Course #

127

Breakfast With The Experts: Ocular Surface Infections
Breakfast with the Experts:
Ocular Surface Infections

Alan G. Kabat, OD, FAAO
Memphis, Tennessee

Course description: This peer-to-peer discussion will be led by an expert in the area of ocular surface infection. Participants will be asked to bring cases and questions, and the leader will facilitate a roundtable discussion on the related topic.

SPEAKER FINANCIAL DISCLOSURE STATEMENT
Dr. Alan Kabat has received honoraria and/or consulting fees during the last twelve months from: Alcon, BioTissue, Nicox and TearScience.

Learning objectives/outcomes: At the conclusion of this lecture, the attendee will be able to...

1. Recognize the broad range of microbial pathogens implicated in ocular surface infection.
2. Identify the key presenting signs and symptoms, as well as appropriate laboratory testing to differentiate these various pathogens.
3. Develop a logical and responsible management strategy for treating these disorders, involving topical and/or oral pharmaceutical agents and surgical intervention where appropriate.

Infectious Microorganisms
- Bacteria
- Viruses
- Fungi
- Protozoa
- Other parasites (e.g. pediculosis)

Anti-infective Therapies
- Antibiotics
  - Most common group of commercially available antimicrobial agents
  - Have specificity for bacteria based upon metabolic and structural differences between host cell and pathogen cell.
  - Must differentiate from preservatives (e.g. benzalkonium chloride, thimerosol), which are non-specific agents that impart toxicity to all cells
- Anti-virals
- Antifungals
- Other antimicrobials (e.g. pediculocides, amoebicides)
Indications for Topical Antibiotic Therapy

- Bacterial Conjunctivitis
- Blepharitis (Acute vs. Chronic)
- Bacterial Keratitis
- Ocular Trauma Prophylaxis
- Surgical Prophylaxis **
  - Accounts for ~85% of antibiotic prescriptions in U.S. today

Antibiotics – Weighing the Options

<table>
<thead>
<tr>
<th>(Chloramphenicol)</th>
<th>Fluoroquinolones</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Tetracycline)</td>
<td></td>
</tr>
<tr>
<td>Polypeptides</td>
<td></td>
</tr>
<tr>
<td>• Bacitracin</td>
<td>• Norfloxacin</td>
</tr>
<tr>
<td>• Polymyxin B</td>
<td>• Ofloxacin</td>
</tr>
<tr>
<td>Sulfacetamide</td>
<td>• Ciprofloxacin</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>• Levofloxacin</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>• Gatifloxacin</td>
</tr>
<tr>
<td>Trimethoprim</td>
<td>• Moxifloxacin</td>
</tr>
<tr>
<td>Aminoglycosides</td>
<td>• Besifloxacin</td>
</tr>
<tr>
<td>• Neomycin</td>
<td></td>
</tr>
<tr>
<td>• Gentamicin</td>
<td></td>
</tr>
<tr>
<td>• Tobramycin</td>
<td></td>
</tr>
</tbody>
</table>

Management of Bacterial Conjunctivitis

- A self-limited disorder... so why treat?
  - Reduce symptoms & shorten course
  - Reduce the risk of contagious spread
- Fluoroquinolones (4th generation or later) represent the current standard of care
- Ancillary treatment:
  - Cold compresses
  - Artificial tears / irrigation
- Corticosteroids are usually not necessary
  - Topical NSAIDs can provide analgesia for symptomatic keratoconjunctivitis
- Educate patients regarding the contagious nature of this condition

Management of Bacterial Keratitis

- Significant risk of permanent visual loss - treatment must be prompt and aggressive
  - Vital MC, Belloso M, Prager TC, Lanier JD. Classifying the severity of corneal ulcers by using the "1, 2, 3" rule. Cornea. 2007;26(1):16-20.
  - 1, 2, 3 Rule defines “potentially sight threatening” ulcers:
    - Anterior chamber reaction ≥ 1+ (≥10 cells in 1 mm beam)
    - Dense infiltrate ≥2 mm in size (greatest linear dimension)
    - Edge of infiltrate ≤3 mm from center of the cornea
- Broad spectrum antibiosis - empirical therapy
  - *Loading dose* and frequent administration, consistent with severity of ulceration
  - Fluoroquinolones: CILOXAN, OCUFLOX, IQUIX
    - “off label” - VIGAMOX
  - Fortified aminoglycosides and/or cephalosporins
    - Fortified antibiotics are not FDA approved for bacterial keratitis management

- The role of corticosteroids in bacterial keratitis management
  - Philosophy:
    - Under ideal conditions, antibiotics rapidly eradicate bacterial pathogens
    - Inflammatory cascade is the body’s natural defense against invasion...
      inflammatory “momentum” persists after pathogen is removed
    - White cells and their by-products (cytokines, proteases, etc.) impact bodily tissues in a negative way – autoimmune disease
    - Suppression of immune response is CRUCIAL to prevent additional tissue damage
      ★ Steroids can potentially hasten symptomatic recovery and diminish scarring
  - References / Scientific Evidence:

Viral Infections of the Anterior Segment
- Adenoviruses
  - Non-specific viral conjunctivitis & pharygoconjunctival fever
  - Epidemic keratoconjunctivitis (EKC - serotypes 8, 19, 37)
  - Clinical signs:
    - preauricular lymphadenopathy
    - follicular conjunctivitis ± pseudomembrane,
    - hyperemia and eyelid edema
    - subepithelial infiltrates
- Herpes viruses
  - H. simplex
  - H. zoster
Indications for Topical Antiviral Therapy

- Herpetic (*Herpes simplex*) keratitis
- Herpetic keratouveitis
- Herpetic blepharoconjunctivitis (prophylaxis)

- What about viral conjunctivitis (e.g. EKC)?
  - Adenoviruses are IMMUNE to all topical antiviral agents; however, some practitioners have achieved success with topical 5% povidone-iodine solution [Melton R, Thomas R. Stop EKC with a ‘silver bullet’. Review of Optometry. 2008 Nov;145(11)].

- What about *Herpes zoster* infections?
  - Zoster infections are treated systemically; the use of topical antivirals is not indicated
  - Options include:
    - Acyclovir – 800 mg PO q4 hrs X 7-10 days
    - Famciclovir (FAMVIR) – 500 mg PO q8 hrs X 7 days
    - Valacyclovir (VALTREX) – 1000 mg PO q8 hrs X 7 days

Herpes Simplex Keratitis – Presentation

- Recurrent disease
- Unilateral in 80% of cases
- Clinical findings:
  - Non-descript epitheliopathy; evolves into dendrite with “terminal end-bulbs”
    - NaFl / rose bengal (or lissamine green)
  - Corneal hypoesthesia
  - Attendant uveitis is common

Herpes Simplex Keratitis – Management

- Self-limiting infection
  - Intact immune system will suppress organism; HOWEVER
  - Visual disability could ensue without treatment
- Corneal debridement
- Topical antiviral therapy...
Topical Anti-Herpetic Agents

**VIROPTIC™** - trifluridine 1% solution

- FDA approved April 10, 1980
- Monarch Pharmaceuticals – Bristol, TN
- Preserved with 0.001% thimerosal
- pH = 5.5 - 6.0
- Indication: for primary keratoconjunctivitis and recurrent epithelial keratitis due to herpes simplex virus, types 1 and 2
- Dosing: 1 drop every 2 hours while awake for a maximum daily dosage of 9 drops until the corneal ulcer has completely re-epithelialized; then, 1 drop every 4 hours while awake for a minimum daily dosage of 5 drops, for an additional 7 days

**ZIRGAN™** - ganciclovir 0.15% gel

- FDA approved September 15, 2009
- Bausch+Lomb – Tampa, FL
- Preserved with 0.0075% BAK
- pH = 7.4
- Indication: for the treatment of acute herpetic keratitis (dendritic ulcers)
- Dosing: 1 drop in the affected eye 5 times per day (approximately every 3 hours while awake) until the corneal ulcer heals; then 1 drop 3 times per day for 7 days

★ **VIROPTIC has been the standard of care in the U.S. for almost 30 years; ZIRGAN offers more convenient dosing and significantly diminished toxicity.**

- Additional considerations:
  - Topical corticosteroids are ABSOLUTELY contraindicated
    - Corticosteroids will suppress the immune response, and can cause the virus to flourish
    - Use of steroids in HSV keratitis is associated with progression to geographic ulceration and secondary scar formation
  - Role of oral antivirals:
    - Can achieve therapeutic concentrations in tears
    - Not helpful when used adjunctively to topical, but may be used in patients who lack dexterity or compliance with topical medications
    - Appropriate therapy is acyclovir 400 mg PO q4h (5 times/day) for 10 days

Herpes zoster (Varicella) infections

- Current therapy for herpes zoster (Varicella) infections:
  - Acyclovir – 800 mg PO q4 hrs X 7-10 days
  - Famciclovir – 500 mg PO q8 hrs X 7 days
  - Valacyclovir – 1000 mg PO q8 hrs X 7 days
Fungal keratitis

- Presentation:
  - Most commonly associated with trauma
  - Approx. 1500 cases a year in the US
- Organisms:
  - Fusarium & Aspergillus (filamentous - hyphae)
  - Candida (yeast - unicellular)
- Can start 48hrs post-trauma
- Feathery stromal infiltrates with dry, gray epithelial surfaces - satellite lesions, ring infiltrates (filamentous fungi)
- Round focal infiltrates with epithelial defects (yeasts)

- Management of fungal infections
  - Ophthalmic antifungal agents are generally NOT commercially available
    - exception: natamycin 5% solution (Natacyn®; Alcon – Ft. Worth, TX)
  - Agents include:
    - Natamycin 5%
    - Amphotericin B 0.15%
    - Miconazole 1%
    - Ketoconazole 1-5%
    - Itraconazole 1%
    - Flucytosine 2%

Acanthamoeba keratitis

- Presentation:
  - Extreme pain common but not absolute
  - Decreased corneal sensitivity
  - Ring infiltrate typical
  - Atypical corneal lesions - mimic HSV
  - Difficult to treat, worsens with delay
  - Contact lens related (92% in recent study)
- More common than you think!
  - Numerous cases reported in the recent literature

- Management of acanthamoeba
  - Therapeutic options:
    - Propamidine isethionate (Brolene)
    - Neomycin-polymyxin-gramicidin
    - Clotrimazole
    - Polyhexamethylene biguanide
  - Bacterial superinfection is common
  - Tx success is 79.3% (Based upon a 1997 study)
  - defined as final visual acuity of 20/40
  - if caught early, 90.8% recover successfully