Assessment of corneal higher order aberrations before and after corneal collagen cross-linking in patients with keratoconus

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

"هُوَ الَّذِي جَعَلَ لَكُمُ اللَّيْلَ لِتَسْكُنُوا فِيهِ وَالنَّهَارَ مُبْصِرًا ۚ إِنَّ فِي ذَٰلِكَ لَآيَاتٍ لِّقَوْمٍ يَسْمَعُونَ (67)"

سورة يونس, آية 67

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List of abbreviations

BAC	Benzalkonium chloride
BSCVA	Best spectacle corrected visual acuity
CCD	Charged couple device
CCT	Central corneal thickness
CXL	Collagen cross-linking
D	Diopter
HOA	Higher order aberration
HPMC	Hydroxypropyl methylcellulose
HS	Hartmann- Shack
J	Joule
LOA	Lower order aberration
RMS	Root mean square
ROS	Reactive oxygen species
SA	Spherical aberration
SD	Standard deviation
TE-CXL	Transepithelial collagen cross-linking
UCVA	Uncorrected visual acuity
UVA	Ultra-violet A
VA	Visual acuity
W	Watt
WAs	Wave aberrations
WF	Wave-front

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Abstract

Abstract:

Purpose: This study aimed to assess the short term effect of corneal collagen crosslinking on higher order aberrations of cornea in patients with keratoconus using corneal topography.

Patients and Methods: the study was a prospective cohort study that was conducted in a private specialized eye hospital on 40 eyes of 28 keratoconus patients. Each patient was fully assessed preoperatively including doing corneal topography using Pentacam® HR. Transepithelial accelerated CXL was done to all patients. Postoperative corneal topography was done at six months and data was retrieved and analyzed.

Results: RMS HOA recorded a higher mean value preoperatively, with an extremely statistically significant difference (p=0.00). All elements of HOAs showed lower postoperative values except for trefoil 30º. The difference was statistically significant in comma 0º, comma 90º, spherical aberrations and fifth order comma 90° (p=0.026, p= 0.003, p=0.005, and p=0.001 respectively).

Conclusion: Transepithelial corneal collagen cross-linking improves corneal higher order aberrations. The maximum effect of the procedure is on comma 0º, comma 90º, spherical aberrations and fifth order comma 90° elements.

Key words: keratoconus, corneal collagen cross-linking, higher order.aberrations.

Introduction

Introduction

The cornea represents a transparent avascular connective tissue that has a primary infection and structural barrier function. With the overlying tear film, it forms the anterior refractive surface of the eye optical system **(Derek and Tim, 2011).**

The adult human cornea has an average horizontal diameter of 11.5 to 12.0 mm with the vertical diameter being 1.0 mm less. Central thickness is about 0.5 mm and gradually increases toward the limbus. Its shape is prolate -flatter in the periphery and steeper centrally- which creates an aspheric optical system **(Rüfer et al., 2005)**.

Both shape and curvature of the cornea are governed by the intrinsic biomechanical structure and extrinsic environment factors **(Muller et al., 2001)**. The human cornea consists of six layers: epithelium, Bowman membrane, stroma, Dua's layer, Descemet membrane and endothelium.

The epithelium is composed of nonkeratinized, stratified squamous epithelium that is 4 to 6 cell layers thick. The most superficial cells form a mean of 2 to 3 layers of flat polygonal cells, then the suprabasal or wing cells layer which is 2 to 3 cells deep with less flat cells **(Farjo et al., 2008)**. The deepest one is

the basal layer, which comprises a single cell layer of columnar epithelium. Beside the stem cells and transient amplifying cells, basal cells are the only corneal epithelial cells capable of mitosis. The basal cells secrete type IV collagen and laminin forming the basement membrane **(Wiley et al., 1991)**.

Bowman layer is an acellular condensate of the most anterior portion of the stroma. It helps the cornea to maintain its shape. It cannot regenerate **(Derek and Tim, 2011)**.

The stroma represents the main bulk of the cornea attributing to 80-85% of its thickness. It is formed of collagen fibers that are arranged in parallel bundles called fibrils, which are packed in parallel arranged layers or lamellae. There is an average of 200 to 250 distinct lamellae, lying at right angles relative to fibers in adjacent lamellae. This special arrangement is the main contributor to corneal transparency **(Maurice, 1971)**. The fibrils are composed of type I collagen in a heterodimeric complex with type V collagen. The fibrils are surrounded by specialized proteoglycans, consisting of keratan sulfate or chondroitin sulfate/dermatan sulfate side chains **(Fini and Stramer, 2005)**.

Descemet membrane is secreted by endothelial cells.

The endothelium is a single layer of flat polygonal cells tightly adherent to each other. It is responsible for keeping the stroma in a relative deturgescence state through the action of their Na,K-ATPase pump **(Stiemke et al., 1991).**

The cornea exhibits elastic and viscous properties, which give it the quality of hysteresis. Elasticity refers to the ability of a substance to deform reversibly under stress. Viscous materials, on the other hand, flow when an external shear force is applied and do not regain their original shape when the force is removed. Viscoelastic materials exhibit characteristics of both viscosity and elasticity, resulting in energy dissipation when stress is applied. The energy lost in this dissipation process is called hysteresis **(Kotecha, 2007)**.

Any disruption of the corneal fiber network can result in decreased structural integrity of the cornea, leading to decreased vision. One of the diseases that exhibit these pathological changes is keratoconus.

Keratoconus is a progressive ectatic disorder. It is usually a bilateral, asymmetric, non-inflammatory degeneration which results in central and paracentral thinning. The degeneration occurs at the level of the chemical composition of the material of corneal stroma, leading to increased strain, and redistribution of

stress **(Dauwe et al., 2009)**.

Etiological factors that may contribute to the disease include eye rubbing, atopy, genetic factors and contact lens microtrauma. The disease may be present solely or in association with various ocular or systemic conditions **(McMonnies, 2008)**.

The onset of the disease starts at puberty with progression for 10-20 years then the condition tends to be more or less stable. Keratoconus affects about 1 in 1750 individuals, and is considered the commonest corneal dystrophy. It has no sex predilection and affects all races **(Rabinowitz, 1998)**.

Keratoconic corneas have normal collagen composition, distribution, and packing, but the native collagen network organization is disrupted **(Meek et al., 2005)** . Irregularities in the collagen network leads to distortion of refractive function resulting in high myopia and irregular astigmatism. There is also high levels of collagenolysis, loss of keratocytes, reduced collagen cross-links, and significantly weakened stress-versus-strain responses in keratoconic corneas **(Zimmermann et al., 1988)**.

One of the important modalities in keratoconus treatment that is gaining more and more importance is corneal collagen

cross-linking (CXL). It is proposed that it slows, stops or even to a limited extent reverses the pathology underlying keratoconus **(Sporel et al., 1998)**.

Corneal collagen cross-linking is a physiological process that occurs in aging corneas via natural enzymatic pathways such as transglutaminase and lysyl oxidase. In 1997, Spoerl and Seiler developed photochemical CXL with Riboflavin (vitamin B2)/Ultraviolet A (UVA) (370 nm) at the University of Dresden **(Sporel et al., 1998)**.

This procedure induces physical cross-linking of collagen by Riboflavin absorbing UVA acting as a photo sensitizer leading to production of free radicals (oxygen singlets), activating the natural lysyl oxidase pathway. Riboflavin absorption of UVA acts as a shield that protects the deeper ocular tissues as endothelium, lens and retina from the damaging effects of UVA **(Wollensak et al., 2003)**.

The exact location of the crosslinks at a molecular level is not determined up till now. The distance between collagen fibrils is too far to form bonds, so it is unlikely that they are formed between them **(Hayes et al., 2013)**.

Since corneal collagen and protoeglycan cross-links cannot