

Clinical Update on Management of Fuchs' Endothelial Dystrophy

Lecture OUTLINE

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Review Normal Corneal Endothelium

- Single layer endothelium covering Descemet's membrane
- Polygonal (mostly hexagonal), uniform tile or mosaic pattern
- Young adults ~ 3500 cells / sq mm
- Normal cell loss ~ 0.5% / year
- **Endothelium functions to pump water OUT of the cornea**
 - Na-K ATPase pumps Na back into the aqueous
 - The water follows Na out of the cornea

Review Injury to Endothelium

Endothelium does not normally divide/multiply

Response to cell Injury/loss

- Remaining cells enlarge to cover the defect (lose hexagonal shape)

Corneal edema

- Remaining cells can't maintain adequate pump function

Discuss New Finding: (Ula Jurkunas, MD et al. – *American Journal of Pathology*)

- Discovered neural crest endothelial stem cells

Key to newest treatment for Fuchs' Endothelial dystrophy

Endothelial stem cells CAN be stimulated to multiply

Review Fuchs' dystrophy/Corneal Edema Differential

- **Primary**
- Dystrophy: **Fuchs' endothelial dystrophy**, Posterior polymorphous corneal dystrophy, Congenital hereditary endothelial dystrophy
- Iridocorneal endothelial syndrome (ICE)
- **Secondary**
- Trauma/Surgery: PBK (Complex phaco, ACIOL, Glaucoma Tube)
- Inflammatory: Herpes, Varicella, uveitis, fungus
- Medications: Carbonic anhydrase Inhibitors (i.e. dorzolamide)
- Hypoxia: Contact lens
- Barrier loss: Epithelial defect/abrasion
- Elevated IOP
 - FUCHS' ENDOTHELIAL CORNEAL DYSTROPHY

Review SIGNS OF FUCHS' ENDOTHELIAL DYSTROPHY

- Vision loss
 - Edema and guttae distort light
 - **Vision often worse in AM and improves during day**
 - Eyes open, surface evaporation helps
 - Unlike dry eye where vision worse as day goes on or with activities like reading or computers
 - Snellen vision may not correspond to visual quality
 - Mild guttae cause significant distortion and glare
- ENDOTHELIAL CELL SPECULAR CHANGES
- Normal Endothelial Histology
- Corneal Histology - Guttae
- Signs and Symptoms

Review Symptoms of Endothelial dysfunction

- Blurry vision worse in AM and may improve

- Glare and difficulty night driving
- Late: constant blurring of vision

Review Signs of Endothelial dysfunction

- Guttae
- Corneal edema (thickened pachy)
 - Waite Beetham lines and Descemet folds
- End stage: Epithelial Bullae

Discuss the Assessment of FUCHS' DYSTROPHY

History

- prior surgery, trauma, family h/o, unilateral or bilateral, age of onset

Exam

- Check IOP, review medications
- **Dorzolamide/CAIs can worsen corneal edema**

Slit lamp

- center thicker than periphery, retroilluminate for guttae/pigment

Discuss Testing for Assessment of FUCHS' DYSTROPHY

Testing:

- Pachymetry >620 CCT (can be normal by itself)
- OCT, ray trace, scanning slit: CCT equal to mid periphery pachy
- Specular microscopy: endothelial cell density, size, and shape
 - Cell counts vary widely (small sample)
 - <1000 CD, <50% hexagonal, coeff variation >0.4

Review Medical management of Fuchs'

Initial therapy can be conservative

- **Hypertonic ointment nightly** (Muro 128, Retaine NaCl)
- Hypertonic drops (Muro 128, Sochlor)
 - Dosing Hypertonic drops: Q5 min x 3 first thing in the AM (NOT QID)
- Gentle hairdryer to face with eyes open

Discuss Who needs Surgery for Fuchs'

Nuanced discussion

- Intervening earlier today as have great surgical options
- Central guttae
- Glare or poor quality of vision? Affecting ADLs?
- Morning blurring?

Testing

- **No set criteria for intervention. Testing is supportive but decision is clinical**

Discuss/review latest Treatment Options for Fuchs'

- PKP - Penetrating Keratoplasty
- DSAEK – Descemet Stripping Automated Endothelial Keratoplasty
- UT-DSAEK – Ultra Thin Descemet Stripping Endothelial Keratoplasty
- DMEK – Descemet Membrane Endothelial Keratoplasty
- PDEK – Pre-Descemet Endothelial Keratoplasty
- DWEK - Desmetorhexis Without Endothelial Keratoplasty
- Descemet Stripping Automated Endothelial Keratoplasty (DSAEK)
- Ultra Thin-Descemet Stripping Automated Endothelial Keratoplasty

Review specifics of Ultra Thin DSAEK

Defined based on graft thickness

- Eye banks improving technique, progressively thinner grafts
- Now ~ 80 to 120 microns is UT-DSAEK

Steps same as for traditional DSAEK

- Graft loaded into injector or placed in the eye by pushing or with forceps
- Graft unfolded and centered easily using air and light taps of the cornea

Review specifics on Descemet Membrane Endothelial Keratoplasty

- DMEK

- Graft loaded into an injector
- Unfolded in the eye using jets of BSS and air and tapping
- Can be more challenging to unfold as graft wants to curl the wrong direction
- No stroma is transplanted, no appreciable graft host interface
- Visual axis often crystal clear and graft nearly imperceptible

Review specifics on Pre-Descemet Endothelial Keratoplasty

- PDEK
- Graft very similar to DMEK but unfolds easier
- Very little stroma transplanted
- Better for eyes with deeper chamber (post PPV, PKP)
- Limited smaller graft size

Discuss Which transplant is best?

Currently limited number of UT-DSAEK vs DMEK studies and PDEK very NEW

UT-DSAEK, DMEK and PDEK are all superior to traditional (thick) DSAEK

- **DMEK offers best quality of vision and fastest vision recovery**
- Limitations on who can undergo DMEK

Review literature on DMEK vs DSAEK: Cornea 2017

- 11 studies (350 DMEK eyes vs 373 DSAEK eyes)
- No difference in total detachment rate, graft failure, rejection
- **DMEK superior in BCVA at 6mon, subjective VA, pt satisfaction**, and was the preferred method by patients
- DMEK had higher partial detachment rate (25% vs 4.4%)
- Limitation: compared DMEK to DSAEK not UT-DSAEK
- DMEK superior but higher risk of rebubbling
- Meta-analysis of postoperative outcome parameters comparing Descemet membrane endothelial keratoplasty versus Descemet stripping automated endothelial keratoplasty. I Pavlovic, MD et.al. Cornea 12/2017. Vol 36;12:1445-1451

Discuss limitations of DMEK

- UT-DSAEK still has a primary role
- Complex cases with ACIOL, Tube shunts, aphakia for example need graft tissue that can unfold easily with minimal manipulation
- Poor visibility from corneal scar may preclude DMEK

Discuss newest Treatment Paradigm Change for Fuchs' - DWEK

- What if we could clear corneal guttae without donor tissue?
 - We CAN!
 - **DWEK needs NO corneal transplant graft**
- Advantages of no graft
 - No risk of rejection
 - No graft host interface
 - No need for rebubbling
 - No complications from long term steroid use

Review Desmetorhexis - DWEK

- Strip central 4mm of Descemet's membrane after cataract surgery
 - Goal to clear guttae out of visual axis
- **NO transplant graft is inserted after stripping of DM**
- Severe post op corneal edema - clears slowly over 6-8 weeks
- **Ripasudil helps it clear faster**
- Nonresponders can still receive endothelial keratoplasty
- Theory: inflammation triggers peripheral endothelial stem cells to proliferate (rather than adjacent cells enlarging)
- DWEK is effective
- DWEK can treat center involving Fuchs' dystrophy with equivalent visual outcomes to the current standard of care
 - My study was recently accepted for publication in Cornea

- DWEK has fewer adverse events and reduces the need for additional procedures and medications
- **Descemetorhexis eliminates the need for immunosuppression and donor corneal tissue**
 - Great for pt with glaucoma or h/o steroid response

Discuss limitations of DWEK

- DWEK not effective when peripheral stem cell population has been damaged
 - Not for PBK and other non-Fuchs' etiologies
 - Not for severe, periphery involving Fuchs'
- Some patients may not tolerate 2 months of blurry vision
 - Limited vision in other eye, type A or anxious personality
 - Multiple reports of corneal clearance despite graft detachment after endothelial keratoplasty (EK)⁵⁻¹⁰
 - corneal clearing began peripherally
 - specular microscopy revealed endothelial cell migration into the areas of bare posterior stroma
- Colby et al. reported clearance in 10 of 13 eyes¹¹
 - Largest series to date
 - 4mm descemetorhexis

Review points/Summary

- Many good treatment options today and can intervene earlier
- Each surgical approach has limitations and advantages
- Key: pairing the patient with the best surgery for a tailored outcome
- Fuchs' patients don't have to suffer with poor quality of vision any longer