness measurements before and after riboflavin instillation were compared. Corneal thickness following epithelial debridement was calculated through subtracting the amount of epithelium removed from the average preoperative pachymetric reading.

Statistical package for social science (SPSS) program version 20.0 was used for the statistical analysis. Wilcoxon test was used to compare corneal thickness before and after instillation of riboflavin 0.1%. A p-value of less than 0.05 was considered to be significant at 95% confidence interval.

3. RESULTS

In this study, 34 eyes of 17 patients were evaluated. 10 participants were females of mean age 29.4 ± 5.32 years and 7 participants were males of mean age 30.14 ± 5.52 years. The mean spherical refractive error for all participants was -2.14 ± 1.95 D and the mean astigmatism was -1.35 ± 1.04 D. Mean spherical refractive error for female subjects was -2.51 ± 2.27 D with -1.46 ± 1.12 D error of astigmatism. Male participants had a mean spherical refractive error of -1.40 ± 1.02 D and astigmatism of -1.12 ± 0.93 D (Figure 1). All subjects had corneal thickness of 400 μm or more.

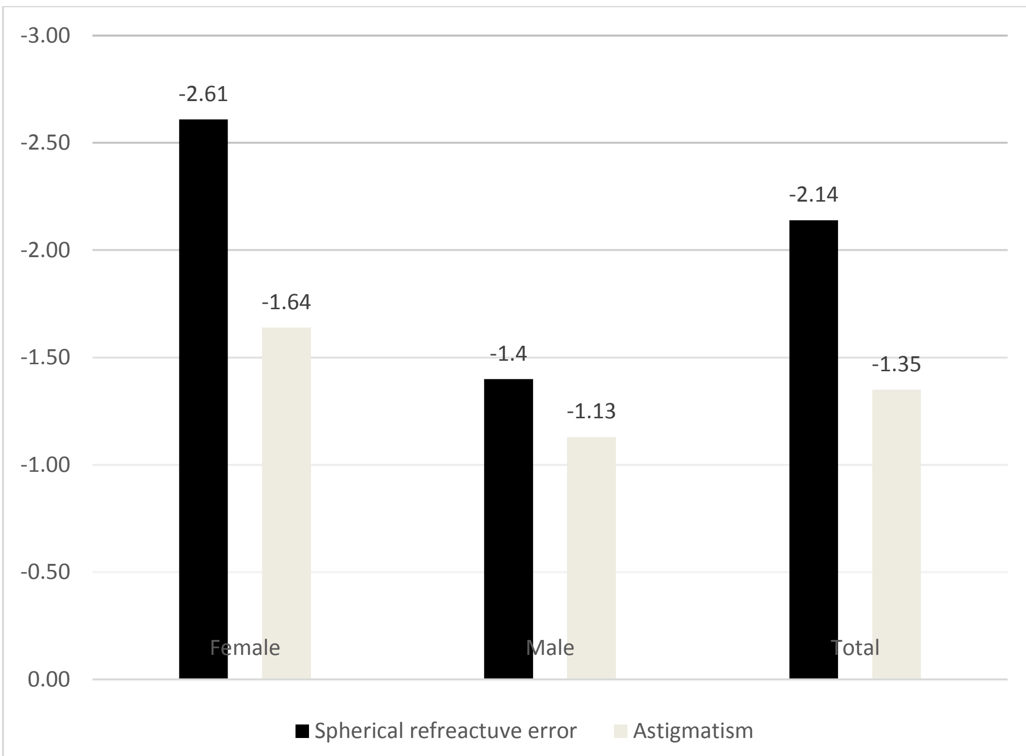

Figure 1 Mean preoperative refractive error.

The mean corneal thicknesses before instillation of iso-osmolar riboflavin for males and females were 407.7 ± 29.5 μm and 427.25 ± 29.9 μm respectively. Corneal thicknesses after the use of riboflavin were 448.24 ± 28.7 μm and 440.88 ± 30.2 μm for males and females respectively.

On observation of central corneal thickness during CXL procedure, it was evident that iso-osmolar riboflavin affects corneal thickness. Corneal thickness was found to be higher following the instillation of iso-osmolar riboflavin. However, this effect was not documented in all participants. Measured pachymetry was significantly higher than calculated pachymetry for all participants, with p-value of less than 0.05 (Figure 2).

In female subjects, the difference between calculated and measured pachymetry was not statistically significant for all eyes. When bed hydration was and was not performed, p-values were 0.508 and 0.93 respectively. In male subjects, the difference between calculated and measured pachymetry was statistically significant for all eyes (p-value of 0.018).

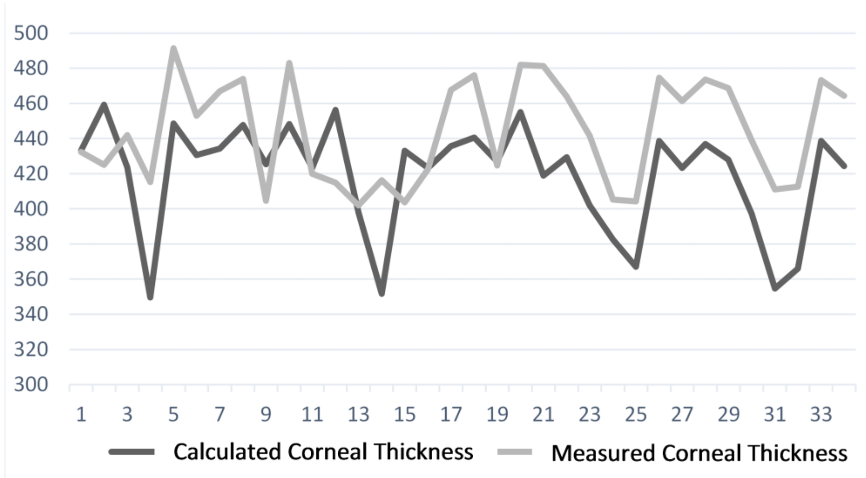

Figure 2 Calculated and Measured Corneal thickness after instillation of iso-osmolar riboflavin 0.1% solution.

4. DISCUSSION

Our results suggest that instillation of iso-osmolar riboflavin into the eye prior to UV exposure causes a statistical significant increase in corneal thickness. Gender differences were evident in the current study. Female subjects showed no statistical significant increase in corneal thickness. Male subjects have showed a significant increase in corneal thickness upon instillation of the iso-osmolar riboflavin. The application of bed hydration had no effect on corneal thickness measurements in all participants.

This study is in agreement with the previous studies conducted by Caca et al., 2014 and Donbaloğlu et al., 2014. The two studies have showed that the use of isotonic riboflavin solution resulted in mild corneal swelling during the procedure. However, none of these studies have considered gender differences.

5. CONCLUSION

Iso-osmolar riboflavin may cause a temporary increase in corneal thickness, although gender differences were noted. However, when corneal swelling is desired in thin corneas, using hypo-osmolar riboflavin may be more effective in preventing any subsequent damage. The use of bed hydration has no effect on corneal thickness.

Conflict of Interest

The authors declare no conflict of interest related to the present manuscript.

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