Education in the Round: My Favorite Meds

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- Optometry Times – Editorial Advisory Board

Prescribing Considerations
- Indications
- Brand vs. generics
- Does the insurance cover prescriptions?
- Costs of medications
- Compliance

Patient Assistance Programs
- Allergan - www.rxhope.com
- Akorn - www.rxassist.org
- Bausch & Lomb - www.valeant.com
- Merck - www.merckhelps.com
- Novartis - www.pharma.us.novartis.com
- Shire - www.shire.com
- www.RxOutreach.org
- www.NeedyMeds.org
- www.pparx.org

Virginia Eye Consultants
Tertiary Referral Eye Care Since 1963
- John D. Sheppard, MD, MMSc
- Stephen V. Scoper, MD
- David Salib, MD
- Elizabeth You, MD
- Thomas J. Joly, MD, PhD
- Dayna M. Lago, MD
- Constance Okeke, MD, MSCE
- Esther Chang, MD
- Jay Starling, MD
- Samantha Dewundara, MD
- Walter O. Whitley, OD, MBA, FAAO
- Cecelia Koetting, OD, FAAO
- Christopher Kuc, OD, FAAO
- Leanna Olennikov, OD
- Christopher Kruthoff, OD
- Jillian Janes, OD

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- www.pparx.org

Barriers to Patient Compliance
- Providers Role
- Side Effects
- # of Meds
- Ability to Take Meds
- Forget
- $$
Patient Compliance and Dosing

- Literature review of 76 studies show:
  - Compliance increases with decreased dosage regimen and complexity\(^1\)
  - 79% compliance with QD regimen vs 51% for QID regimens \((p=0.001)\)\(^2\)
  - Simpler, less-frequent dosing results in better compliance in a variety of therapeutic classes\(^1\)

Prescription Considerations

- Review medical history:
  - Renal function
  - Liver function
- Review current medications
- Side effect vs. true allergies
- Pregnant or nursing
- Rx for children

Prescribing for Women

- Certain medications are OK in pregnancy
- Breast feeding
- Consult OB-GYN if necessary

Updates on FDA Labeling

- Effective June 30, 2015
- Pregnancy and Lactation Labeling Final Rule (PLLR)

- Information to include:
  - Risk / Females and Males of Reproductive Potential

So What Can Be Used During Pregnancy?

- Antibiotics
  - Amoxicillin
  - Amoxicillin/clavulanate
  - Azithromycin
  - Erythromycin
- Antivirals
  - Acyclovir
  - Valacyclovir
- Anti-inflammatory
  - Prednisone
- Analgesics
  - Acetaminophen
  - Ibuprofen
  - Tylenol #3
  - Vicodin
- Allergy
  - Diphenhydramine
  - Loratadine
What About Topical Medications During Pregnancy?

- Category B
  - Antibiotics – tobramycin
  - Allergy – alcaftadine
  - Glaucoma - brimonidine
- Category C
  - Allergy - olopatadine
  - Anti-inflammatory – steroids, cyclosporine
  - Anti-viral – ganciclovir, trifluridine

Prescribing Considerations for Kids

1. Know the age
2. Know the weight
3. Look up the dosage
   - mg/kg/day
4. Be good at math
   - Or call the pharmacist
5. Avoid
   - Tetracyclines
   - Fluoroquinolones

Artificial Tear Supplements

- Improve comfort
- Reduce irritation and friction
- Improve ocular surface
- Store in the fridge

Which Antibiotic Would You Choose?

1) Keflex 500 mg BID po X 7 days
2) Z-Pak UD po
3) Augmentin 500 mg TID po X 7 days
4) Avelox 400 mg QD po x 10 days
5) Does it really matter???
Keflex (cefalexin)

- First generation cephalosporin
  - Bactericidal: Inhibits bacterial proliferation by inhibiting cell wall formation
  - Good gram positive coverage, does cover some gram negative, also covers MSSA
  - Has a 1-10% cross reactivity with penicillin's
  - Effective at treating internal hordeolums, preseptal cellulitis, dacryosystitis and other deep soft tissue infections

Diflucan (fluconazole)

- Effective against candidiasis, cryptococcal meningitis
- Interferes with fungal cytochrome P450 activity (lanosterol14α-demethylase) decreasing ergosterol synthesis
- Pregnancy Category C
- 150 mg as a single oral dose
- Side effect - Headache

Doxycycline

- Bacteriostatic: binds to bacterial ribosome and inhibit bacterial protein synthesis
- Broad spectrum of gram positive and negative, effective against MRSA
- Has anti-inflammatory properties as well and reduces the production of matrix metalloproteinase (MMP).
- Effective at treating conditions such as internal hordeolums, meibomian gland dysfunction, ocular rosacea, recurrent corneal erosions

Zithromax (Azithromycin)

- Inhibit bacterial protein synthesis
- Z pak: 500 mg Day 1, 250 mg Day 2-5 or 1g dose
- Pregnancy Category B
- Side Effects/Contraindications:
  - GI upset
  - Headache
  - Rash
  - May worsen myasthenia gravis symptoms
  - Kidney or liver dysfunction
- Consider risk of fatal heart rhythms

MGD: Azithromycin vs. Doxy

- Purpose: To assess the efficacy and safety of oral azithromycin compared with oral doxycycline in patients with meibomian gland dysfunction (MGD) who had failed to respond to prior conservative management.
- Conclusion: Although both oral azithromycin and doxycycline improved the symptoms of MGD, 5-day oral azithromycin is recommended for its better effect on improving the signs, better overall clinical response and shorter duration of treatment

Case Study - CH

- 07/06/09
- 54 YOMW / Referred from OD for K Ulcer
- Started on levofloxacin 0.5% Q1h OS
- Pain and Redness started 5 days prior
- SCLW / Denies sleeping in lenses
- VAcc OD 20/60 OS 20/200
Case Study

- 3+ injection
- 3.5 mm ulcer
- 2+ cells
- Cultures taken
- Added tobramycin Q2h

Infectious versus Sterile

**Ulcers**
- Rare
- Painful
- AC reaction
- Usually single lesion
- Discharge
- Epithelial staining
- Corneal edema
- > 2.0 mm in size

**Infiltrate**
- Common
- Mild pain
- No AC reaction
- Multiple lesions
- Minimal discharge
- Epithelium intact
- No corneal edema
- < 2.0mm in size

7/7/09

- Cloudy since yesterday
- Labs – No growth
- SLE
  - Conj - 4+ Injection
  - Cornea - 3.5 mm ulcer / Haze / 1+edema / WBC
  - A/C - Rare cell
- Plan
  - Continue present meds
  - Add sub-conjunctival injection of gentamycin
  - Add loteprednol 0.5% tid OS

7/9/09

- More photophobic
- SLE
  - Conj - 2+ Injection
  - Cornea – 3.0 mm ulcer / 1+edema / WBC surrounding ulcer
  - A/C – D/Q
- See lab results

Treatment

- Primary goal – eliminate the pathogens
- Secondary goal – prevent host destruction
- Treated as bacterial initially
- Small infiltrates – Treat empirically (<1.0mm)
- Discontinue CL wear
- Cycloplegics
  - Homatropine 5% tid
  - Scopolamine 0.25% tid
  - Atropine 1.0% tid if hypopyon present
Treatment

- Fluoroquinolones – standard
  - Broad spectrum
  - Bioavailability
  - Biocompatibility
- Peripheral infiltrates – q1-2h
- Medium size – q1h w/ loading dose
- Vision threatening – Fortified antibiotics
  - Tobramycin/gentamycin (15mg/mL) q1h
  - Cefazolin (50mg/mL) or vancomycin (25mg/mL) q1h
  - Fluoroquinolone

Antibiotics

- Fluoroquinolones
  - Besifloxacin
  - Levofloxacin
  - Moxifloxacin
  - Gatifloxacin
  - Ciprofloxacin
- Macrolides
  - Azithromycin
- Aminoglycosides
  - Tobramycin

Treatments for MRSA

- 100% to vancomycin
- 97.7% to sulfisoxazole
- 95% to Polytrim
- 93.2% were sensitive to tetracycline
- 63.6% were sensitive to bacitracin
- 14.8% of MRSA isolates were sensitive to ciprofloxacin and erythromycin
- Besifloxacin has been reported to be effective

ARMOR Updates

- A total of 359 isolates were collected from 11 U.S. sites
- Among all staphylococci, resistance was most notable for:
  - Azithromycin (47-63%)
  - Oxacillin/methicillin (27-43%)
  - Ciprofloxacin (25-30%)
- Non-susceptibility to three or more drug classes was observed in:
  - 24% of Staphylococcus aureus
  - 36% of coagulase-negative staphylococci (CoNS) isolates collected in 2016
- Multi-drug resistance remaining prevalent among methicillin-resistant (MR) S. aureus (70%) and MRCoNS (77%).

ARMOR Updates

- Haemophilus influenzae isolates collected to date from 2016 were susceptible to all antibiotics tested
- Although resistance among Pseudomonas aeruginosa isolates continued to be low, data indicate that non-susceptibility to fluoroquinolones (7%) more than doubled from 2015
- Isolates of Streptococcus pneumoniae exhibited non-susceptibility to azithromycin (31%) and penicillin (38%) while remaining susceptible to fluoroquinolones and chloramphenicol.
ARMOR Updates

• In a second study, ARMOR researchers reported resistance trends in staphylococcal infections from 1/09 through 10/15 – 1597 S. aureus (1400 CoNS) were collected.

• Results
  - Decrease resistance
    • MRSA (~39% to 27%; P<0.001), but not among CoNS, with nearly half of CoNS still demonstrating methicillin resistance.
    • Azithromycin (62% to 47%), ciprofloxacin (39% to 25%), and tobramycin (~24% to 9%) and among CoNS to ciprofloxacin (46% to 39%; P<0.001 for all).
  - Increased resistance
    • CoNS to trimethoprim (26% to 37%; P=0.015).

Treatment for HSV Epithelial Keratitis

• Dendritic keratitis usually resolves within 3 weeks.
• Goal to minimize stromal damage and scarring.
• Consider epithelial debridement.
• Topical / Oral antivirals.
• Topical steroids??

Ganciclovir Mechanism of Action

• Penetrates cell infected with the virus.
• Phosphorylated within the cell to ganciclovir monophosphate by a viral thymidine-kinase.
• Activation continues due to several cell kinases leading to formulation of ganciclovir triphosphate:
  - Inhibits viral DNA polymerase.
  - Incorporates into viral DNA.
  - Prevents replication by chain termination.

Summary of Differences: Zirgan™ Compared to Viroptic® (trifluridine ophthalmic solution) 1%

<table>
<thead>
<tr>
<th>Zirgan</th>
<th>Trifluridine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dosage Forms</td>
<td>5 gram tube</td>
</tr>
<tr>
<td>Storage</td>
<td>Store at 15°C-25°C (59°F-77°F)</td>
</tr>
<tr>
<td>Warnings</td>
<td>For topical use only. Patients should not wear contact lenses if they have signs or symptoms of herpetic keratitis or during the course of therapy with Zirgan. Recommended dosage of administration should not be exceeded. Continuous administration of trifluridine for periods exceeding 21 days should be avoided because of potential ocular toxicity.</td>
</tr>
</tbody>
</table>

Herpetic Eye Disease Study I

• Herpes Stromal Keratitis, Not on Steroid Trial
  - Pred Phosphate faster resolution and fewer treatment failures.
  - Delaying treatment did not affect outcome.
• Herpes Stromal Keratitis, on Steroid Treatment
  - No apparent benefit in the addition of oral acyclovir to the treatment of topical corticosteroid and topical antiviral.
• HSV Iridocyclitis, Receiving Topical Steroids
  - Trend in the results suggests benefit in adding oral acyclovir.

Herpetic Eye Disease Study II

• HSV Epithelial Keratitis Trial
  - No benefit from oral ACV with topical trifluridine in preventing the development of stromal keratitis / iritis.
• Acyclovir Prevention Trial
  - Reduced by 41% the probability of recurrence.
  - 50% reduction in the rate of return of the more severe form.
• Ocular HSV Recurrence Factor Study
  - No results available.
Oral Antivirals

- Inhibit viral DNA polymerase without inhibiting normal cellular activity
- Works best if treatment initiated within 72 hours
- Pregnancy category B
- Caution in patients with renal disease

<table>
<thead>
<tr>
<th>Antiviral Drug</th>
<th>HSV</th>
<th>HZO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acyclovir</td>
<td>400 mg 5x/day for 1 week</td>
<td>800 mg 5x/day for 1 week</td>
</tr>
<tr>
<td>Valacyclovir</td>
<td>500 mg TID for 1 week</td>
<td>1000 mg TID for 1 week</td>
</tr>
<tr>
<td>Famciclovir</td>
<td>250 mg TID for 1 week</td>
<td>500 mg TID for 1 week</td>
</tr>
</tbody>
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Vaccines for HZO - Zostivax

- Zostivax is live attenuated herpes zoster (H2) virus
  - 50% reduction in the incidence of HZ
  - 60% reduction in symptom severity in patients who developed HZ
  - 66.5% reduction in postherpetic neuralgia.
- Must have chicken pox as a child
- May help patients who’ve had HZO already


Recommendations

Improving the Screening, Diagnosis, and Management of Dry Eye Disease

Consensus on Baseline Management

- For all patients:
  - Ocular lubrication
  - Lid hygiene
  - Nutrition
- Topical anti-inflammatories
  - Steroids
  - Cyclosporine
  - Lifitegrast

Slides Courtesy of Milton Hom, OD, FAAO
Effect of Oral Re-Esterified Omega-3 Nutritional Supplementation on Dry-Eye Disease: Double-Masked Randomized Placebo-Controlled Study

- This was a multicenter, prospective, interventional, placebo controlled, double masked, randomized trial.
- 105 patients with dry eye disease
  - Four capsules (2 gm) once a day containing 1680mg EPA and 560mg DHA (PRN Dry Eye Omega Benefits) for 3 months or four capsules of placebo.
  - All patients underwent a screening, baseline, 6 week and 12 weeks visit.
  - On each visit patients were tested for tear osmolarity, MMP-9, fluorescein corneal staining, Schirmer’s testing, and OSDI. On the screening exam and week 12 evaluation patients had their omega index tested.
- This study demonstrated that oral consumption of re-esterified omega-3 fatty acids (1680 mg EPA and 560 mg DHA once daily for 12 weeks) is an effective treatment of dry eye disease and results in a statistically significant improvement in tear osmolarity, OSDI, tear break up time and omega index levels.

Restasis Works on All Three Layers and Underlying Inflammation

Xiidra™

- Lifitegrast is a small molecule integrin antagonist that interferes with binding of ICAM-1 to the integrin LFA-1 on the T cell surface, inhibiting T cell recruitment and activation associated with dry eye disease (DED)
- Lifitegrast ophthalmic solution 5.0% has been investigated in 3 (one Phase 2 and three Phase 3) randomized controlled trials for treatment of DED1-3

Lotemax gel (loteprednol etabonate ophthalmic gel 0.5%)

- Ester based steroid
- Vehicle: Polycarbophil (mucoadhesive polymer matrix)
  - A component of the vehicle DuraSite that adheres to mucous membrane-like tissues
  - This increases retention time and drug penetration
- Added moisturizing agents
  - glycerin and propylene glycol
- Preservative: BAK

Prevalence of Allergy

- A nationwide survey found that more than half (54.6%) of all U.S. citizens test positive to one or more allergens.1
- Allergic diseases affect as many as 40 to 50 million Americans.2
- Greater than 70% of patients with systemic allergy may manifest ocular symptoms.3
**Graded Pharmacotherapy**

**Stepwise Treatment Strategies for Allergic Conjunctivitis**

| Severe | Topical corticosteroids (short course; fluorometholone/dexamethasone/tetrahydrozoline)  
|        | Topical immunomodulating agents (tacrolimus, cyclosporine)  
|        | Oral steroids |
| Moderate | Mast cell stabilizers (treats allergy before mediator is released)  
|        | Combination antihistamine/mast cell stabilizers  
|        | Topical corticosteroids (most beneficial for severe outbreaks) |
| Mild | Avoidance, cold compresses, tears, over-the-counter medications  
| | Topical antihistamines/mast cell stabilizers  
| | Oral antihistamines (allergists may already have patients on orals; may exacerbate the ocular condition while improving the nasal condition)  
| | Montelukast |

**Singulair (montelukast sodium)**

- Leukotriene receptor antagonist
- **Indications:**  
  - Prophylaxis and chronic treatment for asthma  
  - Acute prevention of exercise-induced bronchoconstriction  
  - Relief of symptoms of allergic rhinitis  
- **Dosage:** 10 mg tablet qd  
- **Side effects:**  
  - Behavior or mood changes, URI, fever, headache, sore throat, cough, stomach pain, diarrhea, ear ache or ear infection, flu, runny nose, and sinus infection

**Most Prescription Treatment Options Have a Limited Effect on the Inflammatory Cascade**

**ANTIGEN SKIN TESTING**

**12 Patient Allergy Tips**

- Never rub your eyes  
- Wash your hands  
- Use allergy free pillows  
- Stay indoors  
- Use drops for eyes, sprays for nose  
- Avoid “get the red” out vasoconstrictors  
- Chill your drops  
- Use cool compresses  
- Apply allergy drops proactively  
- Pets out of the house or bedroom  
- Know and avoid your personal antigens  
- Try Montelukast: no sedation, no drying
Durezol (difluprednate 0.05%)

- Indicated for post-operative inflammation and pain and endogenous anterior uveitis
- Ketone based steroid
- Emulsion
  - Oil-water mixture
  - A lipid emulsion has a smaller particle size, which increases bioavailability, provides uniform medication concentration in each drop
- Preservative: Sorbic Acid

Steroid Efficacy

- Difluprednate $>$ Prednisolone $>$ Loteprednol $>$ Dexamethasone $>$ Fluorometholone

Percent of Subjects with Clearing of Anterior Chamber Cells

<table>
<thead>
<tr>
<th>Day 3</th>
<th>Day 7</th>
<th>Day 14</th>
<th>Day 21</th>
<th>Day 28</th>
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<tbody>
<tr>
<td>0</td>
<td>10</td>
<td>30</td>
<td>60</td>
<td>90</td>
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Mean Change from Baseline in Total Symptom Score*

*The total symptom score was the sum of pain/ocular discomfort, photophobia, blurred vision, and lacrimation. Each symptom was graded using a visual analogue scale that ranged from 0-100. Patients were asked to assess these symptoms by using a mark on a 100 mm line where 0 = absent, 100 = maximal.

Steroid Pulse Therapy

- QID to Q 1 Hour for 7 to 10 Days
- Zero Tolerance for AC Cells
- Avoids Surface Toxicity
- Quick & Dirty
- Hit It Hard and Fast: Aggressive
- Treat and Follow

What is Glaucoma??
Consider the Risk Factors

- IOP
- CCT
- C/D ratio
- Age
- Race
- Family History

Glaucoma Diagnosis

- Difficult disease to detect

Glaucoma Diagnosis

IOP: 23
CCT: 450

IOP: 25

3 YEARS

Glaucoma: Medications

First Line Therapy: Prostaglandins

- All active first line drugs are effective compared with placebo in reducing IOP at 3 mos
- Bimatoprost, latanoprost, and travoprost are most efficacious and within-class difference were small

Future Glaucoma Drops

- Latanoprostene bunod (Bausch + Lomb) – Nitric oxide donating prostaglandin analog
- Rhopressa (Aerie) – Inhibition of Rho kinase and of norepinephrine transporter
- Roclatan (Aerie) – Combined mechanisms of Rhopressa and latanoprost
- Trabodenoson (Inotek) – Potent adenosine mimetic specific to the A1 receptor

Advil (Ibuprofen)

- Analgesic, antipyretic, anti-inflammatory properties
- Suppresses inflammatory cascade by inhibiting COX pathway
- Pregnancy Category
  - C – Prior to 30 weeks gestation
  - D – After 30 weeks gestation
- OTC 200 mg tablets/capsules
- Analgesic dosage - 1,200 mg / day
- Anti-inflammatory dosage – 3,200 mg / day
- Generics available
### Topical NSAIDs
- **Bromfenac**
  - Bromday (bromfenac 0.09%)
  - Prolensa (bromfenac 0.07%)
  - **Bromsite (bromfenac 0.075%)**
- **Diclofenac**
  - Voltaren (diclofenac sodium 0.1%)
- **Ketorolac tromethamine**
  - Aclular LS (ketorolac tromethamine 0.4%)
  - Acuvail (ketorolac tromethamine 0.45%)
- **Nepafenac**
  - Nevanac (nepafenac 0.1%)
  - Ilevro (nepafenac 0.3%)

### Extra Strength Tylenol (Acetaminophen)
- Analgesics and antipyretic
- **Indications:**
  - Pain relief associated with corneal abrasions, chemical burns, headaches associated with eye pain, scleritis
- **Pregnancy Category B**
- **Side Effects/Contraindications:**
  - Rash, Hives
  - Itching
  - Difficulty swallowing/breathing
  - Overdose may damage liver

### Oral Narcotic Analgesics
- Centrally acting opioid receptor blockers
- Safe and effective for acute, short-term pain
- Clinically used in combination with acetaminophen
- Generally prescribed as one tablet po q4-6hours prn
- Onset 20 minutes, peak 1 hour, duration 4-6 hours

### Vicodin (hydrocodone/acetaminophen)
- **Dosage:**
  - Vicodin contains 5mg hydrocodone with **300 mg** APAP
  - Vicodin ES contains 7.5mg hydrocodone with **300 mg** APAP
  - Vicoprofen contains 7.5mg hydrocodone with **200 mg** ibuprofen
- **Pregnancy Category C**
- 1 tablet po q4-6 hours
- Indicate how many in writing
- Generics available

### Ultram (tramadol hydrochloride)
- Moderate to severe pain
- Non-narcotic opioid receptor agonist
- **Pregnancy Category C**
- 50-100mg q4-6 hours
- **Side effects**
  - Hallucinations
  - Fever
  - Nausea and vomiting
  - Seizure
  - Skin rash
  - Shallow breathing, weak pulse

### Side Effects of Pain Meds
- **Constipation**
- **Nausea and vomiting**
- **Sedation**
- **Dizziness**
- **Itching**
- **Respiratory depression**
- **Addiction**
Phenergan

- Used to treat allergy symptoms
- Prevents motion sickness
- Treats nausea and vomiting or pain after surgery
- Sedative or sleep aid
- 25 mg QID po

Conclusions

- Know your drugs
- Know your bugs (or causes)
- Practice to the highest level of our great profession!!

wwhitley@vec2020.com

THANK YOU!!