Oral Pharmaceuticals in Ocular Surface Infection and Inflammation

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OSDs are Difficult to Tell Apart: Overlapping Signs/Symptoms

<table>
<thead>
<tr>
<th>Signs</th>
<th>Symptoms</th>
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</thead>
<tbody>
<tr>
<td>Hyperemia</td>
<td>Foreign Body Sensation</td>
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<tr>
<td>Chemosis</td>
<td>Burning</td>
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<tr>
<td>Lid Swelling</td>
<td>Dry, Gritty Ocular Surface</td>
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<td></td>
<td>Itchy Eyes</td>
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<td></td>
<td>Photophobia</td>
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<td></td>
<td>Tearing</td>
</tr>
</tbody>
</table>

CASE

• 20 year old male presents with a red painful eye
  – Started that morning when he woke up
  – Reports a watery discharge, no itching, and is not a contact lens wearer
• SLE:
  – See attached image with NaFl stain

Herpes Simplex Keratitis: Clinical Features

• Characterized by primary outbreak and subsequent reactivation
• Primary outbreak is typically mild or subclinical
• After primary infection, the virus becomes latent in the trigeminal ganglion or cornea
• Stress, UV radiation, and hormonal changes can reactivate the virus
• Lesions are common in the immunocompromised (i.e. recent organ transplant or HIV patients)

Dendritic Ulcers
Herpes Simplex Keratitis

- Topical:
  - Viroptic (trifluridine) q 2h until epi healed then taper down for 10-14 days.
  - Viroptic is toxic to the cornea.
  - Zirgan (ganciclovir) available, use 5 times a day until epi healed then 3 times for a week (US only)
- Oral acyclovir (2 g/day) has been reported to be as effective as topical antivirals without the toxicity
  - Valtrex (valcyclovir) 500 mg TID for 7-10 days
  - Famvir (famciclovir) 250 mg TID for 7-10 days
- If stromal keratitis present, after epi defect has healed, add Pred Forte QID until inflammation reduced and then slowly taper

Prophylaxis??

- Prophylaxis of 400 mg acyclovir BID vs placebo for 1 year resulted in a lower recurrence in the treatment arm (19% vs 32%)
  - Valtrex 500 mg qd was found to be equivalent to acyclovir BID
- Pitfalls to Prophylaxis:
  - Reduction of recurrence does not persist once drug stopped
  - Resistance????
    - van Velzen, et. al., (2013) demonstrated that long-term ACV prophylaxis predisposes to ACV-refractory disease due to the emergence of corneal ACVR HSV-1.

Question

A 30 yr old female patient presents on an emergent basis complaining that she wakes up in the morning with a sharp stabbing pain in her right eye. It gets better as the day goes on but has been happening frequently over the past several months. What would you recommend for this patient?

1. Hyperosmotics
2. Doxycycline 50 mg bid for 6-8 weeks
3. Stromal puncture
4. Amniotic membrane transplant
5. Debridement
6. PTK
Recurrent Corneal Erosion: Treatment

• If severe enough to cause vision loss or repeated episodes:
  • oral doxycycline with/without topical corticosteroid
    – Doxy 50 mg bid and FML tid for 4-8 weeks
    – both meds inhibit key metalloproteinases important in disease pathogenesis
    – Azasite (topical azithromycin) (off label use)
• debridement,
• stromal puncture, or
• PTK
• Latest development: amniotic membrane transplant e.g. Prokera

Amniotic Membrane Transplant

• Amniotic membrane is a biologic tissue with:
  – antiangiogenic,
  – antiscarring,
  – antimicrobial, and
  – anti-inflammatory properties that promotes healing of the ocular surface
• Amniotic membrane grafts have been used for a variety of ocular conditions including:
  – Corneal burns
  – Neurotrophic ulcers
  – Stem cell damage
  – Persistent epithelial defects

Amniotic Membrane Transplant

• Traditionally, amniotic membrane grafts had to be sutured
  – With the advent of tissue adhesives, amniotic transplants can now be sutureless
• ProKera was approved by the FDA in 2003 as a Class II medical device which has a polycarbonate ring which holds a cryopreserved amniotic membrane
• ProKera is indicated in the treatment of corneal erosions, neurotrophic corneas, recalcitrant corneal inflammation, acute ocular surface burns, acute Stevens Johnson syndrome, and descemetoceles.

Question

A 75 year old patient presents with blisters on his forehead and nose and the following ocular presentation. What is your treatment?

1. No treatment
2. Topical trifluridine every 2 hours
3. Oral acyclovir 800 mg 5x/day
4. Topical Pred Forte QID
5. Oral acyclovir 400 mg 5x/day
Herpes Zoster Ophthalmicus

Herpes Zoster

- Associated factors include increasing age, immune deficiency and stress.
- Management includes:
  - oral antivirals (800mg acyclovir 5x/day,
  - valacyclovir (Valtrex) 1g TID,
  - famciclovir (Famvir) 500 mg TID
- effectiveness of therapy is best started within 72 hours
- oral steroids, and
- management of pain (tricyclic antidepressants, gabapentin).
- If ocular complications, consider topical steroids (Pred Forte QID).

Herpes Zoster

- Presents with:
  - pain and tingling in region of skin supplied by V few days before lesions,
  - malaise and fever,
  - papulomacular then pustular rash,
  - mucopurulent conjunctivitis,
  - uveitis, glaucoma, episcleritis, keratitis, and retinitis can all occur.
  - neurological complications include cranial nerve palsies and optic neuritis.

Corneal Ulcers

- Infective bacterial and fungal corneal lesions cause severe pain and loss of vision
- Signs and Symptoms:
  - Pain, photophobia, tearing
  - Mucopurulent discharge with generalized conjunctival injection
  - Decreased VA (esp if on visual axis)
  - Possible AC reaction and hypopyon
  - Dense infiltrate
  - Satellite lesions around main lesion may indicate fungal infection
**Associated Factors**

- Contact lens wear, especially soft and extended wear lens
- Recent history of corneal trauma
- Topical steroid use
- History of exposure to vegetative matter (fungal etiology)

**When to culture?**

- 1,2,3 Rule:
  - 1 mm from visual axis
  - 2 infiltrates (or more)
  - 3 mm or greater in size
- Nosocomial infections
- Immuno-compromised patient
- Post-surgical

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**Sterile vs Infectious Infiltrates**

<table>
<thead>
<tr>
<th>Sterile Infiltrates vs. Infectious Infiltrates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sterile Infiltrates</td>
</tr>
<tr>
<td>Smaller lesion (&lt; 1 mm)</td>
</tr>
<tr>
<td>More peripheral</td>
</tr>
<tr>
<td>Minimal epithelial damage</td>
</tr>
<tr>
<td>(size compared to underlying infiltrate)</td>
</tr>
<tr>
<td>No mucus discharge</td>
</tr>
<tr>
<td>Less pain and photophobia</td>
</tr>
<tr>
<td>Little to no anterior chamber reaction</td>
</tr>
<tr>
<td>No lid involvement</td>
</tr>
</tbody>
</table>


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**Peripheral (Sterile) Corneal Ulcer**

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**Infectious Corneal Ulcer**

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**Corneal Ulcers**

- The Steroids for Corneal Ulcers Trial (SCUT)
- Conclusions:
  - No overall difference in 3-month BSCVA and no safety concerns with adjunctive corticosteroid therapy for bacterial corneal ulcers
  - Researchers did find significant vision improvement for one specific subgroup of the study by using steroid therapy on patients with severe ulcers
- Application to Clinical Practice:
  - Adjunctive topical corticosteroid use does not improve 3-month vision in patients with bacterial corneal ulcers unless in the severe category
Management

- Infective ulcers need to be cultured!
- If contact lens wearer, consider culture of contact lens
- Intensive topical antibiotic regimen, consider fortified preparations, subconjunctival injections.
  - loading dose of Vigamox/Moxeza/Zymaxid/Besivance 2gtts q 15 min x 1 hour,
  - 1gt q 30 min x 6 hours,
  - 1 gt q 1 hr until f/u in 24 hours.

Protein Synthesis Inhibitors

- These antibiotics work by targeting the bacterial ribosome.
  - they are structurally different from mammalian ribosomes,
  - in higher concentrations many of these antibiotics can cause toxic effects.
- This group includes:
  - (a) tetracyclines, (b) aminoglycosides, (c) macrolides,
  - (d) chloramphenicol, (e) clindamycin, (f) quinupristin/dalfopristin and (g) linezolid

Tetracyclines

- Nonresistant strains concentrate this antibiotic intracellularly resulting in inhibition of protein synthesis.
- Broad spectrum, bacteriostatic,
  - effective against gram (+) and (-) bacteria and against non-bacterial organisms
  - widespread resistance has limited their use.
- Drug of choice for Rocky Mountain Spotted Fever, Cholera, Lyme disease, mycoplasma pneumonia, and chlamydial infections.
- Side effects include gastric discomfort, phototoxicity, effects on calcified tissues, vestibular problems, pseudotumor.

Tetracyclines

- This group includes:
  - Tetracycline (250mg - 500 mg cap BID-OID) needs to be taken 1 hour before or 2 hours after a meal.
  - Minocycline (100 mg cap BID)
  - Doxycycline (20mg - 100 mg cap or tab BID)

Anti-inflammatory effects

- Degrade extracellular proteins
- Tetracyclines inhibit MMPs
- Anti-inflammatory

Pseudomonas case report

2 young patients
Severe contact lens-associated Pseudomonas keratitis
Corneal melting
Treated with oral doxycycline and standard topical treatment


Results
Corneal melting stabilized
Perforation avoided

Pseudomonas case report

Doxycycline as an adjunctive therapy...may help to stabilize corneal breakdown and prevent subsequent perforation.

AM. McElvanney

Tetracyclines: Acne Rosacea

- **Acne rosacea:**
  - affects females>males after 30 with peak incidence 4-7th decade of Celtic/Northern European descent. Males more disfigured.
  - 4 subtypes with classic signs of flushing, papules or pustules usually in crops, telangectasia.
    - secondary ocular complications (85% of patients) and often precede other skin manifestations include erythema, itching and burning.
- **Mainstay oral Tx is Oracea (40 mg in morning) or:**
  - tetracycline 500 mg po BID or doxycycline 50 mg po qd or minocycline 100 mg po qd for 4-12 wks.
  - **NOTE: Oracea is subantimicrobial therapy**

Acne Rosacea Treatments

<table>
<thead>
<tr>
<th>Oral Antibiotics</th>
<th>Topical Treatments</th>
<th>Non-Prescription</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythromycin</td>
<td>Retin-A</td>
<td>Rosacea, tol.</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>Benzoyl peroxide</td>
<td>Zenmed.</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>Benzoyl peroxide</td>
<td>Nacea Therapy.</td>
</tr>
<tr>
<td>Minocycline</td>
<td>Tetracycline</td>
<td>Erythromycin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rosacea</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Neova Therapy.</td>
</tr>
</tbody>
</table>

www.internationalrosaceafoundation.org

Hyperacute Conjunctivitis

- Hyperacute conjunctivitis:
  - usually secondary to gonorrhea or chlamydia.
  - profuse purulent discharge.
  - pain.
  - redness.
  - chemosis.
  - papillae.
  - positive nodes

Chlamydia

- **Chlamydia is the most frequently reported bacterial sexually transmitted disease in the United States**
- **Chlamydia is known as a "silent" disease because the majority of infected people have no symptoms**
  - if symptoms do occur, they usually appear within 1 to 3 weeks after exposure
  - women who have symptoms might have an abnormal vaginal discharge or a burning sensation when urinating
  - men with signs or symptoms might have a discharge from their penis or a burning sensation when urinating
  - men might also have burning and itching around the opening of the penis.

www.internationalrosaceafoundation.org

www.internationalrosaceafoundation.org
Chlamydia: Treatment

**Recommended Treatment Regimens:**
- **Azithromycin** 1 g orally in a single dose
- **Doxycycline** 100 mg orally twice a day for 7 days

**Alternative Treatment Regimens:**
- **Erythromycin base** 500 mg orally four times a day for 7 days
- **Erythromycin ethylsuccinate** 800 mg orally four times a day for 7 days
- **Levofoxacin** 500 mg orally once daily for 7 days
- **Ofloxacin** 300 mg orally twice a day for 7 days

Chlamydia: Treatment

**Azithromycin versus doxycycline:**
- For the treatment of genital chlamydial infection treatments were equally efficacious.
- Azithromycin should always be available to treat patients for whom compliance with multiday dosing is uncertain.
- In patients who have erratic health-care-seeking behavior, poor treatment compliance, or unpredictable follow-up, azithromycin might be more cost-effective in treating chlamydia because it enables the provision of a single-dose of directly observed therapy.
- Levofloxacin and ofloxacin are effective treatment alternatives but are more expensive and offer no advantage in the dosage regimen.
- Other quinolones either are not reliably effective against chlamydial infection or have not been evaluated adequately.

Gonorrhea

- Some men with gonorrhea may have no symptoms at all.
- Signs or symptoms appear 1 to 14 days after infection.
- Signs and symptoms include a burning sensation when urinating, or a white, yellow, or green discharge from the penis.
- Sometimes men with gonorrhea get painful or swollen testicles.

- In women, the symptoms of gonorrhea are often mild, but most women who are infected have no symptoms.
- Symptoms can be so non-specific as to be mistaken for a bladder or vaginal infection.
- Initial symptoms and signs in women include a painful or burning sensation when urinating, increased vaginal discharge, or vaginal bleeding between periods.
- Risk of developing serious complications from the infection, regardless of the presence or severity of symptoms.

Gonorrhea Treatment

- **Adult cervical/urethral infection:**
  - **Ceftriaxone** (Rocephin) IM injection of 250 mg in a single dose.
  - If not an option then:
    - **Cefixime** (Suprax) 400 mg oral in a single dose.

- **Alternative treatments include:**
  - **Azithromycin** 1 gram single dose.
  - **Doxycycline** 100 mg BID 7-10 days.

- **Neonatal:** 25-50 mg/kg, up to 125 mg IV/IM ceftriaxone daily for 7 days.

- Syphilis, gonorrhea, chlamydia, chancroid, HIV infection, and AIDS are reportable diseases in every state.

Allergic Conjunctivitis

- Allergies affect as many as 40 to 50 million Americans.
- Incidence and prevalence of allergic conjunctivitis has been rising over the last 40 years.
**Signs and Symptoms of Allergic Conjunctivitis**

Clinical presentation – bilateral

**Signs:**
- Conjunctival edema
- Conjunctival hyperemia
- Chemosis
- Lid edema
- Watery discharge

**Symptoms:**
- Itching
- Burning
- Photophobia
- Foreign body sensation
- Blurred vision

**Mast Cell Cascade**

**Treatment**

• Ocular allergy sufferers need:
  – fast relief of signs and symptoms,
  – long-lasting therapeutic effects,
  – comfortable and safe topical drugs,
  – convenient treatment regimen

• Therapeutic focus is mostly confined to the suppression of mast cells, their degranulation and the effects of histamine and other mast-cell derived mediators.

**Treatment of Ocular Allergy**

**Medications:**
- Topical OTC drops
- Oral antihistamines (prescription and OTC)
- Topical NSAID drops
- Topical antihistamines
- Topical mast cell stabilizers
- Topical steroid drops
- Topical dual-action drugs (antihistamine/mast cell stabilizers)

**Oral Allergy Medications**

• Oral antihistamines (pills and liquids) ease symptoms such as:
  – swelling,
  – runny nose,
  – itchy or watery eyes, and
  – hives (urticaria).

• Some oral antihistamines may cause dry mouth and drowsiness.

• Older antihistamines such as diphenhydramine (Benadryl), chlorpheniramine (Chlor-Trimeton) and clemastine (Tavist) are more likely to cause drowsiness and slow reaction time.
  – these sedating antihistamines shouldn’t be taken when driving or doing other potentially dangerous activities.

**OTC Allergy Medications**

<table>
<thead>
<tr>
<th>Generic</th>
<th>Brand</th>
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<tbody>
<tr>
<td>Diphenhydramine</td>
<td>Benadryl</td>
</tr>
<tr>
<td>Chlorpheniramine</td>
<td>Chlor-Trimeton</td>
</tr>
<tr>
<td>Clemastine</td>
<td>Tavist</td>
</tr>
<tr>
<td>Loratadine</td>
<td>Claritin</td>
</tr>
<tr>
<td>Cetirizine</td>
<td>Zyrtec</td>
</tr>
<tr>
<td>Fexofenadine</td>
<td>Allegra (both OTC and Rx)</td>
</tr>
</tbody>
</table>
Prescription Allergy Medications

<table>
<thead>
<tr>
<th>Medication</th>
<th>Brand Names</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbinoxamine maleate</td>
<td>ARBINOXA, PALGIC (tabs, solution)</td>
</tr>
<tr>
<td>Diphenhydramine HCl</td>
<td>BENADRYL Injection</td>
</tr>
<tr>
<td>Hydroxyzine HCl</td>
<td>HYDROXYZINE HCL (tabs, syrup)</td>
</tr>
<tr>
<td>Desloratadine</td>
<td>CLARINEX (tabs, ODT, syrup)</td>
</tr>
<tr>
<td>Fexofenadine HCl</td>
<td>ALLEGRA (tabs, ODT, suspension)</td>
</tr>
<tr>
<td>Levocetirizine dihydrochloride</td>
<td>XYZAL (tabs, solution)</td>
</tr>
<tr>
<td>Montelukast</td>
<td>SINGULAIR (tabs, chew tabs, granules)</td>
</tr>
<tr>
<td>Cromolyn sodium</td>
<td>GASTROCRAM (oral solution)</td>
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Ocular Allergy Medication Options

<table>
<thead>
<tr>
<th>Medication</th>
<th>Brand Names</th>
</tr>
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<tbody>
<tr>
<td>Tetrahydrazoline HCl</td>
<td>VISINE*, MURINE® Plus</td>
</tr>
<tr>
<td>Naphazoline HCl</td>
<td>NAPHCON® eye drops, VASOCOM®</td>
</tr>
<tr>
<td>Phenylephrine HCl</td>
<td>PREFRIN</td>
</tr>
<tr>
<td>Oxytetrahydrozoline HCl</td>
<td>VISION® L.R.*</td>
</tr>
<tr>
<td>Naphazoline/Antazoline</td>
<td>VASOCOM®-A</td>
</tr>
<tr>
<td>Naphazoline/Pheniramine</td>
<td>VASOCOM®-A</td>
</tr>
<tr>
<td>Ketorolac</td>
<td>ACULAR*</td>
</tr>
<tr>
<td>Suprofen</td>
<td>PROFENAL® solution</td>
</tr>
<tr>
<td>Diclofenac</td>
<td>VOLTAREN®</td>
</tr>
<tr>
<td>Lodoxamide</td>
<td>ALOMIDE® solution</td>
</tr>
<tr>
<td>Ketotifen</td>
<td>OPTIVAR®, LASTIN*.</td>
</tr>
<tr>
<td>Pemirolast</td>
<td>ALAMAST®</td>
</tr>
<tr>
<td>Azelastine</td>
<td>ALOCRIL®, TILAVIST*</td>
</tr>
<tr>
<td>Emadastine</td>
<td>EMADINE® solution</td>
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<tr>
<td>Loteprednol</td>
<td>ALREX®</td>
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<tr>
<td>Rimensol</td>
<td>VELOX® suspension</td>
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<tr>
<td>Levocabastine</td>
<td>LIVOSTIN®</td>
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<tr>
<td>Epinastine</td>
<td>ELESTAT®</td>
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<tr>
<td>Olopatadine</td>
<td>PATANOL®</td>
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<tr>
<td>Nedocromil</td>
<td>PATADAY®</td>
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<td>Bepotastine</td>
<td>BEPREVE®</td>
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<td>Azelastine</td>
<td>ALAWAY®</td>
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<tr>
<td>Ketotifen</td>
<td>ZAZITOR®, CLARITIN, ALAWAY®</td>
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<tr>
<td>Epinastine</td>
<td>ELESTAT®</td>
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<td>Rimexolone</td>
<td>PATADAY®</td>
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<tr>
<td>Nedocromil</td>
<td>BEPREVE®</td>
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<tr>
<td>Alcaftadine</td>
<td>LASTACAFT</td>
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Sinusitis Red Eye

- With a sinus infection or inflammation, the sinuses swell and mucus cannot properly drain.
- The increase in mucus and the narrow passage through which it tries to escape creates pressure in the sinuses that leads to pain.
- The sinuses surround the ocular region—pressure from sinuses may feel like eye pressure.
- Swollen sinuses and nasal membranes can push against ocular nerves resulting in pain.
- Pooled mucus can result in infection that increases the pain in the sinus and ocular region even more.

Sinusitis Treatment

- The infection is likely bacterial and should be treated with antibiotics if:
  - symptoms last for 10 days without improvement, or
  - include fever of 102 degrees or higher;
  - nasal discharge and facial pain lasting three to four days
- Because of increasing resistance to the antibiotic amoxicillin—the current standard of care—the ISDA recommends Augmentin
- Augmentin 250/500 TID for 5-7 days for adults, 10-14 days for children
  - If allergic or failure with Augmentin then Keflex 500 mg QID for 7-10 days

Blepharitis

Icare in America

- Expert group convened to review the results of a recent landmark survey of patient and eye care specialist perceptions regarding the impact of Blepharitis in America
  - Survey conducted July through September of 2008
- Methodology:
  - A telephone survey of a representative sample of the adult US population (N=5000)
    - Purposes was to elucidate the frequency of common symptoms associated with blepharitis
  - A study that queried ophthalmologists (n=120) and a similarly selected group of optometrists (n=84) about the frequency of:
    - Blepharitis in their clinical practice,
    - The existence of comorbid conditions, and
    - Their management strategies
Current Prevalence of Blepharitis

• Although blepharitis may be a frequently overlooked condition in the United States, ophthalmologists and optometrists report that blepharitis is commonly seen in 37% and 47% of their patients, respectively.

Blepharitis Patients Initial Motivation for Seeking Treatment

Tear Film & Ocular Surface Society (TFOS): Meibomian Gland Workshop

• The MGD Workshop was conducted to provide an evidence-based evaluation of meibomian gland structure and function in health and disease.
• MGD is an extremely important condition, conceivably underestimated, and very likely the most frequent cause of dry eye disease.
• The Report required over 2 years to complete and involved the efforts of more than 50 leading clinical and basic research experts from around the world.
• The International Workshop on Meibomian Gland Dysfunction: March 2011; 52 (4)

Differential Diagnosis of Blepharitis

Spectrum of Blepharitis

Anterior Blepharitis

Mixed

Posterior Blepharitis (MGD*)

Most Common

MGD

Stage Clinical Presentation Treatment

1

No symptoms of ocular discomfort, itching or photophobia
Clinical signs of MGD based on gland expression
Minimally altered secretions: Grade >2-<4 Expressibility: 1 No ocular surface staining

Inform patient about MGD, the potential impact of diet and the effect of work/home environments on tear evaporation, and the possible drying effect of certain systemic medications. Consider eyelid hygiene including warming/expressing as described below (D).

2

Minimal to mild symptoms of ocular discomfort, itching or photophobia
Minimal to mild MGD clinical signs
Scattered lid margin features
Mildly altered secretions: Grade >4-<8 Expressibility: 1
None to limited ocular surface staining

[DEWS grade 0-7; O xford grade 0-8]

Advise patient on improving ambient humidity, optimizing workstations and increasing dietary omega 3 fatty acid intake (D).
Institute eyelid hygiene with eyelid warming (minimum of four minutes, once or twice daily) followed by moderate to firm massage and expression of MG secretions (+).
All the above, plus (D)
Artificial lubricants (for frequent use, non-preserved preferred)
Topical emollient lubricant or liposomal spray
Topical tetracycline
Consider oral tetracycline derivatives

3

Moderate symptoms of ocular discomfort, itching or photophobia with definite limitations of activities
Moderate MGD clinical signs lid margin features: plugging, vacuole
Moderately altered secretions: Grade >8-<13 Expressibility: 2
Mild to moderate conjunctival and peripheral corneal staining often inferior [DEWS grade 8-23; Oxford grade 4-10]

All the above, plus (D)
Oral tetracycline derivatives (+)
Lubricant ointment at bedtime (D)
Anti-inflammatory therapy for dry eye as indicated (D)

4

Marked symptoms of ocular discomfort, itching or photophobia with definite limitations of activities
Severe MGD clinical signs lid margin features: dropout, displacement
Severely altered secretions: Grade >13 Expressibility: 3
Increased conjunctival and corneal staining, including central staining [DEWS grade 24-33; Oxford grade 11-15]
Signs of inflammation: e.g. moderate conjunctival hyperemia, phlyctenules

All the above, plus
Anti-inflammatory therapy for dry eye (+)
Signs and Symptoms of Blepharitis

- **Symptoms**
  - Burning
  - Irritation
  - Foreign body sensation (FBS)
  - Itching
  - Tired eyes
  - Photophobia
  - Contact lens intolerance

- **Signs**
  - Injected lid margin / conjunctiva
  - Telangiectasia (dilated blood vessels)
  - Swollen lid margin
  - Plugged, inflamed meibomian glands
  - Thickened meibomian gland secretion
  - Saponification
  - Lid debris

Pathophysiology of Blepharitis

- Inflammatory condition of the anterior lid margin and eyelashes
  - Bacterial exotoxins and/or delayed hypersensitivity to antigens
- Tends to be staphylococcal and/or seborrheic in nature
- Staphylococcal infection can be purulent or ulcerative and often causes angular blepharitis

Pathophysiology of MGD (previously Posterior Blepharitis)

- Altered meibomian gland (MG) secretions
  - Thickened secretion (rich in keratin)
  - Cicatricial obstructive disease with duct exposure and retroplacement of orifices
  - Epithelial hyperplasia/hyperkeratinization
  - Cystic dilation of ducts and acini
  - Atopy, psoriasis

- Inflammation
  - Hyperemia of the lid margin
  - Lid swelling

- Bacterial
  - Secretion of toxins, enzymes (lipases, esterases)

- Hypersecretory
  - Meibomian seborrhea
  - Acne rosacea

Treatment Goals for Blepharitis

- Long-term control of underlying pathophysiology:
  - Bacteria, inflammation and meibomian gland secretions
  - Improvement of signs and symptoms
  - Improve health of tear film lipid layer
- Reduce risk of fluctuating visual acuity
  - Reduce possible risk of progression to other conditions such as dry eye disease or chalazion
  - Improve outcomes in surgical procedures and comfortable contact lens wear time

Physicochemical Differences in Normal vs MGD Patients

- The thickened and turbid MG secretions in patients with MGD can be attributed to a more ordered lipid structure.
- Increased phase transition temperature noted with MGD correlates with the more ordered lipid structure seen in the graph on the left.

Treatment/Management

- **Lid hygiene (warm compresses and lid “scrubs”)**
  - New product:
    - Cliradex: incorporates “tea tree oil”
- **Oral doxycycline**
  - 50 mg bid for 7-14 days then qd for next 6-8 weeks
- **Topical azithromycin (off label)**
  - 1 gtt BID for 2 days then qhs for next 28 days
- **Omega 3 supplements**
Benign Eyelid Lesions: Hordeola
- Acute purulent inflammation
  - Internal occurs due to obstruction of MG
  - External (stye) from infection of the follicle of a cilium and the adjacent glands of Zeiss or Moll
- Painful edema and erythema,

Benign Eyelid Lesions: Hordeola
- Typically caused by Staph and often associated with blepharitis
- Treatment includes:
  - hot compresses,
  - topical antibiotics (?)
  - possibly systemic antibiotics
- Treat concurrent blepharitis

Benign Eyelid Lesions: Chalazia
- Focal inflammatory lesion resulting from obstruction of a meibomian or Zeis gland
- Results in a chronic lipogranulomatous inflammation

Benign Eyelid Lesions: Chalazia
- May drain spontaneously or persist as a chronic nodule
- Recurrent lesions need to exclude a sebaceous gland carcinoma
- Treatment varies from:
  - hot compresses/massage,
  - intralesional steroid injection or
  - surgical drainage.

Preseptal Cellulitis
- Infection and inflammation located anterior to the orbital septum and limited to the superficial periorbital tissues and eyelids.
- Usually follows sinus infection or internal hordeolum (possibly trauma)
- Eyelid swelling, redness, ptosis, pain and low grade fever.
- Tx:
  - Augmentin 500 mg TID or 875 mg BID for 5-7 days
  - Keflex 500 mg QID 5-7 days
  - or if moderate to severe IV Fortaz (ceftazidime) 1-2 g q8h.

Prevalence of Dry Eye Disease (DED)
- Prevalence estimated from 7.4% to 33.7% depending on study quoted, how DED is defined and patient population studied
- Affects women more than men
- Increases as patient population ages
- 14.4% of patients self-report history of dry eye
- 7.8% of women aged 45 to 84 were clinically diagnosed with DED (Beaver Dam Study)
- Affect on quality of life (QOL):
  - Mild DED = psoriasis
  - Moderate DED = moderate angina
  - Severe DED = class III/IV angina or disabling hip fracture
Case

- 55 yr white female complains of fluctuating vision
  - Worse at near
  - Spends 8-10 hours/day on the computer
- Medical Hx:
  - Hypertension for 10 years
  - Joint pain
- Medications:
  - HCTZ for HTN
  - Celebrex for her joint pain

Exam Data

- PERRL
- EOM β: FROM
- CVF: FTFC
- SLE:
  - TBUT 5 sec OD, OS
  - Positive NaFl staining and Lissamine green staining of conj and cornea
  - Decreased tear prism

Additional Testing/Questions

- Schirmer: < 5 mm of wetting in 5 minutes OD, OS
- RF and ANA: normal for patients age
- SSA: 2.0 (normal < 1.0), SS-B: 1.9 (normal < 1.0)
- Additional symptoms reported:
  - Patient experiences dry mouth and taking Salagen

  Diagnosis: Sjogren’s Syndrome

Differential Diagnosis of Dry Eye

InflammaDry

  • Point of care testing to measure MMP-9 levels
  - MMP-9 is an inflammatory biomarker found to be elevated in patients with dry eye
  - Marketed by RPS
Treatment

• We initiated:
  — Omega-3 supplements (3-4 grams per day)
  — Recommended warm compresses and lid washes qhs
  — Testosterone cream 3% applied to upper lid bid
• Patient had significant improvement in symptoms with the use of the topical testosterone cream.
  — However, she was still symptomatic at the end of the day and she still had significant staining on her cornea and conjunctiva
  — Initiated FML tid for 1 month, restasis bid after 2 weeks
  • 2 months later patient reported further improvement in her symptoms
  • No conjunctival staining was noted and only slight SPK
  • Schirmer values improved to OD: 9 mm, OS: 10 mm

Role of Androgens?

• Recent studies have suggested that androgen deficiency may be the main cause of the meibomian gland dysfunction, tear-film instability and evaporative dry eye seen in Sjogren patients
• Transdermal testosterone 3% promotes increased tear production and meibomian gland secretion, thereby reducing dry eye symptoms (Dr. Charles Connor).
• Progesterone 0.05%/Testosterone 0.05% Ophthalmic Solution BID (available from Leiter’s Pharmacy)

SJOGREN’S SYNDROME:
OLD/NEW CLASSIFICATION

• Old:
  — 1st Sjogren’s occurs when sicca complex manifests by itself
    • no systemic disease present
  — 2nd Sjogren’s occurs in association with collagen vascular disease such as
    • RA and SLE
    • significant ocular/systemic manifestations
• New:
  — The diagnosis of SS should be given to all who fulfill the new criteria while also diagnosing any concurrent organ-specific or multiorgan autoimmune diseases, without distinguishing as primary or secondary.

Ocular Surface Score (OSS)

• The ocular surface score (OSS) is the sum of:
  — 0-6 score for fluorescein staining of the cornea and
  — 0-3 score for lissamine green staining of both the nasal and temporal bulbar conjunctiva,
  — yielding a total score ranging from 0-12.

Diagnosis: New Criteria

• Sjogren & International Collaborative Clinical Alliance (SICCA) was funded by the National Institutes of Health to develop new classification criteria for SS
• New diagnostic criteria requires at least 2 of the following 3:
  — 1) positive serum anti-SSA and/or anti-SSB or (positive rheumatoid factor and antinuclear antibody titer >1:320),
  — 2) ocular staining score >3, or
  — 3) presence of focal lymphocytic sialadenitis with a focus score >1 focus/4 mm2 in labial salivary gland biopsy samples

Sjö Diagnostic Test
Sjo Diagnostic Test

Sjo: new diagnostic test for Sjogrens

- Novel biomarkers:
  - SP-1 (salivary gland protein-1),
  - CA-6 (carbonic anhydrase-6) and
  - PSP (parotid secretory protein).
- Traditional tests use ANA, SS-A and SS-B and RF antibodies which have significant limitations of sensitivity and/or specificity and are associated with later-stage disease.
- During studies, these novel antibodies were found in 45% of patients meeting the criteria for Sjogren’s Syndrome who lacked the traditional antibodies for SS-A and SS-B.

Dry Eye and Lid Disease?

- It is estimated that 67-75% of patients who have dry eye have some form of lid disease
  - it is often the most overlooked cause for dry eye symptoms
- Important to address the lids in any treatment plans for patients with dry eye

Treatment/Management

<table>
<thead>
<tr>
<th>TIS Severity</th>
<th>Treatment Recommendation</th>
</tr>
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<tbody>
<tr>
<td>Tier 1</td>
<td>No treatment</td>
</tr>
<tr>
<td>Tier 2</td>
<td>Use of hypoosmotic products</td>
</tr>
<tr>
<td>Tier 3</td>
<td>Water intake</td>
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<tr>
<td>Tier 4</td>
<td>Psychological support</td>
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<tr>
<td>Tier 5</td>
<td>Avoidance of drugs contributing to dry eye</td>
</tr>
<tr>
<td>Tier 6</td>
<td>Secretagogues</td>
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<tr>
<td>Tier 7</td>
<td>Tears and ocular surface</td>
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<tr>
<td>Tier 8</td>
<td>Setting factors with dry eye</td>
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<tr>
<td>Tier 9</td>
<td>Topical steroids</td>
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<tr>
<td>Tier 10</td>
<td>Topical cyclosporine</td>
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<tr>
<td>Tier 11</td>
<td>Nutrition support (lactate acid)</td>
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<td>Punctal plugs</td>
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<tr>
<td>Tier 13</td>
<td>Surgery</td>
</tr>
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<td>Prosthetic devices</td>
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<tr>
<td>Tier 16</td>
<td>Oral cyclosporine</td>
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<tr>
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<td>Contact lenses</td>
</tr>
<tr>
<td>Tier 18</td>
<td>Moisture plugs</td>
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Thank You!!!