Clinical Dry Eye Management: Diagnostics, and Treatment Methodologies

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Overview

• Nomenclature used in the past:
  – Dry Eye Syndrome
  – Tear Dysfunction Syndrome
  – Ocular Surface Disease
  – Aqueous Deficiency
  – Keratoconjunctivitis Sicca
  – Etc. etc. etc.

• BEGINS as Tear Dysfunction
  – Imbalance in some aspect of tear chemistry/physiology
  – Increased Osmolarity? Decreased Lipid Layer?

• PROGRESSES to Ocular Surface Disease
  – Affects underlying structure and ability for compensatory mechanisms to restore homeostatic balance

Symptoms: What are they?

• Def: “a physical or mental feature that is regarded as indicating a disease; particularly such a feature that is apparent to the patient” (Oxford dictionary)
• Downstream effect of a pathology or disruption to normal physiologic processes
• Result from breakdown in innate coping mechanisms
• Questions:
  – Do we wait for symptoms?
  – What symptoms present at the earliest levels?
  – Are there other methods?

Disclosures

• Paid Consultant, Speaker, or Advisor to:
  – Alcon Pharmaceuticals Inc.
  – Allergan Inc.
  – Bausch+Lomb, Inc.
  – BioTissue, Inc.
  – NicOx Inc.
  – TearScience, Inc.

• Some of the information in this lecture may represent off-label uses of approved drugs or devices.
Early Symptoms

- Less than 60% of patients with observable dry eye are symptomatic
- For earlier diagnosis, blur or fluctuating vision may be one of the best indicators
- PROOF study (Progression of Ocular Findings)\(^2\)
  - 58.5% of ITF Stage II dry eye presented with moderate or greater complaint of blurred vision vs. 13.7% of controls
  - Both groups had baseline of 20/20 vision

Changes to The Dry Eye Workup

- Newer technologies entering the clinical setting
  - Tear osmolarity, interferometry, cytokine assays, protein assays
  - Attempt to measure core mechanisms of dry eye

Diagnostic Testing: Dry Eye workup

- Interferometry (LipiView)
- Osmolarity (TearLab)
- MMP-9 (InflammaDry)
- Ocular Surface Assessment
  - External lids, lid margin, conjunctiva/cornea
- TBUT
- Volumetric Assessment*
  - Schirmer/ZoneQuick
- Meibum Assessment**
- Diagnostic Gland Expression
- Meibography
- Biomarker testing (Sjö)

Tear Quality Tests

- Are they valid measures?
  - Each is based on detecting a contributing factor of the core mechanisms for dry eye progression
- Are they essential for every dry eye patient?
  - Each gives valuable insight to understand a different aspect of the tear film
  - Perimetry, OCT, examples of parallel technologies for glaucoma
  - Restoring physiological normality is achieved most rapidly by increasing both tear film stability and quieting inflammation

Understanding Osmolarity

- Definition: number of moles of solute in 1L of solution
  - Ionic/electrolyte content of tear film
- Dynamic measurement: in normals, fluctuates small amount throughout day (evaporation/compensatory mechanisms/temperature)
  - Garcia: 270 +/- 4.4 mOsm/l
- "Normal": <308 mOsm/l eye, <5 mOsm difference between OD/OS and CONSISTENT over time
  - Multiple measurements needed to assess trends
  - Higher number = greater degree of tear film disruption = higher potential for inflammation and tissue degradation

Osmolarity as result of stressors

- Increased osmolarity is a result of different stressors in Aqueous deficient vs. Evaporative dry eye
- End result = decreased sensation, decreased TF integrity, lacrimal flow
Inflammation as a role in Dry Eye

- Inflammation primarily mediated through T- and NK-cells
- Triggered by APC – activated likely via dessicating stress and in lymphatics
- Upregulation of several cytokines (IL-17, TNF-a, IL-1B, et c.) present in patients with dry eye – No specific cytokines or groups correlate with presence or severity of disease
- Elevated levels of MMP-9 associated with:
  - Increasing symptom scores
  - Decreased low-contrast visual acuity
  - Inversely correlated with TBUT
- Likely is associated with tissue remodeling

Understanding MMP-9

- Proteolytic enzyme useful in degrading extracellular matrix – Has positive effects in small amounts (<41ng/ml)
- Higher amounts result in dissolution of gelatinous basement membrane and intracellular junctions
- Increase in staining, changes in surface morphology
- Amount in tear fluid may be driven up via increased osmolarity

Meibomian Gland Assessment

- Following expression, may evert lids for more detailed examination of condition of glands
- Visualize by transilluminator, or via other device (infrared via Keratograph-5, confocal microscopy)
- Grade:
  - Length/presence of truncation (shortening)
  - Absence of glands where there should be some (dropout)

Biomarker Assays

- Systemic disease may leads to increased severity of dry eye
- Several autoimmune conditions contribute
- Immune panels may help bridge professions and lead to improvements in patient care
- Sjögren’s (NicOx; Immco):
  - ANA, rheumatoid factor, ESR, SSA (Rho), SSB (La)
- Immunoglobulin levels of: SP-1, PSP, CA-6
- In Sjögren’s patients, may have dry eye for 10 years prior to emergence of other complications

Understanding MMP-9}

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- RPS InflammaDry:
  - Sensitivity & specificity: 85% and 94%, respectively
  - Predictive values: (+) 73%; (-) 97%

Lid Function Tests

- Close attention to blink function reveals that the outer portion of the lid margin do not close completely
- Needs to be enough closure to grab the lower tear meniscus and drag it up over the cornea and conjunctival surface
- Blinks is dynamic – not 100% every time
- Calculate percentage over 20-30 seconds
- Lift lids – check for increased laxity (Floppy Lid Syndrome)
- TBUT, Meibomian Gland Function done prior to Lid Function tests to minimize expression of glands

TREATMENTS
### Treatment Goals

- "Successful" treatment = alleviation of symptoms?
  - Patient-dependent vs. objective
- Successful treatment now includes:
  - 1) Restoration of normal anatomy & physiology (as much as possible)
  - 2) Halting/eliminating inflammatory processes which lead to further disruption of tissues
  - 3) Reduction of symptoms
- Without #1 and #2, #3 is more difficult to achieve

### Therapies

#### Basics:
- Increase hydration
- Nutritional recommendations

#### Tear supplementation:
- Drive down osmolarity
- Non-preserved v. preserved tears
- Oil based v. aqueous supplements
- Gels/ointments
- Lacrisert (hydroxypropyl cellulose)

#### Warm compresses:
- 10-15 min once to twice per day
- Good apposition to lid surface
- Constant temperature (near 120°F – not to induce pain)

### Therapies

#### Anti-inflammatories:
- Essential for halting progression of immune-mediated disruption
- Steroid therapy – short v. long term
- Cyclosporine, Tacrolimus
  - Increased dosing may result in improved results\(^{34}\)
- NSAIDs
- Doxycycline/Minocycline/Azithromycin

#### Secretagogues
- Pilocarpine PO 5mg

#### Other:
- Autologous serum (1:5 serum with BSS) q2h x 2 weeks then QID x 3 months

### In-office treatments

#### Supportive:
- Bandage CL
- Scleral contact lenses
  - Creates reservoir of fluid to protect corneal surface
- Amniotic membrane
  - Allows for a “boost” to allow healing of epithelial defects

#### Therapeutic:
- Punctal occlusion
- Manual gland expression
- Mastroda paddle, Hardten compression forceps
- Maskin probing
- Thermal Pulsation (LipiFlow)
- Intense Pulsed Light

### Thermal Pulsation (LipiFlow)

- More effective than at-home warm compresses
- Provides heat and pressure to therapeutically express the meibomian glands of both upper and lower lids
- Improvement in LLT, TBUT, and patient symptoms lasting up to 12 months from single treatment\(^{17}\)
  - 2.75 years from personal experience

### SUMMARY
Wrapping it up

- Ocular Surface Disease is still very dynamic and undergoing change in a rapid pace
  - Continued evolution of diagnostic and therapeutic technology
- Efforts towards prevention, early diagnosis, and normalization of tissues
  - Restoring homeostasis vs. chasing symptoms
- Utilize all tools available
- Patient education and setting proper expectations is key:
  - It pays to take time to closely examine the ocular surface in its entirety
  - This area offers an opportunity for subspecialty like no other in ophthalmology
  - No shortage of patients

References

The Impact of Dry Eye on Contact Lens Wear

London Business School Study

- CL patients are 60% more profitable than spectacle only wearers
- Spectacle wearers = Higher initial profit
- CL patients = ↑ Frequency of eye exams
- Many contact lens patients also buy spectacles
- “We realized that much of the optical industry is ironically very myopic.”
- Lost CL Patient = Lost Revenue

What is the impact of contact lenses on the tear layer?

TFOS: Contact Lens Discomfort: Definition

- A condition characterized by episodic or persistent adverse ocular sensations related to lens wear, either with or without visual disturbance, resulting from reduced compatibility between the contact lens and the ocular environment, which can lead to decreased wearing time and discontinuation of contact lens wear
Categorizing Contact Lens Discomfort

How do we get out CL wearers more comfortable?

Eliminating Corneal Staining

• Differentiate between Dry Eye Induced Staining and solution or lens induced hyperfluorescence

The Staining Grid

PATH

Preservative-Associated Transient Hyperfluorescence (PATH)

• NaFl adheres to MPS PHMB on the eye
  — Fluorescein’s affinity for PHMB is up to 50-times greater than for PQ-1

Eyes evaluated 2 hours after lens application
PHMB release over time

Proactively Look for Hyperfluorescence

• If it is solution induced – change solutions or go to DD
  – Peroxide if possible
• If it is lens induced, consider if you can improve the fit of the lens on eye
• If it is staining due to dry eye, treat dry eye aggressively
• If you don’t check for and attack staining proactively, you will have CL dropouts

Corneal Infiltrative Events (CIE)

• Higher rate in silicone hydrogels due to lipid build-up rather than protein build-up
• Higher rate with some care systems than others

Choose the Solution

• MPS for new fits
• MPS for those that may be non-compliant or not get 6 hours of sleep
• Peroxide in any instance where there are symptoms
• Add lubricant to the lens if needed with Peroxide


How much do lubricant drops help?

A B C D E

CL Insertion 3 min Drop Instillation 2 min 4 min

How much do lubricant drops help?

1 min points

How much do lubricant drops help?

Punctal Occlusion and Contact Lenses

Inferior punctal occlusion with removable silicone punctal plugs in the treatment of dry eye related contact lens discomfort.

Evaluation of 35 patients who were not satisfied with previous management were retrospectively reviewed. The outcome of treatment was scored and evaluated with the DED-Q and MEIS questionnaire and the Ocular Surface Disease Index (OSDI).

CONCLUSION: Punctal occlusion transiently increased tear film volume in symptomatic and asymptomatic lenses wearers. A longer duration in the symptomatic group. For both symptomatic and asymptomatic lenses wearers, the increased meibomian volume was associated with improved tear film.

The impact of punctal occlusion on soft contact lens wearing comfort and the tear film.

Kathy T. (on behalf of)

How much do lubricant drops help?

Restasis and Contact Lenses

Use of cyclosporine 0.05% ophthalmic emulsion for contact lens intolerant patients.

RESULTS: Five-weeks of cyclosporine treatment significantly improved dry eye symptoms (mean improvement of 0.86 ± 0.68 with cyclosporine; mean change of 1.56 ± 1.05 with placebo). Patients using cyclosporine decreased the use of artificial tears by 96% on average, compared to 84% for placebo users. Mean tear break-up time increased 2.10 ± 0.50 with cyclosporine and 0.00 ± 0.64 with placebo, TUT increased 5.70 ± 0.54 with cyclosporine and 0.43 ± 0.53 with placebo. There were no significant differences in mean central keratometric readings. After 5 weeks, patients using cyclosporine showed statistically better improvements in temporal barry conjunctival fluorescein staining (improvement of 0.06 ± 0.50 vs. increase of 0.07 ± 0.67 with placebo). Both treatments were tolerated well.

How much do lubricant drops help?

Contact Lenses and Meibomian Glands

Contact lenses wear is associated with decrease of meibomian glands.

CONCLUSION: Contact lens wear is associated with a decrease in the number of functional meibomian glands. This decrease is proportional to the duration of CL wear.
Contact Lenses and the Lid Wiper

Lid Wiper

Lid Wiper Epitheliopathy and Contact Lenses

Treating LWE

Contact Lens Materials and Dry Eye

1. Pathophysiology of LWE
   - Dry eye states and/or contact lens surfaces
   - Inadequate lubrication
   - Mechanical trauma to epithelium of lid wiper
   - Staining of epithelium of the Lid Wiper
   - Triple Response of Lenses
   - Inflammatory cascade
   - Sequele

2. Prevalence of LWE
   - 80% of symptomatic CL wearers demonstrated LWE vs. 13% for asymptomatic controls
   - LWE with SCL and RGP wearers
   - Prevalence or LWE when dry eye symptoms present, but no signs in non-CL wearers (Huk et al., 2006)
     - 79% of asymptomatic non-CL wearers demonstrated LWE vs. 12% for asymptomatic controls
   - Conclusion: A significant proportion of the population with dry eye exhibits lid wiper epitheliopathy.

3. Prevalence of LWE when both dry eye symptoms and signs are present in non-CL wearers (Koth et al., 2006 – 2008)
   - 80% of symptomatic non-CL wearers had LWE compared to 16% for asymptomatic patients. The prevalence of LWE was 5 times greater for those with symptoms compared to the control group, and the prevalence of LWE grade 2 was 16 times greater for the symptomatic group than for the control group (Grade 0 – 3)

• What considerations are there for comfort?
  - % of water – demand on tear volume
    - Higher % = more evaporation, more interactive with tear layer
    - Lower % = less evaporation, less interactive with tear layer
  - Coefficient of Friction – lid wiper epitheliopathy
    - Lower = less friction
    - Higher = more friction

• Same as treating dry eye disease
  - Lubricants
  - Anti-inflammatory meds
  - Treat MGD
  - Restasis
  - Ointments or Gels qHS
Dry Eye and Contact Lenses

- Treat Dry Eye!
- Stain to try to catch early signs and treat early
- Evert lids – look for LWE
- Use plugs / restasis / meds just like in any Dry Eye Patient
- Use Diagnostic Tools to educate and monitor treatment efficacy
- Choose the best solution and lens combination
- Daily Disposables can help many patients

We’re not just providing good vision…

We’re Protecting It

Scleral Contact Lenses
For our Dry Eye Patients

OPENING THOUGHTS ON SCLERAL CONTACT LENSES…

Why do we do what we do?

- Take care of people
- Change lives for the better

How we do it!

- Improve Vision
- Relieve pain and suffering

Indications of scleral contact lenses

WHO: PATIENTS with painful and damaged eyes.

- Lid coloboma
- Lagophthalmos
- Exophthalmos
- Corneal Degenerations
- Trichiasis
- Atopic Keratoconjunctivitis
- Ectropion / Entropion
Who are these patients, exactly?

- Ocular manifestations of systemic disease
  - Steven Johnson’s Syndrome, Sjogren’s Syndrome, Ocular Cicatricial Pemphigoid, GVHD, Neurotrophic Keratitis
- Dry eye and Ocular surface disease
  - ABMD, Terrien’s Marginal Degeneration, LSCD, Corneal scars
- Also successful in pediatric populations

How can we help these patients?

Scleral Lenses for Ocular Surface Disease

- In a study of 517 patients, 69% of scleral lens wearers reported previous failures with other contact lens modalities.

How do scleral lenses work?
Key Components of Scleral CLs

- **Liquid Reservoir**
  - No disruption of surface epithelium!
  - Shield to environment and lid friction
- **High Oxygen Transmission**
  - High Dk materials
  - >97-160
- **Non-preserved environment**
  - Sodium Chloride Inhalation Solution 0.9%
- **Must protect the limbus**

Fitting Pearls for Scleral Lenses to Achieve Maximum Patient Success

- Amount of corneal vault
- Limbus concerns
- Landing Curves
- Lens diameter
- Solutions and Saline
- Artificial tears and Scleral contact Lenses

Patient Education

- Scleral Lenses are part of therapy, not a cure
- Vision fluctuations: “You still have a dry eye”
- Average / Expected wearing time
- Rinsing mid-day is normal and sometimes necessary

Ouch!

- VA 20/100
- Slit Lamp:
  - Anterior stromal corneal haze
  - Small epithelial defect
- Current therapy includes topical antibiotic and artificial tears, prescribed by other eye care provider

KF [Aug 1, 2012]

- 59 Year old Caucasian Male
- Referred to OMD
- Visits our office after one month of consistent blurry vision, burning sensation and photophobia OD
  - Hx of Herpes Zoster “Shingles” 4 months ago
  - On renal dialysis

Course of Treatment

- We added Pred Forte QID
- Maintain: Topical lubricants, topical antibiotics
- Diagnosed with Zoster Keratitis
- VA improved to 20/50 at **Aug 7th visit**
- Corneal surface is improved but still irregular
- Maintain course of treatment (Oflox, Pred, AT’s)
- Patient returns **Aug 21st, 2012**
- Vision is not getting better, eye is sore
- VA 20/60 and SLE reveals new epithelial defects
Course of Treatment

• Sept 5th 2012: Patient returns, eye is hurting
  – Vision down to 20/200
  – Defect enlarged to 3mm x 4mm

• Added Polytrim and Erythomycin Ung to Ocuflox and Pred Forte

• Sept 12th: Defect better, VA 20/60
• Sept 18th: Defect worse, VA 20/60, Added BCL
• Sept 25th: Defect better, VA 20/80 – kept BCL
• Oct 2nd: BCL falls out, defect is very large
  – Added autologous serum, ordered custom soft large
diameter BCL to hopefully keep in eye
• Oct 9th: VA 20/125 BCL maintained, healing
• Oct 16th: BCL falls out, defect enlarges
• Oct 17th: BCL falls out
• Oct 19th: Lost BCL, defect enlarged again, VA 20/300
• Oct 23rd: Replaced BCL, defect 2mmx3mm
  (13 visits)

WHAT IS GOING ON?

Ophthalmology Management, Sept 2012

Neurotrophic Keratopathy

• Impaired innervation to the cornea contributes to a
degenerative corneal epithelium
• Can produce epithelial keratopathy, ulceration and
eventual perforation
• Most common cause is a herpetic lesion of the ophthalmic
branch of the trigeminal nerve (V1)

Treatment Options

• Goal is to maintain corneal lubrication to promote corneal healing
• Bandage CLs were used for several weeks to protect the corneal surface, with no improvement
• VA was down to 20/300, patient was
  – Hardly spoke at visits, refused to read VA
  – A tarsorrhapsy was recommended.
• But the sharp and knowledgeable OD
  “WAIT! There’s a better answ
Scleral Lens Fitting

- Lens was applied on Visit 14, Oct 23rd 2012
  - Jupiter 18.2 / 46.00 BC
  - Careful watch, RTC 48 hours
  - Use medication drops over scleral lens
  - EW x 2 days

- Visit 15: “Eye feels calm”
  - Defect is smaller, VA 20/200
  - RTC 4 Days, continuous wear of scleral lens

- Visit 16, Nov 6th: NO EPITHELIAL DEFECT!
  - Epithelium still irregular, but intact. VA 20/50

A light at the end of the tunnel

- After 1 week of extended wear, vision improved to 20/50
- Patient was followed weekly for nearly 6 weeks, neovascularization began to develop inferiorly.
- At visit 19, Dec 12, patient was instructed to begin wearing the lens only during the day, which he does most of the time. He occasionally wears the lens a few nights per week if eye feels sore.
- Visit 21, Jun 11 2013: Patient regained 20/20 vision through a scleral contact lens. Discontinued Pred Forte drops.
- Last seen 10/29/13: Doing well, minimal haze, epith smooth

Thank you!