New Advances in the Management of Viral Eye Disease

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- Corneal Services and Ocular Disease Research
- Koffler Vision Group

Anterior Seg Grand Rounds Case III

68 y.o. Caucasian female

CC: photophobia and blurred vision
As well as a headache over right eye for 2 days

Slit lamp exam:

- Grade 2- injection:
- Irregular SPK and staining
- AC: grade 3 cell & flare

Diagnosis?

__________________

Not enough information provided.

Sign:

- Nearly 1 Million Americans develop ______ each year
- ______ accounts for up to 25% of presenting cases
- Over ___% incur ocular damage

- Lesion on the tip of the nose
- Nasociliary branch of ophthalmic division of trigeminal nerve (V)
- Nasal means possibly ciliary (ocular) involvement
Ocular findings:

According to a study by Thean what was the most common complication associated with HZO?

A. Iritis  
B. Optic neuritis  
C. Neurotrophic keratitis  
D. Scleritis

Iridocyclitis and HZO

- Most common and most often overlooked ocular complication (43%)
- Highly elevated IOP
- Study by Thean, Hall & Stawall - clinical Ophthalmology Dec 2001
- 56% of patients developed _________!!

Treatment: Iridocyclitis

- Pred Acetate 1% q1 or q2h
- Durezol (Difluprednate) 0.05%
- Lotemax Long term
- Cycloplegia
  - Homatropine 5% bid
  - Cyclopentolate 1% bid

Six Rules of Iritis Management

Also added medication to lower the IOP

- Diamox 500 mg (non-sequels) after asking about sulfa allergies and kidney problems
- Beta-blocker gtts (after asking about heart rate and breathing problems)
- Iopidine/Alphagan
- Better yet: Combigan
Treatment:

- PO Acyclovir 800 mg 5x/day or new to generic: __________ mg __ x/day
- or Famvir 500 mg 3x/day or
- Advantages:
  - Easier to take 3x Vs. 5x
  - Decreased post-herpetic neuralgia, faster resolution of patient (Ormrod - Drugs June 2000)
  - 25% more bioavailable

Treatment:

- When should you begin therapy?
- Prior to ___ hours proven for Acyclovir (HE Kaufman)
- Not as critical for Valacyclovir or Famvir* (Ormrod)

Treatment:

- Duration?
- ___ days for most patients although newer studies (Zaal - Am J or Ophthal. Jan 2001) suggest
- ___ days for patients over age 66 due to shedding

New Vaccine: __________

- Live attenuated zoster vaccine
- Indicated for patients above age 60 who had chicken box as a child but have not had shingles
- Doesn’t work in 100% of cases and decreased effect with age

New Vaccine: __________

- In the Shingles Prevention Study 38,000 patients 60 and older were enrolled
- 51.3% reduction of herpes zoster
- 61.1% reduction in the severity of herpes zoster
- 66.5% reduction in the incidence of post-herpetic neuralgia

Case History II

- 28 y.o. Caucasian female
- CC: photophobia, red eye and blurred vision
- Been going on for 1 week and symptoms getting worse
- Had a friend with ‘pink eye’ that she saw the week prior
Case History II

• VA: 20/30 OD, 20/40+ OS
• Conjunctiva: grade 2+ injection, no pseudomembrane
• Cornea - as per image
• AC: D&Q
• All other structures unremarkable

Differential Diagnosis?

• Symptoms?
• Discharge?
• Lymph adenopathy?
• History of family member of friend with eye

Diagnosis?

• __________________________

Treatment

• _______ ______ rinse vs. ______

Povidone Iodine 5%

• Verify no allergy to iodine
• Proparacaine x 2 or tetravisc/proparacaine gel x 2
• 2-3 drops in each eye
• Have patient roll around closed eye for
• Lavage extensively
• Rx: Steroid such as lotemax QID x 2 w
• Rx: NSAID such as Bromaday QD
Zirgan

- Rx Zirgan 5x per day x 1 week
- Then TID x 1 week

Patient LBV: CASE HISTORY III

- 38 y.o. African American Female
- Complaint of decreased vision for about 1 week
- Longstanding contact lens wearer
- Vision seems to be getting worse over last few days
- No significant pain
- No corneal staining

What test would you perform?

- A. Jones Test
- B. RPS Adenodetector
- C. Culture
- D. Corneal sensitivity

Testing??

______________________________

______________________________

Diagnosis??

______________________________

______________________________
Infectious Epithelial Keratitis: Cornea Vesicles

- Cystic lesion of the epithelium
- Contains active virus
- No epithelial defect
  - Negative staining early
  - Late staining

Infectious Epithelial Keratitis: _______ Ulcer

- Branching linear ulceration
- Swollen epithelial borders
- Contain active virus
- Most common presentation for HSK

Infectious Epithelial Keratitis: Geographic Ulcer

- Enlarged dendritic ulcer
- Scalloped borders
- Contains active virus

Infectious Epithelial Keratitis: Marginal Ulcer

- Begins as ulcer
- Stromal infiltrate rapidly develops
- Dilated limbal vessels
- Peripheral corneal NV

Immune Stromal Keratitis (Interstitial Keratitis)

Clinical Findings

- Stromal haze or infiltrate
- Neovascularization
- Immune ring
- Intact epithelium
Disciform Endotheliitis

- Most common form
- Central or paracentral disc-shaped area of edema
- KP corresponding to edema
- Iritis
- Elevated IOP

Treatment: Epithelial Involvement

- In the past: trifluoridine - Viroptic q2h
- New replacement: Zirgan 5 x per day until ulcer disappears then TID x 1 week
- PO Valtrex 500mg TID
- PF artificial tears
- Follow-up (next day), day 3-4, day 7-10

Zirgan™ (Ganciclovir Ophthalmic Gel) 0.15%

Indication and Usage

- Zirgan is a topical ophthalmic antiviral that is indicated for the treatment of acute herpetic keratitis (dendritic ulcers).

Ganciclovir Mechanism of Action

- Penetrates cell infected with the virus
- Phosphorylated within the cell to ganciclovir monophosphate by a viral thymidine-kinase
  - Affinity for thymidine-kinase allows for specificity in its action
- Activation continues due to several cell kinases leading to formulation of ganciclovir triphosphate, which:
  - Inhibits viral DNA polymerase
  - Incorporates into viral DNA preventing replication

Zirgan™ (ganciclovir ophthalmic gel) 0.15% Indication

Dosage and Administration

- The recommended dosing regimen for Zirgan is 1 drop in the affected eye 5 times per day (approximately every 3 hours while awake) until the corneal ulcer heals, and then 1 drop 3 times per day for 7 days.
Properties of Zirgan™ Gel

- Polyfoil 5 gram tube with dropper fitting
- Gel formulation (due to carbomer-based vehicle)
  - Allows for more prolonged contact time with the eye than oil-based formulations
- Aqueous gel allows for ganciclovir concentration of 0.15%
  - Sufficient to ensure good tolerability and efficacy in treatment of superficial acute herpetic keratitis
- pH = 7.45
- Osmolality = 300 mOsmol

Zirgan™ Clinical Efficacy Results

Results from a open-label, randomized, controlled, multicenter clinical trial evaluating ganciclovir ophthalmic gel 0.15% compared to acyclovir ophthalmic ointment 3% in patients with dendritic ulcers

<table>
<thead>
<tr>
<th>Clinical Resolution By Day 7</th>
<th>GCV 0.15% N = 77</th>
<th>ACV 3% N = 67</th>
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<td>55 (77%)</td>
<td>48 (72%)</td>
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Zirgan™ Clinical Efficacy Results

Results from 3 randomized, single-masked, controlled multicenter clinical trial evaluating ganciclovir ophthalmic gel 0.15% compared to acyclovir ophthalmic ointment 3% in 213 patients with dendritic ulcers

<table>
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<tr>
<th>Clinical Resolution By Day 7</th>
<th>GCV 0.15% N = 57</th>
<th>ACV 3% N = 49</th>
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<tbody>
<tr>
<td></td>
<td>41 (72%)</td>
<td>34 (69%)</td>
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Treatment: Stromal keratitis or Endotheliitis

- Durezol QID
- Pred Forte QID
- Cover with PO Acyclovir (400 mg bid) or Valtrex (1000mg QD) or topical (Zirgan TID)

When to use Oral Therapy

- Toxicity of Viroptic requires lower dosing
- Patient with stromal keratitis
- Prevention of HSV stromal keratitis
- Children -primary HSV
- Prior to surgery
- In all cases?
  - Trigeminal ganglion suppression