Innovations in Dry Eye and Primary Eye Care

What's Here, What's Coming, and What You Need to Know

2-Hour Course

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Category:

General Optometry (GO)

Course Description:

This course will reveal, feature, and spotlight innovations in dry eye and primary eye care that will impact every optometrist.  Technologies, pharmaceuticals, products, services, and processes that advance eye care will be discussed in a rapid-fire presentation. This course will keep you "in the know" for delivering advanced patient care.

Objectives:

1. Introduce the innovation to the clinician in each of the topic areas
2. Discuss how the innovation will impact the diagnosis and treatment in eye care
3. Reveal the benefit of embracing the innovation
4. Demonstrate how it will impact patient care
5. Demonstrate how to integrate the innovation into the clinician’s practice
6. Enhance the clinician’s knowledge of selected innovations that impact eye care

Outline:

1. Disclosures- Greg Caldwell, OD, FAAO
   1. Will mention many products, instruments and companies during our discussion, I don’t have any financial interest in any of these products, instruments or companies
   2. Lectured for: will provide most updated list at lecture
   3. Advisory Board: will provide most updated list at lecture
   4. Envolve: PA Medical Director, Credential Committee
   5. Optometric Education Consultants- Scottsdale, Quebec City, and Nashville- Owner
2. How Many People With:
   1. Diabetes 30 million
   2. Thyroid 30 million
   3. Glaucoma 3-6 million
   4. Dry Eye 30 million
3. Vital Dyes
   1. Fluorescein
      1. Detects disruption of intercellular junctions
      2. Positive (stain)-pooling
      3. Negative (stain)-high or elevated areas
   2. Rose bengal and Lissamine green
      1. Stains devitalized cells and cells that have lost normal mucin surface
      2. Detects abnormal epithelial cells
   3. Why are Conjunctival Staining and SPK Often Missed or Under Scored?
4. Aqueous Deficient vs Evaporative
   1. What’s the common denominator?
      1. Eyes burn/discomfort/pain
      2. pH
   2. What’s the next question?
      1. When is it worse?
      2. AM/PM
   3. AM- bacteria/parasite related
   4. PM- aqueous deficient
5. 48-year-old man; OU red, gritty, sandy and dry feeling
   1. Diagnosis
      1. Rosacea
   2. What findings support your diagnosis?
      1. Telangiectasias
      2. Erythema of the cheeks, forehead and nose
      3. Rhinophyma
         1. Indicates chronic
   3. Let us get a closer look
      1. Meibomian Gland Dysfunction- Exacerbated by Rosacea
      2. Treatment?
         1. Warm compresses
         2. Lid hygiene
         3. Artificial tears
         4. Omega 3 fatty acid
            1. EPA and DHA total 1500 mg (1000 mg minimum)
         5. Dermatological consult (Acne Rosacea)
         6. Oral antibiotics…???
            1. Which one and why??
            2. Minocycline
   4. Clinical Pearl- Treatment Failure
      1. If you continue to think of doxycycline and minocycline as antibiotics, treatment failure will be the result
      2. From this point on consider them a steroid
6. Minocycline / Doxycycline
   1. Drug of choice for marginal inflammatory blepharitis (posterior blepharitis)
   2. AB, anti-inflammatory and anti-collagenase
   3. Inhibits lipase enzyme
   4. No renal adjustment
   5. 50-100 mg qd-bid 2-12 weeks (pulse)
   6. Lower maintenance dose
   7. 20 mg Periostat (Doxycycline)
7. Hyclate vs Monohydrate
   1. Calls from the pharmacist
      1. Doxycycline
         1. Doryx- Enteric coated hyclate pellet)
         2. Adoxa - Monohydrate
8. Precautions with Oral Tetracycline Analogs
   1. Enhanced photosensitivity
   2. Avoid in children and pregnancy (Category D)
   3. Enhances the effects of
      1. Coumadin
      2. Digoxin
   4. Idiopathic intracranial hypertension
      1. Pseudotumor cerebri
   5. Hyperpigmentation
9. Case example - Benign intracranial hypertension
10. Case example – Hyperpigmentation
    1. 6 Month Later
    2. 1 Year Later
11. Innovations- Dry Eye Disease
    1. Procedures Currently Represent 4% of all US Dry Eye Revenue
       1. Procedures AM, plugs, Lipiflow, Miboflo
       2. Why we are seeing more devices and innovations
    2. Heat to the MG
       1. Bruder Moist Heat Eye Compress
          1. Moist heat treatment
          2. Stabilize the tear film, improve oil gland function, slow tear evaporation
          3. Ready in seconds, easy to use
          4. Patient compliance increases
          5. Patented MediBeads
          6. Self-hydrating (no need to add water)
          7. Anti-bacterial and non-allergenic
          8. Washable and reusable
          9. Safe for frequent use
          10. Microwave for 20-25 seconds
          11. Apply for 10 minutes
          12. Unique pod design provides improved fit and performance
       2. Mibo Heating Pad
          1. 5 settings
          2. Aromatherapy
          3. Lavender
          4. USB powered
       3. Mibo Thermoflo
          1. Ultrasound gel, heat, skin
          2. Comfortable treatment, no pressure
          3. No disposables (ROI for the practice)
          4. Technician driven eliminating the need to burn the doctors chair time
          5. Dry eye maintenance
    3. Pharma Innovations
       1. Nuzyra™(omadacycline)
          1. Tetracycline antibiotic
          2. Approved 2018
          3. Approved for PO/IV treatment of patients
             1. Bacterial skin infections
             2. Community-acquired bacterial pneumonia
             3. ADRs: Nausea, vomiting, diarrhea, constipation, insomnia
             4. Chelation issues JUST like other tetracyclines!
       2. Seysara™ (sarecycline)
          1. Tetracycline drug
          2. Approved 2018
          3. Indicated for the treatment of inflammatory acne in non-nodular, moderate to severe acne vulgaris
          4. Can be taken WITH or WITHOUT food!
          5. ADRs: nausea
       3. Xerava™ (eravacycyline)
          1. Tetracycline antibiotic
          2. Approved 2018
          3. Indicated for the treatment of intra-abdominal infections in adults
          4. IV ONLY
       4. Xiidra™ (lifitegrast) 5%
          1. Company: ShireTakeda
          2. Approved July 2016
          3. Specific treatments/indication: dry eye disease
          4. Signs and symptoms of dry eye
          5. Dosage: one drop twice daily in each eye, 12 hours apart
          6. Dysgeusia, site irritation, blurred vision
          7. Relief as soon as 2 weeks with symptoms
             1. Eye Dryness Score
          8. Signs improve as soon as 12 weeks
             1. Inferior cornea staining
          9. Mechanism of Action
             1. Lymphocyte function-associated antigen-1 antagonist
             2. LFA-1 is found on the T-cell
             3. Blocks ICAM-1/LFA-1 interaction
             4. Intercellular adhesion molecule-1
             5. ICAM is overexpressed in dry eye

Cornea, conjunctiva, lacrimal gland

* + - * 1. Anti-inflammatory by inhibiting

T-cell activation

T-cell migration

Cytokine Release

* + 1. CequaTM (cyclosporine ophthalmic solution) 0.09%
       1. Sun Pharmaceuticals
       2. Approved August 2018
       3. Dosed BID
       4. Single-use vials
       5. “New Nanomicellar Ophthalmic Solution for Treatment of Keratoconjunctivitis Sicca”
       6. Formulation technology uses micelles
       7. Gelatinous aggregates of amphipathic molecules
       8. Hydrophobic and hydrophilic molecules
       9. Ease of entry into conjunctiva and cornea
       10. High delivery of cyclosporine A (CsA)
       11. Indication and Important Safety Information
           1. A calcineurin inhibitor immunosuppressant indicated to increase tear production in patients with keratoconjunctivitis sicca
       12. Warnings and Precautions:
           1. Potential for Eye Injury and Contamination: To avoid the potential for eye injury and contamination, advise patients not to touch the vial tip to the eye or other surfaces.
           2. Use with Contact Lenses: CEQUA should not be administered while wearing contact lenses. If contact lenses are worn, they should be removed prior to administration of the solution. Lenses may be reinserted 15 minutes following administration of CEQUA ophthalmic solution
       13. Adverse Reactions:
           1. The most common adverse reactions reported in greater than 5% of patients were pain on instillation of drops (22%) and conjunctival hyperemia (6%)
           2. Other adverse reactions reported in 1% to 5% of patients were blepharitis, eye irritation, headache, and urinary tract infection
       14. Novel, aqueous, nanomicellar formulation of cyclosporine A 0.09%1–4
       15. Unpreserved, isotonic, neutral pH fluid that is supplied in unit dose vials
       16. Well tolerated in a 12-week phase 2b/3 study5
    2. Systane Complete
       1. The core SYSTANE® technology includes HP-Guar (hydroxypropyl-guar)
       2. Polymer that becomes a gel on instillation, the lubricant propylene glycol as the active ingredient, and the inactive ingredients phospholipid DMPG and mineral oil to help deliver the active ingredient.
       3. Lipid nanodroplet technology that results in better coverage of the ocular surface vs. SYSTANE® BALANCE Lubricant Eye Drops
       4. Designed to minimize blur upon instillation due to its nanodroplet formulation
       5. Completely free of benzalkonium chloride
       6. Contains 3 times the concentration of HP-Guar per unit volume, compared to SYSTANE® BALANCE Lubricant Eye Drops
       7. This permits greater cross-linking and persistence of the protective elastic matrix, resulting in better retention of the propylene glycol lubricant and protection against tear evaporation.
       8. Nanodroplet technology provides better coverage of the ocular surface, fast-acting hydration, and long-lasting relief compared to SYSTANE® BALANCE Lubricant Eye Drops.
       9. Supports all layers of the tear film and helps protect against tear film evaporation
  1. Hygiene Solutions
     1. Hypochlorous Acid
        1. Natural antibacterial agent
        2. Found in white blood cells
        3. Different mechanism of action of antibiotics
        4. Oxidant; bactericidal
        5. Skin microbiome contributes to infection, blepharitis, and MGD
        6. Staphylococcus aureus, Staphylococcus epidermidis, Corynebacterium, and Propionibacterium acnes
  2. Nutraceutical Therapies
     1. Looking for anti-inflammatory fatty acids
     2. Dry eye efficacy
     3. Gamma-Linolenic Acid GLA
     4. Specific action that ”fish oil” omegas lack
     5. 7 randomized controlled trials for dry eye
        1. Aqueous-deficient (Barabino S et al. Cornea 22: 97–101, 2003.)
        2. PRK (Macri A et al. Graefes Arch Clin Exp Ophthalmol 241:561-6, 2003.)
        3. Sjögren's (Aragona P, et al. Ophthalmol Vis Sci 46:4474-9, 2005.)
        4. Contact lens (Kokke KH et al. Contact Lens Ant. Eye 31:141-6, 2008.)
        5. MGD (Pinna et al. Cornea 26:260-264, 2007.)
        6. Mild-moderate DE (Brignole-Baudouin et al. Acta Ophthalmologica 89:e591-7, 2007.)
        7. Post-menopausal women (*HydroEye*) (Sheppard JD, Pflugfelder SC, et al. Cornea 32 :1297-1304, 2013.)
     6. Nutraceutical Therapies
        1. Prostaglandins- Myth buster- they are not all bad
           1. Prostaglandin E1 (PGE 1) -good

Shown to stimulate lacrimal production *(Phalpramool, 1980, 1983)*

Supports mucin production

Conjunctiva, other membranes *(Viau, 2009, Willemsen, 2003, Nygren, 1984)*

Experimental deprivation of vitamin C a required cofactor for PGE 1

Stops lacrimal production, produces Sjögren's-like signs & symptoms *Wood, 1970*

Precursor GLA

* + - * 1. Prostaglandin E2 (PGE 2) – bad

Precursor AA

* + - * 1. Prostaglandin E3 (PGE 3)- good

Precursor Omega-3 “fish oil”

* + - 1. Gamma-Linolenic Acid GLA
         1. Consistently shown improvement in markers of inflammation / inflammatory mediators in dry eye
         2. Shown promise in other inflammatory diseases, like rheumatoid arthritis, IBD, dermatitis, and diabetic retinopathy
         3. In Sjögren's increases tear production, raises PGE1 in tears *(Aragona, 2005)*
         4. Supports meibomian glands *((Pinna, 2007)*
         5. Probably through anti-inflammatory action
         6. 2,000-3,000 mg omega-3s usually required to have significant effect
         7. In contrast 235 mg of GLA significantly reduced 2 different inflammatory markers (HLA-DR, CD11c) in the HydroEye trial (*Sheppard, Pflugfelder, Whitley et al. Cornea, 2013)*
      2. Is GLA offered in the triglyceride (TG) form? aka “re-esterified”
         1. These forms of omegas triglyceride (TG) vs ethyl ester (EE) mainly apply only to fish oils
         2. Fish oil when it’s purified is transformed from the natural TG form in fish to the EE form
         3. Which allows the omegas to be concentrated & purified
         4. Fish oil companies have heavily marketed re-esterified or TG fish oils as vastly more absorbable and bioavailable
         5. GLA only comes as TG form
         6. No other form
         7. TG vs EE discussion is purely about different fish oils
  1. Regenerative Healing
     1. Amniotic Membrane
        1. To help reset the eye from a stage 3-4 back to something manageable
        2. Failure on multiple therapies
        3. Sjogren’s and the rheumatological patient
        4. Dry Eye and Amniotic Membrane
  2. Neurostimulation
     1. Ocular Surface Disease/Dry Eye
     2. Aqueous production
     3. True Tear-Allergan
        1. FDA approved (April 25, 2017)
        2. New development for treatment of ocular surface disease
        3. Intranasal Tear Neurostimulator
        4. Uses mild electric pulse to stimulate branch of trigeminal V1
        5. Research showing stimulates all 3 layers of the tear film
        6. Disposable end caps need to be replaced daily
        7. Sold by docs and/or Allergan and tips prescribed by optometrist
  3. In-Office Lab Testing
     1. Helps with:
        1. Switching patient to dailies
        2. Starting nutraceuticals
        3. Starting pharmaceuticals
        4. Following patients over time
     2. TearLab Osmolarity Test
        1. 300 and above
           1. Helps confirm dry eye
        2. Asymmetry
           1. Helps confirm unstable tear film
     3. TearLab Discovery™ Assay Platform
        1. Panel Testing of Tear Fluid Biomarkers
        2. Tear Osmolarity plus inflammatory marker
        3. Capable of quantitative measurement
        4. Single 100 nanoliter tear collection.
        5. Fluorescent Immunoassay
        6. Rapid < 2 minutes from collection to result
        7. Study Panel: DED + Inflammation
        8. Expected approval 🡪 2019
     4. InflammaDry®-
        1. For inflammatory dry eye detection normal levels of matrix metallopepidase (MMP-9) in human tears ranges from 3-41 ng/ml
     5. *Sjö* Diagnostic Test
        1. Uses proprietary biomarkers to create an advanced diagnostic panel
        2. Early detection of Sjögren’s syndrome in your patients
  4. Innovations -Outside of Dry Eye
     1. Pharma Update- Glaucoma
        1. Xelpros™ (latanoprost ophthalmic solution 0.005%)
           1. Sun Pharmaceuticals
           2. Approved September 2018
           3. Dosage: QD
           4. Reduce IOP in open-angle glaucoma and ocular hypertension
           5. Xelpros is the first latanoprost product not formulated with the preservative benzalkonium chloride
           6. Potassium sorbate 0.47% - preservative
           7. Reduces IOP in patients with open-angle glaucoma and ocular hypertension
           8. Up to a mean of 6 mm Hg to 8 mm Hg in randomized clinical trials
           9. Not available in pharmacies

A direct pay between patient and partnering pharmacies

Capstan Pharmacy

Transition Pharmacy

* + - * 1. Xelpros Xpress offers:

No prior authorizations

No coupon activation

No callbacks

Prompt fulfillment and refills

$55 for 30 days, $110 for 90 days

* + - 1. Rhopressa™ 0.02%- (netarsudil ophthalmic solution)
         1. Aerie Pharmaceuticals
         2. Approved December 2017
         3. Treatment of glaucoma or ocular hypertension
         4. Rho kinase inhibitor

ROCK-NET Inhibitor

* + - * 1. Once daily in the evening
        2. Twice a day dosing is not well tolerated and is not recommended
        3. Side Effects

Conjunctival hyperemia

Corneal verticillata

Conjunctival hemorrhage

* + - * 1. Rhopressa (ROCK-NET Inhibitor) Triple-Action

1. Wang SK, Chang RT. An emerging treatment option for glaucoma: Rho kinase inhibitors. *Clin Ophthal* 2014;8:883-890.

2. Wang RF, Williamson JE, Kopczynski C, Serle JB. Effect of 0.04% AR-13324, a ROCK, and norepinephrine transporter inhibitor, on aqueous humor dynamics in normotensive monkey eyes. *J Glaucoma* 2015. 24(1):51-4.

3. Kiel JW, Kopczynski C. Effect of AR-13324 on episcleral venous pressure (EVP) in Dutch Belted rabbits. *ARVO* 2014. Abstract 2900

* + - * 1. Causes Expansion of TM in Donor Eyes  
           Increases TM Outflow Facility in Clinic
        2. No labeled contraindications for Rhopressa™
        3. No clinically relevant effects on vital signs

Blood Pressure- Changes were generally small and not clinically relevant in both groups

Heart Rate- Timolol caused statistically significant reduction in the phase 3 studies by an average of 2-3 beats per month

* + - * 1. Cornea Verticillata Observed in Phase 3 Studies

Cornea verticillata refers to a whorl-like pattern of deposits typically localized to the basal corneal epithelium

Subjects are asymptomatic

The onset was ~6 to 13 weeks (netarsudil QD)

Cornea Verticillata Due to Phospholipidosis

* + - 1. Rocklatan™ (netarsudil/latanoprost ophthalmic solution) 0.02%/0.005%
         1. Approved March 14, 2019
         2. Aerie pharmaceuticals
         3. Treatment of ocular hypertension or primary open angle glaucoma
         4. Once-daily eye drop
         5. First PGA combination in USA
         6. Passed superiority testing
      2. Bimatoprost SR - Sustained Release
         1. Allergan
         2. Phase 3 Clinical Trial Update

20 month efficacy and safety study

528 people with POAG or Ocular HTN

30% reduced IOP over 12 week primary efficacy period

Met predefined criteria for noninferiority to the comparator- Timolol

These results similar to topical PGA

* + - * 1. Designed to lower IOP for 4 months
        2. Well tolerated to this point
        3. New drug application most likely second half of 2019
  1. Innovation- Neurotrophic Keratitis
     1. Oxervate™ (cenegermin-bkbj)
        1. Approved 2018
        2. Dompé farmaceutici SpA
        3. Ophthalmic solution indicated for the treatment of neurotrophic keratitis
        4. Dosing: Instill 1 drop in affected eye 6 times per day (at 2 hour intervals) for 8 weeks
        5. Storage issues: in the freezer at the pharmacy; patient keeps the individual vials in the fridge – once “actively ready” for use, then it is only stable for 12 hours
        6. ADRs: eye pain, inflammation, corneal deposits
  2. Innovation- loteprednol etabonate- Lotemax
     1. Lotemax SM 0.38%
  3. Innovations- Glaucoma
     1. Minimally Invasive Glaucoma Surgery- MIGS
        1. The iStent *inject* Trabecular Micro-bypass
           1. For patients with cataracts and glaucoma, iStent *injec*t is:
           2. FDA approved therapy for the treatment of elevated IOP in adult patients with mild-to-moderate primary open-angle glaucoma in conjunction with cataract surgery
           3. The first available *ab interno*, micro-bypass system designed to restore natural physiological outflow through two openings through the trabecular meshwork
  4. Innovations - Instruments
     1. OCT-A (Angiography)
        1. Normal Retinal Vasculature
           1. What Does Glaucoma Look Like?
           2. Case Presentation of Patient with Diabetes

Diabetes 12-19-2018 OD

Diabetes 12-19-18 OS

* + 1. Visual Field Threshold Strategy
       1. Sita Faster
          1. Turns off False Negatives
          2. Turns off Blind Spot monitor
          3. Leaves on False Positives
          4. Leaves on Gaze Tracking
          5. Faster test with same reliability
       2. Visual field threshold pattern 24-2C
          1. Glaucomatous damage of the macula is common and can occur early in the disease
          2. Can be missed or underestimated or both, with standard 24-2 VF tests that use a 6°grid
          3. Highest Importance Locations Chosen from 10-2 Pattern
          4. The expert group selected specific 10-2 test point locations
          5. Prevalence and depth of glaucomatous macular defects were systematically evaluated to select optimum test points
          6. Pattern covers areas known to be susceptible to glaucomatous defects both from structural and functional studies
          7. SITA Faster 24-2C showed enhanced sensitivity to detect visual field loss in Central 10 degrees
          8. SITA Faster 24-2C showed an enhanced sensitivity to detect visual field loss in the central 10 degrees over the SITA Fast 24-2 pattern
          9. Increased total and pattern deviation flagging of the ten additional SITA Faster 24-2C points corresponded to the flagging of the same points tested on the SITA Fast 10-2 test
          10. Minimize Time and Maximize Information with HFA3
          11. More information in the central field
          12. ~20% faster than SITA Fast 24-2
    2. The Icare® HOME tonometer
       1. Handheld
       2. Battery operated device
       3. Without the need for topical anesthetic
       4. Intended as an adjunct for monitoring IOP of adult patients (self-use)
       5. Caregivers in cases where the patient is not able to obtain their own measurements
       6. Light weight (26.5 mg) probe touches the cornea with low speed (0.25-0.30 m/s)
       7. IOP, date, time, eye recognition (right/left) and measurement quality are all stored in the internal memory.
       8. Data is transferred to a PC for further analysis by the prescribing physician.
       9. New features: positioning light, automatic eye recognition system, series or single measurements, new user interface panel.
       10. IcareEyeSmart:Automatic Eye Recognition
           1. The tonometer includes an automatic eye recognition system that identifies which eye is being measured.
           2. Two infrared LED transmitters below probe (1)
           3. One infrared LED sensor above probe (2)
           4. The infrared light is reflected from nose back to the sensor
           5. The sensor knows from which transmitter the reflected infrared light came from and thus which eye, right or left, was measured
       11. The resulting eye indication is stored into the memory of the tonometer
       12. Rebound Tonometry is Safe
           1. No significant safety issues reported for the Icare® ic100 & TA01i tonometers with a large number sold worldwide (40,000) and in the United States (9,000)
           2. In use by health care personnel with varying degrees of tonometer experience and some of which have little or no ophthalmic training.
           3. No significant safety issues reported for the Icare® HOME tonometer or its predecessor, Icare ONE; over 2,000 tonometers in use worldwide
           4. Majority in Europe after Icare ONE received CE mark in late 2009 and was introduced in 2010.
       13. Why 24 Hr Monitoring?
           1. 24 hour IOP monitoring can reveal higher peaks and wider fluctuations of IOP than those found during routine office visits. Research reports a steady daily increase in IOP in some patients being treated for glaucoma.
           2. Barkana Y, Anis S, Liebmann J, et al. Arch Ophthalmol. 2006;124:793-797.
           3. Studies have shown IOP rises when a patient is supine; IOP peaks were measured upon awakening and declined within 30 minutes.
  1. Innovations in Wide Field Technology
     1. *Optos- Monaco*
        1. The only ultra-widefield retinal imaging device with integrated OCT enabling eye care professionals enhance their clinical exams and improve practice economics
        2. provides more information faster
        3. *Monaco* can capture color and optomap *af* images along with posterior pole OCT scans of both eyes in as little as 90 seconds.
        4. This quick, comprehensive look inside the eye has been shown to enhance pathology detection and significantly improve clinic flow.
     2. Zeiss- Clarus
        1. Case Presentation
        2. Case Presentation
        3. Case Presentation

1. Questions
2. Thank you!