COLLAGEN CROSS - LINKING IN MANAGEMENT OF CORNEAL ECTASIA DISORDERS

ESSAY

SUBMITTED IN PARTIAL FULFILMENT FOR
MASTER DEGREE OF OPTHALMOLOGY
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CAIRO
2009

الترابط التقاطعى للألياف الكولاجينية بالقرنية فى علاج امراض بروز القرنية

تمهيدا
للحصول على درجة الماجستير فى طب وجراحة العيون

مقدمة من

الطبيبة/رانيا ابراهيم الدسوقى على

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القاهرة
2009

LIST OF ABBREVIATIONS

ACGIH…...American Conference of Governmental Industrial Hygienists

ALDH…….Aldehyde Dehydrogenase

Am J Med Genet ……...American Journal of Medical Genetics

Ann Ophthalmol ……Annals of Ophthalmology

Arch Ophthalmol. ……..…….Archives of Ophthalmology

ARVO ….....Association for Research in Vision and Ophthalmology

ASCRS……...American Society of Cataract and Refractive Surgery

BSCVA…….Best Spectacle Corrected Visual Acuity

BFS……Best-Fit Float Sphere Size

Biochem Biophys Res Commun……...Biochemical and Biophysical Research Communications

Biochem. J. ……....Biochemical Journal

Biochim Biophys Acta…….Biochimica et Biophysica Acta: A Journal published by Elsevier Science

BMJ …….…….British Medical Journal

C3R……..……..Corneal Collagen Cross-Linking with Riboflavin

CH……..Corneal Hysteresis

CLAO ….....Contact Lens Association of Ophthalmologists

CLEK ……...Collaborative Longitudinal Evaluation of Keratoconus

Coll Relat Res ……..Collagen and Related Research

Comp. Ophthalmol. Update .....Comprehensive Ophthalmology Update

Curr Opin Ophthalmol ……Current Opinion in Ophthalmology

CXL……...Collagen Cross-Linking

Dextran-T-500……..Technical Dextran with average molecular weight of 500,000 Daltons

Eur J Implant Ref Surg …….European Journal of Implant and Refractive Surgery

Exp. Eye Res. …….Experimental Eye Research

G…….Glucose

Ger J Ophthalmol. …….....German Journal of Ophthalmology

Graefe's Arch Clin Exp Ophthalmol ……Graefe's Archive for Clinical and Experimental Ophthalmology

ICNIRP……...International Commission on Non-Ionizing Radiation Protection

Int Cont Lens Clin. ……..International Contact Lens Clinic

Int J Biol Macromol…….....International Journal of Biological Macromolecules

Int J Dev Biol. ……International Journal of Developmental Biology

J Struct Biol. …….....Journal of Structural Biology

J Ultra Mol Struct Res ….....Journal of Ultrastructure and Molecular Structure Research

J. Anat. …….Journal of Anatomy

J. Microsc. ……...Journal of Microscopy

JCRS ……...Journal of Cataract and Refractive Surgery

KC……...….Keratoconus

K reading……..Keratometric Reading

Lab Invest ……Laboratory Investigation is the Official Journal of the United States and Canadian Academy of Pathology

LED……...…Light Emitting Diode

MDA……..Malondialdehyde: a natural by-product of fat digestion known to increase the risk for heart disease and other chronic conditions.

Methods Mol Biol……...Methods in Molecular Biology

Ophthalmol Clin North Am …...Ophthalmology Clinic of North America

Ophthalmologica.....…….....International Journal of Ophthalmology. It is an official publication of the International Society for Clinical Electrophysiology of Vision

PMCD…….Pellucid Marginal Corneal Degeneration

PMMA……..…...Polymethyl Methacrylate

Q Rev Biophys …….Cambridge Journals Online – Quarterly Reviews of Biophysics

RGP……Rigid Gas Permeable

RNFL…….Retinal Nerve Fiber Layer

SPIE Digital library……..is the most extensive resource available on optics and photonics from 1990 to the present (2009)

Surv Ophthalmol……....Survey of Ophthalmology

Trans Am Ophthalmol Soc……..…Transaction of the American Ophthalmological Society

UCVA…….....Uncorrected Visual Acuity

LIST OF CONTENT

ACKNOWLEDGEMENTS

Thanks first and last to ***Allah*** *as we owe him his great care, support and guidance in every step in our life.*

I'd like to express my sincere appreciation to Prof. Dr. ***Saad Mohammed Rashad*** *Professor of Ophthalmology, Faculty of Medicine, Ain Shams University, for his great help, constructive criticism and kind supervision. No word can fulfill the feeling of gratitude and respect I carry for hem.*

I would like to express my sincere thanks to Lecturer ***Ahmed Abd Elmeguid Abd Ellatef*** *Lecturer of Ophthalmology, Faculty of medicine, Ain Shams University, for his continuous work, wise advice, and cooperation through this work.*

At last, but definitely not least, I would like to thank my great husband and my son's father Ahmed, Dr. ***Abd Elmonem Elshazly*** *for his great help, support and encouragement; also I would like to thank my father, my mother, my brother and my sister for their support, advice and motivation.*

Rania Ibrahim Eldesoky Aly

INTRODUCTION

The biomechanical properties of cornea are determined by the collagen fibers and the degree of interfibrillar linkage. Ectatic conditions of cornea may result from inflammation or they may be non inflammatory in origin. The non inflammatory ectasias are Keratoconus, Keratoglobus & Pellucid marginal degeneration, Keratoconus being the most common **(Wollensak, 2003)**.

Keratoconus is a degenerative non-inflammatory disorder of the eye in which structural changes within the cornea cause it to thin and change to a more conical shape than its normal gradual curve. Keratoconus can cause substantial distortion of vision, with multiple images, streaking and sensitivity to light all often reported by the patient, because of induced myopia, and both regular and irregular astigmatism. Incidence of Keratoconus in general population is 1 in 2000. It is more common in females and is usually bilateral. There is no specific hereditary pattern **(Seiler, 2006)**.

Corneal Ectasia is a condition resembling Keratoconus but comes from a different origin. Almost invariably the cause is refractive eye surgery, specifically LASIK. After LASIK, the cornea has been made thinner. SO, internal pressure from within the eye can cause expansion or distension of the cornea. The resultant distorted corneal surface will usually make it impossible to have clear vision with eyeglasses or soft contact lenses. A special gas permeable contact or scleral lens will be needed to restore lost vision. These special lenses will act to create a new

corneal surface allowing the patient to regain clear vision **(Mazzotta, 2006)**.

Pellucid marginal corneal degeneration (PMCD) is a sub-category of Keratoconus. It is a peripheral ectatic corneal disorder. Typically bilateral, non-inflammatory peripheral corneal thinning occurs over a 1-2 mm clear crescentric area, between the 4 and 8'o clock position, located 1-2 mm from the inferior limbus. The uninvolved area separating the thinning from the limbus is normal while the apparently normal area superior to it is ectatic without associated inflammation, vascularisation, scarring, or lipid infiltration. The topography usually (beer belly contour) shows 'against the rule' astigmatism, with a sagging bow-tie configuration, oblique inferiorly. The steepest meridian is located 90 degree to the area of thinning. Fitting this type of cornea can be more challenging; a much larger gas-permeable scleral lens is needed. Scleral lens vault the entire cornea and are supported by the sclera. A special liquid fills the space between the back surface of the lens and the front surface of the cornea. This liquid acts as a buffer and protects the compromised corneal tissue. These lenses are comfortable and vision provided by them is good **(Sridhar, 2004)**.

The treatment of patients with Keratoconus depends of the degree of ectasia and the resultant irregular astigmatism. Early cases can be treated with astigmatic spectacle correction and soft toric contact lenses. As the disease progresses rigid contact lenses become the mainstay of treatment. Between 10-25% of patients with Keratoconus progress to a point where surgical intervention is required. Surgical options include:

- Corneal transplantation (or grafting)
- Intra-corneal ring segment insert
- Ultraviolet-A/Riboflavin corneal cross linkage (C3R) **(Caporossi, 2006)**.

Collagen cross-linking is a new treatment for corneal ectasia that uses a photosensitizing agent, riboflavin (vitamin B2) & ultraviolet light (UVA, 365nm) exposure. In extensive experimental studies (including biomechanical stress & strain measurements) researchers have demonstrated a significant increase in corneal rigidity / stiffness after collagen cross-linking using this riboflavin/UVA treatment. Collagen cross-linking treatment is not a cure for ectasia; rather, it aims to halt the progression of the condition. This is important to understand. Patients will continue to wear spectacles or contact lenses (although a change in the prescription may be required) following the cross-linking treatment. The main aim of this treatment is to arrest progression of ectasia by increasing the mechanical stability of the cornea and its resistance to enzymatic digestion, by inducing cross linkage between the corneal collagen fibers, and thereby prevents further deterioration in vision and the need for corneal transplantation **(Tan, 2007).**

Aim of the Work

To highlight the role of cross-linking of corneal collagen in reducing progression of ectatic corneal conditions such as Keratoconus, Pellucid Marginal Degeneration and Iatrogenic Keratectasia after LASIK.

CONTENTS

SURFACE ANATOMY

The cornea is a transparent avascular tissue with a smooth, convex outer surface and concave inner surface, which resembles a small watch-glass. The main function of the cornea is optical; it forms the principal refractive surface accounting for 70% (40-45 dioptres) of the total refractive power. Most of the refraction of the eye occurs not in the lens but at the front surface of the cornea at the tear/air interface. The resistance of the cornea which provides a protective layer and resists the ocular pressure is due to the stromal collagen **(O'Donnell and Wolffsohn, 2004).**

Transparency of the cornea is achieved by:

1. The regularity and fineness of its collagen fibrils.

2. Active metabolic pump of endothelium which prevents corneal edema.

3. Absence of the blood vessels except the peripheral 1mm.

4. Non myelination of the corneal nerve fibers.

5. Uniform refractive indices of epithelium, endothelium and Descemet's.

The cornea protrudes slightly beyond the scleral globe because the curvature of the cornea is greater than that of the sclera so that a slight external furrow (the sulcus sclerae) separates it from the sclera, in the living subject it corresponds roughly to the periphery of the visible

iris. It demarcates the limbus which is defined in two ways. The histological limbus is the full thickness annular interface that separates the optically transparent corneal stroma from the opaque sclera. The surgical limbus is the annular region bound by a line from the anterior surface termination of bowman's layer to the posterior surface termination of descemet's membrane and by a line oriented perpendicular to the external scleral surface that intersects schlemm's canal in the angle of the anterior chamber **(Bores et al., 1993).**

TEAR FILM:

The precorneal tear film is approximately 7 μm thick with a volume of 6.2 ± 2 μL during normal tear production. Tear fluid is typically produced at a rate of 1.2 μL/minute, with a major portion drained from the palpebral fissure through the nasolacrimal duct and a smaller volume lost through evaporation from the ocular surface. Tear chemistry is complex; ingredients include various electrolytes, metabolites, proteins, enzymes, and lipids. The functional significance of the tear film is broad. It provides lubricating qualities and a smooth optical interface with the air. It also protects the epithelium from airborne contaminants and provides natural immunity to infectious agents through secretory immunoglobulin molecules. The most anterior layer is the lipid or oily layer derived from secretions of the Meibomian glands located in the eyelid and caruncle. This layer is between 0.1 and 0.5 μm thick. The aqueous lacrimal tear layer is at least 5 μm thick and often thicker, depending on tear production by the lacrimal glands located in the superiotemporal margin of the orbit. The posterior mucous layer is

approximately 1μm thick and is derived from secretions of conjunctival goblet cells. The hydrophilic nature of mucus substantially reduces surface tension and provides a smooth, wettable surface for the aqueous tear layer **(Gipson et al., 1992).**

DIMENSIONS:

In front, the cornea appears elliptical, being 11.7 mm wide in the horizontal meridian and 10.6 mm in the vertical. The posterior surface of the cornea appears circular, about 11.7 mm in diameter. This difference is due to the greater overlap of sclera and conjunctiva above and below than laterally. The cornea is 1% wider in males. The axial thickness of the cornea is 0.52 mm with a peripheral thickness of 0.67 mm. At birth, the cornea is slightly thicker than that in children, perhaps reflecting the onset of endothelial function close to the time of birth**.** Its surface area is about 1.3 cm2, one-sixth of the surface area of the globe. Its refractive index is 1.37. The cornea forms part of what is almost a sphere, but it is more curved in the vertical than the horizontal meridian, giving rise to "astigmatism with the rule". In its central third, **the optical zone,** the radius of curvature of the anterior surface is about 7.8 mm and that of the posterior is 6.5 mm, in adult male. The difference in curvature between the anterior and posterior corneal surfaces results from the central cornea which is thinner than the periphery. Peripheral cornea is more flattened **(Safir et al., 1983).**