Evaluation of Posterior Corneal Surface in Keratoconus Patients after Corneal Cross-Linking by Pentacam

Thesis

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Rami Abdallah Kamel Hassouna

List of Contents

List of Tables

List of Figures

List of Abbreviations

Abb.	Full term
BCDVA	Best corrected distance visual acuity
BFS	Best fit sphere mode
BFTE	Best fit toric ellipsoid mode
CKI	Center Keratoconus-Index
CXL	Corneal Cross-linking
DALK	Deep lamellar keratoplasty
DALK	Deep Anterior Lamellar Keratoplasty (
ICRS	Intracorneal ring segments
IHA	Index of height asymmetry
IHD	Index of height decentration
ISV	Index of surface variance
IVA	Index of vertical asymmetry
KC	Keratoconus
Kf	Flat Keratometry
Kmax	Maximum keratometry
Ks	Steep Keratometry
MMP-2	Matrix metalloproteinase-2
PK	Penetrating keratoplasty
PMMA	Polymethyl methacrylate
SE	Spherical equivalent
UVA	Ultraviolet A

INTRODUCTION

Keratoconus is a non-inflammatory bilateral progressive but asymmetrical disease. Described as corneal ectasia, thinning, gradual corneal protrusion and irregular astigmatism[1]. It usually starts during puberty with 75% of cases diagnosed before the age of 25 years[2].

Pentacam HR has helped us to detect early topometric, pachymetric aberrometric, and posterior corneal changes, in subclinical and definite Keratoconus cases hence facilitating early diagnosis.

Corneal cross-linking has been described as the only modality in halting the disease progression over the past decade[3], by using Riboflavin eye drops and UVA light this creates bonds between corneal collagen fibers in the stroma[4]. Cross-linking has been shown to generate various effects in the cornea such as increased stiffness, changes in biomechanical and bioelastic behavior of corneal collagen tissue and different visual, refractive, topographic and abberometric changes[5]. Cross-linking has been proving it's efficacy in stabilizing ectatic corneas by changing anterior keratometry readings at the keratoconus apex (K max) hence flattening the cornea[6]. Few studies have been evaluating its effect on the posterior corneal surface.

Aim of the Work

To evaluate the posterior corneal surface changes in keratoconus cases after 6 months following treatment with corneal collagen cross-linking using Pentacam (Oculus, Germany).

Chapter 1
ANATOMY OF THE CORNEA

Our cornea forms the anterior portion of the outer layer of the eye, it has a dual function; protecting the inner contents of the eye and providing about two thirds of the eye's refractive power[7]. The Cornea is a transparent avascular tissue, it consists of three cellular layers the epithelium, stroma and endothelium and four interfaces the basement membrane of the epithelium, Bowman layer, Dua's layer and Descmet's membrane. The average size of the human cornea is 11–12 mm horizontally and 9–11 mm vertically. It is approximately 0.5 mm thick, and the thickness increases gradually toward the periphery[8]. The shape of the cornea is prolate; flatter in the periphery and steeper centrally thus creating an aspheric optical system[9].

- **The Epithelial Layer:**

A non-keratinized, stratified squamous epithelium that is 4 to 6 cell layers thick (40 um to 50 um)[10]; two to three rows of flat polygonal cells, two to three rows of wing cells and a monolayer of columnar basal cells that adheres to its basement membrane by a hemidesmosomal system. Basal cells are the only corneal epithelial cells that are capable of mitosis[11]. Corneal epithelial cells have an average lifespan of 7 to 10 days[12] it undergoes apoptosis and desquamation. The basement membrane of the epithelium cells measures around 0.05 um and

formed of type IV collagen and laminin. It is produced by the basal columnar layer of epithelium.

- **The Bowman Layer:**

Is located in the anterior part of the stroma is a condensation of the stroma rather than a true membrane, it is acellular and when disrupted it will not regenerate[3].

- **The Corneal Stroma:**

Is the cornea's thickest part, it represents 90% of its thickness. Its main function is the maintenance of the corneal shape, physiologic hydration, and thus transparency[13]. It is composed of extracellular matrix; proteoglycans, stromal cells; keratocytes and collagen fibers. These collagen fibers are arranged in parallel bundles called fibrils and these fibrils are packed in parallel arranged lamellae. The stroma contains 200 to 250 distinct lamella, each arranged at right angles relative to fibers in adjacent lamellae. This highly organized network reduces light scatter thus contributes to the transparency and mechanical strength of the cornea[14]. Collagen fibrils are composed of type I and type V collagen mainly, and they are surrounded by proteoglycans which regulate hydration of the cornea[15]. Keratocytes are the main cell type of the stroma and their function is to produce components of the extracellular matrix.

- **Dua's Layer:**

Recent studies in the United Kingdom have discovered a new layer in the cornea which they called Dua's Layer after its main discoverer Prof. Harminder S. Dua of Nottingham University[16]. It is found between the stroma and the Descmet's membrane, its main significance is in endothelial Keratoplasty. After performing various lamellar corneal surgeries. Dr. Dua hypothesized that another layer of the cornea might exist. To confirm this, he and his colleagues simulated corneal transplants by injecting air into corneal grafts to carefully separate the distinct layers of the cornea. Then, they closely examined the layers using electron microscopy. They found that the separation of layers that yielded the strongest tissue was not between the stroma and the DM, as believed. Rather, the ideal separation was between the deep stroma and this unrecognized layer.

- **Descemet Membrane:**

Is the basement membrane of the corneal endothelium. It is has two distinct parts: an approximately 3 um thick anterior banded layer, which is formed during fetal development, and a posterior non-banded layer that is produced throughout life and whose thickness ranges up to 8–10 um[17]. If injured it does not regenerate.

- **The Endothelial Layer:**

Is a monolayer, which appears as a honeycomb-like mosaic. It maintains corneal clarity by ensuring its relative state of deturgescence. It covers the entire posterior corneal surface and fuses with the cells of the trabecular meshwork[18]. Adjacent endothelial cells share extensive digitations and possess gap and tight junctions along their lateral borders which also contain plenty of Na+, K+-ATPase pump sites[19]. The endothelial cell density changes throughout life, it declines from 4000 cells/mm2 to around 2600 cells/mm2[20] at a rate of 0.6% per year. The activity of the endothelial cells keep the corneal stroma in a state of deturgescence[21].

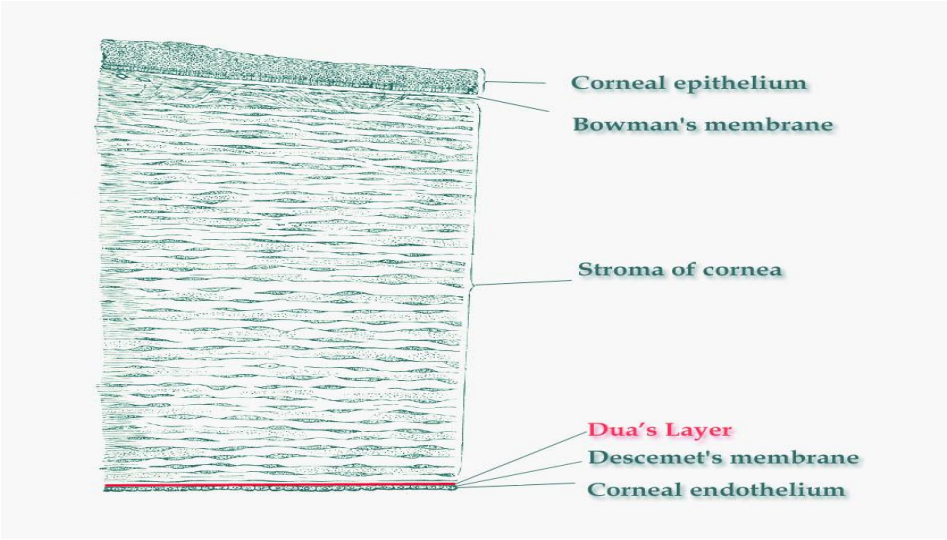

Figure (1): Cornea layers

Chapter 2
KERATOCONUS

First described by german professor Burchard Mauchart in 1748 at the University of Tubingen, Germany. Keratoconus is a progressive non-inflammatory, degenerative disease that affects the integrity of the collagen matrix within the corneal stroma. Its hallmark is the formation of a localized cone-shaped ectasia, it is accompanied by thinning of the stroma in the area of the cone. This might cause irregular astigmatism and a steeper corneal curvature[22].

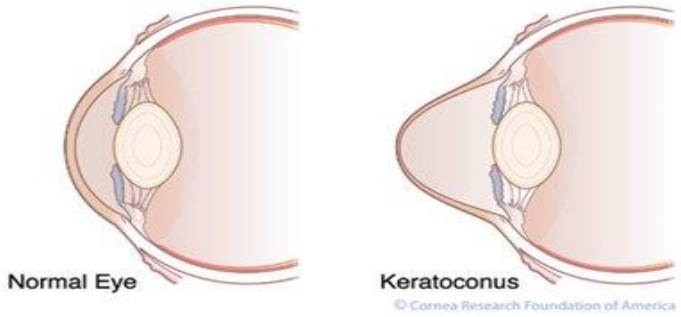

Figure (2): Difference between normal and keratoconus corneas shape.

- **Epidemiology:**

It usually starts at puberty generally before the age of 25[23]. Prevalence in Asians is 4.4 to 7.5 greater than in Caucasians denoting a significant role in ethnicity[24]. Its prevalence in the general population is between 4/1000 and 6/1000[25]. However this number has been multiplied by 100 fold in places where refractive surgery was relatively recent due to

keratoconus patients self-selecting laser vision correction to treat their poor visual acuity[26]. Since Keratoconus is a bilateral disease it often arises in one eye before the fellow eye, this lapse gives rise to a different appearance of signs in fellow eyes which is a useful indicator of the disease. However it may remain latent at a subclinical state or completely uninvolved in the other eye in up to 6% of cases[27].

- **Etiology:**

Although it was described above that Keratoconus is a non-inflammatory disease, new studies believe that inflammatory mediators play a major role in its development[28]. An imbalance between degradative enzymes such as; lysosomal enzymes, cathepsins and matrix metalloproteinase-2 (MMP-2) and their inhibitors; Alpha-1 proteinase inhibitor, alpha-2 macroglobulin and tissue inhibitor of metalloproteinase-1 and 3 is now understood to be the reason behind the development of Keratoconus[29].

Atopy and rubbing the eyes are epidemiologically linked, a study reported that 48.2% of patients with keratoconus vigorously rubbed both eyes and only 2.2% rubbed significantly only one[30]. It was also found to be associated with ocular diseases such as Leber's congenital amaurosis, granular corneal dystrophy, Avellino corneal dystrophy and posterior polymorphism dystrophy[31,32,33] and some systemic diseases

such as Down syndrome, Ehlers-Danlos syndrome and osteogenesis imperfecta[34].

The disease was reported in identical twins and multigenerational families[35]. Prevalence of keratoconus is 3.34% in families with first degree relatives having the disease which is 15 to 67 times higher than the general population[36]. It is recently understood that KC has multiple genes responsible for its development.

- **Clinical Picture:**

  - ***Symptoms:***

Clinically KC presents with unstable refraction usually consisting of myopia and astigmatism and variable visual acuity impairment however normal visual acuity may be present but only in early stages. Often the patient is symptom free until a relative advanced disease stage. It usually starts with the patient complaining of decreased visual acuity at all distances, which cannot be compensated by correction, as well as distortion of images. Photophobia, glare and eye irritation making contact lenses uncomfortable are often characteristic symptoms of the disease grade[37].