الجديد فى تشخيص و علاج القصور الوظيفى للخلايا البطانية لقرنية العين

رسالة مقدمة توطئة للحصول على درجة الماجستير فى طب و جراحة العيون من الطبيب

رامى رياض فكرى
بكالريوس طب و جراحة العيون
جامعة القاهرة

تحت اشراف

د/ هيثم عزت نصر
أستاذ طب و جراحة العيون
كلية الطب
جامعة القاهرة

د/ رياض بهى الدين شلش
أستاذ طب و جراحة العيون
كلية الطب
جامعة القاهرة

د/ أحمد حسنين ابراهيم
أستاذ مساعد طب و جراحة العيون
كلية الطب
جامعة القاهرة

كلية الطب
جامعة القاهرة
٢٠٠٩

Abstract

The corneal endothelium is functionally essential to the cornea. Dysfunction of the endothelial cell layer provokes hydration of the cornea and thus results in corneal edema. Corneal endothelial cell density and corneal thickness are essential in evaluating the status of the cornea. Penetrating keratoplasty has been the standard of care for treating endothelial cell failure however, The Deep Lamellar Endothelial Keratoplasty DLEK, Descemet-stripping with endothelial keratoplasty DSEK and Descemet-stripping automated endothelial keratoplasty DSAEK procedures represent posterior lamellar corneal transplantation that allows for the selective replacement of diseased recipient endothelium and leads to improved visual outcomes.

Key Words :

Endothelial – Decompensation – Dlek .

Recent Trends in Diagnosis and Management of Corneal Endothelial Decompensation

Essay

Submitted in partial fulfillment of the master degree of ophthalmology

By

Ramy Riad Fikry

M.B.B.ch

Supervisors

Dr. Haytham Ezzat Nasr

Professor of ophthalmology

Faculty of medicine

Cairo University

Dr. Riad Bahey Eldin Shalash

Professor of ophthalmology

Cairo University

Dr. Ahmed Hassanein Ibrahim

Assistant professor of ophthalmology

Faculty of Medicine

Cairo University

Faculty Of Medicine

Cairo University

2009

Acknowledgments

- First and foremost I am grateful and thankful to **GOD** for all the blessings in my life.

- Words can not express how indebted I am to my **father**, for all what he has done for me.

- I would like to express:

    - My appreciation to my **wife** for all her support.

    - My respect and gratefulness to ***Dr. Haitham Nasr*** for his valuable supervision and support.

    - My sincerest gratefulness and appreciation to ***Dr. Riad Shalash*** for his continuous contribution and supervision throughout this work.

    - My deepest appreciation and gratitude to ***Dr. Ahmed Hassanein*** for his Guidance, support, and supervision.

    - My gratefulness to ***Dr. Wael Eweiss*** for his help and kind support.

- Finally I thank the Ophthalmology department; my professors and colleagues.

-

Table of contents

Introduction

The cornea is a unique portion of the outer, fibrous ocular tunic that is transparent and serves a refractive function while maintaining a mechanically tough and chemically impermeable barrier between the eye and the environment. The cornea became structurally and functionally specialized to achieve the required optical properties.

The corneal endothelium is functionally essential to the cornea. Normally the endothelium enjoys a privileged and protected place in the anterior chamber, but it remains a fragile cell layer whose integrity and viability must be guarded to ensure the success of any intra-ocular procedure.

Dysfunction of the endothelial cell layer provokes hydration of the cornea and thus results in corneal edema, which may be reversible or irreversible (decompensated). The corneal edema is at first stromal the epithelium becomes involved as well, and may even swell producing bullae. These bullae may rupture and impair the integrity of the epithelial surface.

There are both primary intrinsic and secondary extrinsic causes of endothelial failure examples of which are age related, Fuch's endothelial dystrophy, surgical trauma, elevated intra-ocular pressure and intraocular inflammation. Viscoelastics facilitate cataract surgery and protect the corneal endothelium during the procedure.

Corneal endothelial cell density and corneal thickness are essential in evaluating the status of the cornea. Optical slit lamp and ultrasonic Pachymetry are used routinely to measure corneal thickness.

However several new instruments have been recently developed to determine corneal thickness; these include Optical coherence tomography, confocal microscopy, Ultrasonic biomicroscopy and the Scheimpflug camera.

The aims of treatment of corneal edema are:

- Withdrawal of fluid from the corneal tissue
- Suppression of any underlying factor as inflammation or raised IOP
- Relieving any discomfort or pain that may be present in severe cases
- Restoration of a clear cornea

The aims of treatment can be achieved with conservative medical measures during the early phases of corneal edema for up to three month to elicit a compensated cornea; if not possible this denotes a decompensated cornea, which entails surgical intervention.

Penetrating keratoplasty has been the standard of care for treating endothelial cell failure however, the disadvantages of this procedure include prolonged visual rehabilitation, high astigmatism and suture related complications.

The Deep Lamellar Endothelial Keratoplasty DLEK, Descemet-stripping with endothelial keratoplasty DSEK and Descemet-stripping automated endothelial keratoplasty DSAEK procedures represent posterior lamellar corneal transplantation that allows for the selective replacement of diseased recipient endothelium and leads to improved visual outcomes.

Aim of work

To review the literature about the pathogenesis and different etiologies of corneal endothelial decompensation, review recent modalities in diagnosis and finally describe new methods of treatment aiming at the best possible visual outcome.

List of figures

List of abbreviations

FED: Fuchs endothelial dystrophy

IOP: Intra-ocular pressure

SMA-2: Citrate acetate bicarbonate solution

NGOIS: New generation ophthalmic irrigation solution

HPMC: Hydroxy-propyl methyl cellulose

BAC: Benzalkonium chloride

MMC: Mitomycin C

SL: Slit lamp

TSCM: Tandem Scanning Confocal Microsope

SSCM: Slit Scanning Confocal Microscope

CCT: Central corneal thickness

OCT: Ocular coherence tomography

VSI: Volume Stress Index

CACI: Continuous anterior chamber infusion

OVD :Ophthalmic Viscosurgical device

RCE: Reccurent corneal erosions

ASP: Anterior stromal puncture

PTK: Photo therapeutic keratectomy

DLEK: Deep lamellar endothelial keratoplasty

LASIK: Laser-assisted in situ keratomileusis

DSEK: Descemet-stripping with endothelial keratoplasty

DSAEK: Descemet-stripping automated endothelial keratoplasty

DMEK: Descemet membrane endothelial keratoplasty

HCEC: Human corneal endothelial cells

CECs: Corneal endothelial cells

Chapter 1

Corneal Endothelium Structure and Function

Anatomy of the corneal endothelium

Corneal endothelium is the single layer of cells forming a boundary between the corneal stroma and the anterior chamber. Descemet's membrane is the basement membrane of the corneal endothelium. It is synthesized by the corneal endothelium and assembled at the basal surface of the cell layer.

The posterior cell surface contains numerous microvilli, [1] whereas the lateral and basal plasma membranes are interdigitated.[2,3] Gap junctions located in the basal aspect of the lateral plasma membrane connect adjacent cells allowing intercellular communication.[4]

Ultrastructural studies of corneal endothelial cells reveal the presence of abundant mitochondria indicating that these cells are highly metabolically active. During eye development, both cell proliferation and migration contribute to the formation of the endothelium from neural crest derived mesenchymal cells.[5,6] There is ample evidence, however, to indicate that once the mature corneal endothelial monolayer has formed, human corneal endothelium does not normally replicate in vivo at a rate sufficient to replace dead or injured cells.[7]

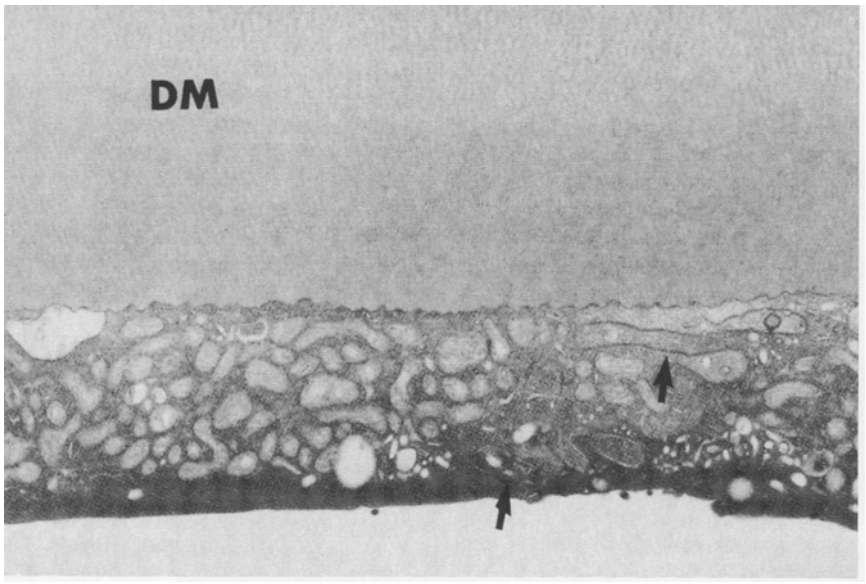

Figure 1: Descemet's membrane and the corneal endothelium the portion of the endothelial cell visible in the micrograph shows the presence of numerous mitochondria and an interdigetating lateral membrane [8]

Though significant proliferation is not seen in vivo, evidence shows that endothelial cells actually retain proliferative capacity. These cells have not exited the cell cycle, but instead, are arrested in the G1 phase.[9]

Overall the relative lack of proliferation in the endothelium results in an age-related decrease in cell density throughout life, with an average cell loss of 0.3% to 0.6% per year.[10] At birth cell densities range from 3500 to 4000 cell/mm^2. Adult corneas have endothelial cell density of 1400 to 2500 cell/mm^2. A lower limit to the ability of the endothelial cells to maintain corneal hydration is at densities of 400 to 700 cell/mm^2.[11]

Physiology of the corneal endothelium

Hydration of the cornea is controlled by the active transport of water back into the anterior chamber after stromal proteoglycans create an oncotic pressure gradient that results in drawing fluid into the cornea.

The primary site of fluid regulation through the endothelium's activity is the corneal stroma. As a result of this endothelial activity, the stroma is maintained in a relatively deturgesced state, which allows an orderly lattice of collagen fibrils to enmesh in glycosaminoglycans and create a transparent tissue.[12]

At Least three endothelial "pumps" have been identified a Na^+/K^+-ATPase, a bicarbonate-dependent Mg^{2+}-ATPase and aquaporins or water-selective channels. As reviewed by Gipson and Joyce, Aquaporin-1 (AQP-1) is the specific isoform that has been described in corneal endothelial cells.[4, 9]

Sanchez et al in 2002 promote the idea that endothelial fluid transport involves electro-osmosis through the intercellular junctions as the primary process in a sequence of events secondary to iron transport.[13] Ruberti et al in 2003 suggest that transendothelial fluid may be rapidly self-modulating to control stromal hydration in response to small osmotic stresses, and this may assist in the regulation of corneal hydration.[14]

In summary, the corneal endothelium secretes solutes into the aqueous humour and this transport system creates an osmotic gradient that draws fluid out of the stroma to balance its swelling tendency.

Pathogenesis of corneal Edema

The model discussed in the previous section for the control of corneal hydration concerns itself with the normal healthy cornea with intact functioning membranes and avascular, compact corneal stroma. However, these normal properties are modified by disease and the reaction of the cornea can be complex.[8]

Although acute corneal edema is usually reversible, chronic corneal edema is usually irreversible and treatment varies according to the nature of the disease. The endothelium under stress changes in a few non-specific, but characteristic ways. Thus, in acute inflammation, or in trauma, rapid cell degeneration and death may occur in a focal manner that is then repaired by sliding and rearrangement of neighboring cells. The resulting endothelium is characterized by decreased cell number and enlarged and irregularly shaped cells (polymegathism and pleomorphism). [8]

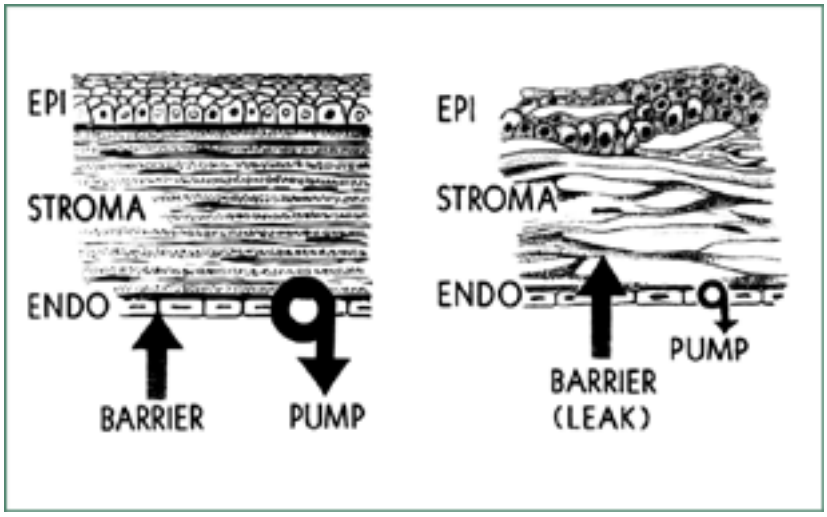

Figure 2: Mechanism of Development of stromal edema due to endothelial dysfunction[8]