The State of Therapeutics in Eye Care
(Part II)
Ron Melton, OD, FAAO
Randall Thomas, OD, MPH, FAAO

“The comprehensive ophthalmologist should be comfortable in using and prescribing the treatments for stages 1 through 3. In stage 4, topical steroids are added. The same clinician may be uncomfortable with this treatment recommendation because of the possible complications of topical steroids and so may want to obtain a second opinion from a cornea or external disease specialist before starting the patient on topical steroids.”

Physician Care of Dry Eye Patients
“Surprisingly, the cornea specialists did not show better conformance (to established Preferred Practice Patterns) than other ophthalmologist subtypes because they received special training in the diagnosis and management of dry eye syndrome.”

It is our opinion that an attentive, compassionate doctor of optometry should be the best at caring for patients with dry eye disease!

THERMODYNAMIC TX TO EXPRESS AND EVACUATE MGs
A new thermodynamic treatment to express & evacuate the MGs
Heat applied to both inner lid surfaces
Pulsatile pressure applied to outer lids

THE LIPIFLOW
(TearScience Inc., Morrisville, NC)

The device applies controlled heat to the inner upper and lower palpebral conjunctival surfaces and lid margins, while simultaneously applying pulsating pressure over the upper and lower (outer) eyelids.

A NEW INSTRUMENT & METRIC
STANDARDIZED DX EXPRESSION FOR MG FUNCTIONALITY

THREE DIAGNOSTIC QUALIFIERS
1. Standard force to mimic force of blink - 1.0 gram/mm² (.3 PSI)
2. Application = 15 seconds
3. Secretion must be liquid (MGYLS)

A new metric allowing standardized expression for diagnosis & quantification of MG functionality

SUMMARY– NEW PARADIGM
“It is important to note that MGD, a condition of MG obstruction, may be the leading cause of dry eye syndrome throughout the world.”
TFOS 2008, Report to professions, 2011

- Lipid deficiency & not aqueous deficiency is usually the catalyst for DRY EYE & inflammatory cascade
- In contrast to conventional models and treatment
- MGD and MG OBSTRUCTION may be obvious or non-obvious, most frequently non-obvious
- Dx of MG functionality requires expression – new metrics
- Treatment of MGD with new technology can treat obstruction improving meibomian gland function to effectively treat dry eye disease & CL intolerance
Anti-infective/Anti-inflammatory Combinations

<table>
<thead>
<tr>
<th>Prednisolone</th>
<th>Dexamethasone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blephamide</td>
<td>Maxitrol</td>
</tr>
<tr>
<td>Isopto-Cetapred</td>
<td>Dexacidin</td>
</tr>
<tr>
<td>Vasocidin</td>
<td>Neo-Decadron</td>
</tr>
<tr>
<td>Metimyd</td>
<td>TobraDex (ST)</td>
</tr>
<tr>
<td>Sulfrin</td>
<td></td>
</tr>
<tr>
<td>Poly-Pred</td>
<td>Loteprednol</td>
</tr>
<tr>
<td>Pred-G</td>
<td>Zylet</td>
</tr>
<tr>
<td>Fluorometholone</td>
<td>Hydrocortisone</td>
</tr>
<tr>
<td>FML-S</td>
<td>Cortisporin</td>
</tr>
</tbody>
</table>

Tobramycin and Dexamethasone

- Excellent coverage against most ocular pathogens with minimal concern of aminoglycoside toxicity
- Effective suppressor of inflammation
- Guard against prolonged use with dexamethasone
- Marketed as TobraDex Suspension and Ointment (tobramycin 0.3% and dexamethasone 0.1%) by Alcon. (Suspension available generically)
- Also available as TobraDex ST (tobramycin 0.3% and dexamethasone 0.05%) by Alcon

Neomycin, Polymyxin B, and 0.1% Dexamethasone

- Excellent coverage against most bacteria
- Effective suppressor of inflammation
- Has been a time honored work horse in medical eye care
- Guard against IOP increase by limiting use to 1-2 weeks
- Marketed as Maxitrol and generically

Tobramycin 0.3% and Loteprednol etabonate 0.5%

- Excellent coverage against most ocular pathogens with minimal concern of aminoglycoside toxicity
- Safe, effective suppressor of inflammation
- Marketed as Zylet Ophthalmic Suspension by B&L Pharmaceuticals
- Available in 5 and 10 ml bottles

Treatment of Blepharitis-Related Dry Eye

- “Antibiotic/steroid combination agents can play an important role in a rational, stepwise dry eye treatment plan.”
- “These drugs do not appear to alter meibomian gland secretions. However, they can effectively reduce both bacterial proliferation and inflammation of the lid margins.”
- “Treat with “…combination antibiotic/steroids as needed on a pulsed basis as part of a long-term treatment plan for recalcitrant or recurrent blepharitis.””

Reference: Refractive Eyecare, December 2011

Obviously, in chronic conditions, an aminoglycoside combined with loteprednol would be the wisest choice

Cliradex for Demodex

- A derivative of Tea Tree Oil ingredients
- Terpinen-4-ol (T4o) is the most demodexicidal
- For cleansing the face and eyelid skin
- Has a transient slight stinging, menthol-like sensation
- If ocular contact, rinse with saline or artificial tear
- Must keep eyes closed, and allow to air dry for 1 minute
- Try this once daily for 6-8 weeks (bid if severe)
- Available from BioTissue, Doral, FL
- See www.cliradex.com for more information
Resistance and Unnecessary Antibiotic Use

• “Now that we know that unnecessary treatment fosters resistance, and resistance has become a significant threat to our patients, we cannot simply prescribe for any conjunctivitis on the grounds that it may be bacterial. Fortunately, there is now a test available that will detect adenovirus, the most common cause of viral conjunctivitis.”
• Dr. McDonald is referring to the RPS Adenodetector (www.RPSdetectors.com)

Reference: M. McDonald. Refractive Eyecare, September 2011

AdenoPlus™

• Convenient in-office, 10 minute immunoassay
• Detects all known serotypes of adenovirus
• Clinical Laboratory Improvement Amendment (CLIA) waived
• Has sensitivity of 90% and specificity of 96%
• Adenoviral infection is commonly a clinical diagnosis
• Helpful for challenging cases, and for primary care physicians
• CPT code 87809QW
• www.nicox.com

Clinical Perspective on AdenoPlus Immunoassay

• Adenovirus can cause: nonspecific follicular conjunctivitis, PCF, acute hemorrhagic conjunctivitis, and EKC
• Clinical diagnostic accuracy ranges from 40-70%
• AdenoPlus is a rapid in-office assay having 90-95% sensitivity and specificity
• AdenoPlus results correlates with disease infectivity (i.e. the intensity of the positive result line is directly proportional to the amount of antigen present)
• “In addition to the typical management strategy for adenovirus conjunctivitis, 2 novel treatments, topical povidone iodine and ganciclovir gel, have become more widely used.”
• www.nicox.com

Reference: JAMA-Oph, January 2013

Povidone - Iodine 5% ophthalmic solution

• Broad spectrum microbicide
• Indicated for “irrigation of the ocular surface”
• “Off label” use: Tx adenoviral keratoconjunctivitis
  • Anesthetize with proparacaine
  • Instill 1 or 2 drops of NSAID
  • Instill several drops Betadine 5% in eye(s), close eye(s)
  • Swab or rub excess over eyelid margin
  • After 1 minute, irrigate with sterile saline
  • Instill 1 or 2 drops of NSAID
  • Rx steroid qid x 4 days
• No reports in clinical trials of adverse reactions.
• Marketed as Betadine 5% ophthalmic prep solution (30 ml opaque bottle) by Alcon surgical
• CPT 99070 supply code

Ganciclovir 0.15% Gel: A new Treatment for EKC

• “36 patients beginning an acute EKC were treated QID with ganciclovir 0.15% gel. All eyes were culture positive on 1-3 days.”
• “Ocular discomfort was alleviated in one week. No keratitis developed in any patient with this type 8 infection.”
• “Ganciclovir 0.15% gel must be prescribed as soon as possible. It does not blur vision owing to its water miscible property.”

Reference: Verin, et al. Ophthalmic Research, 1997; 29 (suppl. 1) 12-27 (France)

Ganciclovir Effects in EKC

• “Patients treated with topical ganciclovir 0.15% ointment showed resolution of EKC within 7.7 days (range 7-12 days) compared with 18.5 days (range 7-30 days) in the control group.”
• “22% of cases developed subepithelial opacities in the treatment group compared to 77% in the control group.”
• “Conclusions: Topical ganciclovir 0.15% ophthalmic ointment is safe and effective in the treatment of adenoviral keratoconjunctivitis”

Reference: Tabbara, KF. The Eye Foundation For Research in Ophthalmology. Riyadh, Saudi Arabia
Cost Analysis of Povidone-Iodine for Ophthalmia Neonatorum Prophylaxis

“Topical azithromycin is likely as effective for the important causes of ophthalmia neonatorum as its fellow macrolide erythromycin.”

“A controlled clinical trial comparing erythromycin, 0.5%, povidone-iodine, 2.5%, and silver nitrate, 1%, for ophthalmia neonatorum prophylaxis demonstrated that povidone-iodine was more effective than the other agents for preventing infectious conjunctivitis, including chlamydial conjunctivitis.”

“We believe povidone-iodine would be a suitable and perhaps preferable alternative to azithromycin for ophthalmia neonatorum prophylaxis.”


Anti-Viral Medicines

<table>
<thead>
<tr>
<th>Topical</th>
<th>Trifluridine</th>
<th>Viroptic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral</td>
<td>Acyclovir</td>
<td>Zovirax</td>
</tr>
<tr>
<td></td>
<td>Valacyclovir</td>
<td>Valtrex</td>
</tr>
<tr>
<td></td>
<td>Famciclovir</td>
<td>Famvir</td>
</tr>
</tbody>
</table>

- These are anti-herpetic drugs and are ineffective against the various adenoviral serotypes -

Triflorothymidine (Trifluridine)

- A halogenated pyrimidine analog of thymidine
- Inhibits both virally-infected and non-infected cells
- Possesses good activity against both HSV-I and HSV-II
- Approved down to age 6
- Penetrates into epithelium, stroma, and aqueous
- Once dispensed by pharmacy, refrigeration not required
- Heals most herpetic ulcers in 5 to 8 days
- Use q 2h for first 4 to 5 days, then taper PRN
- Marketed as: Viroptic 1% (7.5 ml) by Monarch Pharmaceuticals and generic

Topical Ganciclovir

- Used systemically to treat CMV retinitis
- A new topical “pro-drug” for treating epithelial HSV
- Only acts on virally infected cells
- Used 5 x D for 4 to 6 days, then tid for 3 to 4 more days
- Is a 0.15% ophthalmic gel-drop with BAK
- Marketed as Zirgan ophthalmic gel
- Comes in a 5 gram tube
- Marketed by B+L Pharmaceuticals

Topical Antiviral Options

<table>
<thead>
<tr>
<th>Trifluridine</th>
<th>Ganciclovir</th>
</tr>
</thead>
<tbody>
<tr>
<td>Old drug</td>
<td>New drug</td>
</tr>
<tr>
<td>Indiscriminate expression</td>
<td>Infected cell-specific</td>
</tr>
<tr>
<td>Potentially toxic</td>
<td>Minimally toxic</td>
</tr>
<tr>
<td>More frequent dosing</td>
<td>Less frequent dosing</td>
</tr>
<tr>
<td>Refrigerate until opened</td>
<td>No refrigeration needed</td>
</tr>
<tr>
<td>Thimerosal preserved</td>
<td>BAK preserved</td>
</tr>
<tr>
<td>Solution (7.5 ml bottle)</td>
<td>Gel (5 gram tube)</td>
</tr>
<tr>
<td>Viroptic and generic</td>
<td>Zirgan by B+L</td>
</tr>
</tbody>
</table>

Acyclovir (ACV)

- Analog of guanosine
- Specifically targets virally-infected cells
- Minimally toxic to uninfected cells
- Best to initiate therapy within 72 hours
- Tx: 800 mg by mouth 5 x D for 7 days for HZO; 400 mg 5 x D for 7 days for HSK
- Main side effect: occasional nausea
- Use with caution in kidney disease
- Available generically
Valacyclovir vs. Acyclovir for Recurrent HSV

“One-year suppression therapy with oral valacyclovir (500-mg tablet daily) was shown to be as effective and as well-tolerated as acyclovir (400-mg tablet twice daily) in reducing the rate of recurrent ocular HSV disease.”


Study on Stromal HSK

- OD response rate, 6% - MD response rate 15%
- ALL: 95% treated epithelial keratitis correctly
- For stromal immune keratitis
  - 54% OD correct
  - 74% MD correct
  - 82% corneal subspecialist correct
- Correct = topical steroids with antiviral cover
- Correct use of oral antiviral prophylaxis for recurrences
  - 51% - OD, 60% - MD, 62% corneal subspecialist
- “Training” was most significant determining factor

Reference: Letters – Arch. Oph., December 2010

Preventing HSV Disease Recurrences

- Patients being treated with oral antiviral therapy were 9 times less likely than untreated patients to develop recurrent keratitis
- Recurrence rates:
  - 27% at 1 year
  - 50% by 5 years
  - 57% by 10 years
  - 63% by 20 years
- Stromal disease is more likely to recur than epithelial disease
- Length of prophylaxis: Generally 5 disease-free years


Pediatric Herpes Simplex Disease

- Herpes simplex virus (HSV) and herpes blepharocconjunctivitis (HSB) frequently misdiagnosed
- Recurrence of HSV more common in children (50%) than adults
- 30% of patients with HSK initially misdiagnosed
- Suspect HSV keratitis in recurrent unilateral keratoconjunctivitis with corneal neovascularization and decreased corneal sensation
- Peds patient HSV shows severe inflammation and stromal keratitis; in adults, most common manifestation is dendritic keratitis
- Tx: Oral ACV

Reference: Ophthalmology, October 2012 (Lin, Pavan-Langston, Colby)

Treatment and Prophylactic Dosages for Acyclovir in Children

<table>
<thead>
<tr>
<th>Age</th>
<th>Treatment Dose Thrice Daily</th>
<th>Prophylactic Dose Twice Daily</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants (up to 18 mos)</td>
<td>100 mg (2.5 ml)</td>
<td>100 mg (2.5 ml)</td>
</tr>
<tr>
<td>Toddlers (18 mos-3 yrs)</td>
<td>200 mg (5 ml)</td>
<td>200 mg (5 ml)</td>
</tr>
<tr>
<td>Young children (3-5 yrs)</td>
<td>300 mg (7.5 ml)</td>
<td>300 mg (7.5 ml)</td>
</tr>
<tr>
<td>Older children (6 yrs and older)</td>
<td>400 mg (10 ml)</td>
<td>400 mg (10 ml)</td>
</tr>
</tbody>
</table>

Reference: Ophthalmology, October 2012

Zostavax

- Vaccine for prevention of shingles in adults age 50 and older
- Marketed by Merck as Zostavax and is given as a single dose by injection
- Anyone who has been infected by chicken pox (more than 90% of adults in US) is at risk for developing shingles
- Contraindicated if Hx of allergy to gelatin, neomycin; Hx of acquired immunodeficiency states; pregnancy
- In landmark Shingles Prevention Study, Zostavax reduced risk of developing shingles by 51% (4 yrs of follow-up)
- Duration of protection after vaccination unknown

References: www.cdc.gov/vaccine/vpd-vac/shingles; FDA News Release, March 24, 2011 “FDA approves Zostavax vaccine to prevent shingles in individuals 50 to 59 years of age.”
**Antiviral Treatment for VZD**

- Unlike stromal keratitis and uveitis, the dendriform lesions do harbor active virus, and respond to oral and topical antiviral therapy.
- Such “late dendriform keratopathy” occurs in 2-10% of patients after HZO.
- While corticosteroids are commonly used to treat the sequelae of HZO, if the tissues do not respond as expected, perhaps trying a seven day course of oral antiviral could be tried.

*Reference: Arch. Oph. January 2012*

---

**Zoster Disease: Young (<60) vs Old (>60)**

- Overall peak incidence of HZO: 50-59 years of age.
- Because of childhood chickenpox immunization, there will be an increased incidence of younger people developing HZ for a few decades.
- Younger: secondary inflammation “flares” (pseudodendrites, keratouveitis) more common.
- Older: neurotrophic keratitis in about 25%, therefore need to enhance tear film function.
- Long-term oral antiviral and corticosteroid therapy may be indicated in many HZO patients.

*Reference: Ophthalmology, November, 2011*

---

**Prostaglandin Receptor Agonists**

- Latanoprost (Xalatan and generic) 0.005%
- Travoprost (Travatan Z) 0.004%
- Bimatoprost (Lumigan) 0.01%
- Tafluprost (Zioptan) 0.0015%

---

**Tafluprost Ophthalmic Solution**

- FDA approved February 2012.
- First “preservative-free” prostaglandin.
- Reduces IOP similarly to the other prostaglandins.
- Dosage: once daily, preferably in the evening.
- Most common side-effect – conjunctival hyperemia.
- Available in unit dose containers.
- Marketed as Zioptan 0.0015% ophthalmic solution by Merck.

---

**After a Prostaglandin; What to Add**

- Meta-analysis of studies regarding what drug to add to a prostaglandin.
- Is it brimonidine, a beta-blocker, or a CAI?
- Conclusions: “All 3 classes are similarly effective in lowering mean diurnal IOP when used in combination with PGAs. Brimonidine is statistically less effective in reducing IOP at trough compared with the beta-blockers and CAI’s.”
- Additional lowering of IOP was, on average, 2.5 to 3 mmHg for all 3.

*Reference: Arch. Oph. July 2010*
**RESCLULA (unoprostone isopropyl) ophthalmic solution 0.15%**

- RESCLULA may be used as a first-line agent or concomitantly with other topical ophthalmic drug products to lower intraocular pressure
- Reduces IOP 2-4 mmHg
- Rescula is supplied 5 mL in a 7.5 mL bottle
- Marketed by Sucampo Pharma Americas, LLC

---

**Prostaglandin-Associated Periorbitopathy**

- A more newly recognized side effect of prostaglandin therapy
- Periorbital fat atrophy gives rise to marked deepening of the superior lid sulcus, which can result in ptosis and enophthalmos
- Beyond the obvious cosmetic concerns, such altered lid/orbital anatomy can make applanation tonometry quite challenging
- Probably expressed more in middle-aged patients than in older patients
- Tends to be at least partially reversible over a few months.

*Advanced Ocular Care. July-August 2011.*

---

**Timoptic in OcuDose**

- Only preservative-free glaucoma medicine
- Niche product: indicated when ocular preservatives, particularly benzalkonium chloride (BAK), impair surface tissues of the eye
- Available as .25% and .5% in .2mL individual units of solution from Aton Pharma, Inc.

---

**β-Blockers May Reduce Mortality and Risk of Exacerbations in Patients with Chronic Obstructive Pulmonary Disease**

Conclusion: Treatment with β-blockers may reduce the risk of exacerbations and improve survival in patients with COPD, possibly as a result of dual cardiopulmonary protective properties.


---

**Higher β-Blocker Doses Lead to Better Outcomes in Heart Failure Patients**

*Titrating doses to higher levels, as tolerated, seems reasonable*

β-blockers prevent cardiovascular-related morbidity and mortality in patients with heart failure and reduced ejection fractions. But does a strong dose-response relation exist between β-blockers and clinical outcomes?

*Kirsten E. Fleischmann, MD, MPH*

*Published in Journal Watch General Medicine May 22, 2012*

---

**Dorzolamide Hydrochloride 2% — Timolol Maleate .5% (Cosopt)**

- Both components decrease IOP by reducing aqueous humor secretion
- Because of the CAI, must be used bid, which results in excessive beta-blocker therapy
- Contraindications: patients with asthma, heart disease, or allergy to sulfa drugs
- Ocular side effects: burning/stinging and perversion in taste
- Marketed as Cosopt by Merck bottle and PF and generic
Combigan Ophthalmic Solution

- If using timolol and not quite to target IOP, then trying Combigan would be rational
- If using brimonidine and not quite to target IOP, then rational to try Combigan
- If a prostaglandin does not reach target IOP, then trying a once daily beta-blocker like timolol. If this two drop therapy approaches, but does not achieve target IOP, then trying a combination drug is rational
- Marketed as Combigan by Allergan in 5, 10, and 15 ml opaque white bottles, preserved with BAK 0.005%

Simbrinza - New Combination Drug

- Combination drug without a beta blocker where both ingredient drugs are dosed the same (b.i.d.)
- Combines 1% brinzolamide (Azopt ophthalmic suspension) with 0.2% brimonidine
- Offers a wide range of treatment possibilities due to its strong efficacy and ability to decrease elevated IOP by 21-35%
- Marketed by Alcon under the brand name Simbrinza

Laser Trabeculoplasty for Open-Angle Glaucoma

- The IOP-lowering effect and complications of treatment are similar for SLT compared with ALT.
- “At present, there is no literature that establishes a clear clinical superiority of any one type of laser for trabeculoplasty.”
  
  Oph. November 2011

Alert on Topiramate (Topamax)

- Approved for seizure disorders and migraine headache prevention
- Unapproved: Weight loss, depression, bipolar disorder
- Mechanism of action is unknown
- Because of a topiramate-associated risk for oral clefts, the FDA has now designated topiramate as a pregnancy category D drug.
- Numerous reported cases of acute, bilateral, simultaneous angle-closure glaucoma
- Onset usually within first 2 weeks of therapy
- Most common presenting symptom: blurred vision
- Choroidal effusion physically closes the angle
- Tx: Stop the topiramate; STAT consult with prescribing physician; then aqueous suppressants, oral CAI, cycloplegia (retracts ciliary body) - no miotics
- IOP and myopia normalizes in 1-4 days, no laser Tx indicated

Topiramate (Topamax) and Vision

- Uses: anticonvulsant, migraine prevention, bipolar disorder, obesity, OCD, IIH, neuropathic pain, essential tremor, post-herpetic neuralgia, and other esoteric uses.
- Topiramate is a sulfa derivative (like CAI's)
- Idiosyncratic ciliochoroidal effusion is the most common ocular side effect, and most always results in a myopic shift with or without increased IOP
- This rare event usually occurs within 2 weeks of initiation (or doubling) of dosing
- First described in 2001 – 70% are female
- Tx: D/C the medicine; use (PRN) beta-blocker, brimonidine, or, in refractory case, oral prednisone or IV methylprednisolone. Also, instill cycloplegic agent, and do not use pilocarpine. Reference: Clinical Ophthalmology. January 2012

Qsymia: Potential for Decreased Weight and Increased Risk of Angle Closure

- New drug for weight loss patients who are overweight or obese and also have at least one weight-related condition such as high blood pressure, diabetes or high cholesterol.
- Combination of two older drugs
  - Phentermine (appetite suppressant)
  - Topiramate (feeling of satiation)
- Lesser dosages of each component drug tend to act synergistically
- On average, patients lose about 10% of their body weight over one year
- Marketed by Vivus Inc (Mountain View, California)
- FDA approval July 17, 2012
Treatment Options - Ocular Allergy

- Artificial Tears
- Mild Vasoconstrictors
- Decongestant / Astringents
- Vasoconstrictor / Antihistamines
- Antihistamines
- Antihistamine / Mast Cell Stabilizers
- Mast Cell Stabilizers
- Non-steroidal Anti-inflammatories
- Mild Corticosteroids
- Systemic Antihistamines
- Potent Corticosteroids
- Homeopathic Formulations

Antihistamine/Mast Cell Stabilizer

- Highly selective H1 receptor blockers with prolonged receptor binding
- Good mast cell stabilization
- All bid dosing, except Pataday and Lastacaft qd

<table>
<thead>
<tr>
<th>Medication</th>
<th>Concentration</th>
<th>Brand Names</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olopatadine</td>
<td>0.1%</td>
<td>Patanol (5 ml)</td>
</tr>
<tr>
<td></td>
<td>0.2%</td>
<td>Pataday (2.5 ml)</td>
</tr>
<tr>
<td>Bepotastine</td>
<td>1.5%</td>
<td>Bepreve (5, 10 ml)</td>
</tr>
<tr>
<td>Epinastine</td>
<td>0.05%</td>
<td>Elenz (5 ml)</td>
</tr>
<tr>
<td>Alcaftadine</td>
<td>0.25%</td>
<td>Lastacaft (3 ml)</td>
</tr>
<tr>
<td>Azelastine</td>
<td>0.05%</td>
<td>Optivar and generic</td>
</tr>
<tr>
<td>Ketotifen</td>
<td>0.025%</td>
<td>(generic and OTC)</td>
</tr>
</tbody>
</table>

Systemic Antihistamines

OTC
- Chlorpheniramine (Chlor-Trimeton)
- Diphenhydramine (Benadryl)
- Loratadine (Claritin) - 10 mg qd
- Fexofenadine (Allegra) - 60 mg bid; 180 mg qd
- Cetirizine (Zyrtec) - 5 or 10 mg qd

Rx
- Desloratadine (Clarinex) – 5 mg qd
- Levocetirizine (Xyzal) – 5 mg qd
  - Metabolized by the liver
  - Excreted in bile and urine (1/2 dose if renal disease)

Loteprednol Etabonate

- Only ester-based, site-specific steroid
- Works at target tissues, and then is quickly metabolized into inert compounds
- LE has high intrinsic activity when applied locally
- 0.5% loteprednol similar in therapeutic equivalence on the ocular surface to 1% prednisolone acetate, yet causes little, if any, increase in IOP
- Available as 0.5% (Lotemax) and 0.2% (Alrex) ophthalmic suspensions

Intranasal Steroids for Ocular Symptoms in Allergic Rhinitis

- In a randomized trial, intranasal steroids relieved both nasal and ocular symptoms.
- Because intranasal steroids are the most effective medications for allergic rhinitis symptoms (especially congestion), guidelines recommend them as first-line agents for moderate-to-severe disease
- As many as 85% of patients with seasonal allergic rhinitis also have ocular symptoms
- For these patients, many clinicians prescribe oral antihistamines or ocular products rather than (or in addition to) intranasal steroids

Reference: journalwatch.com, June, 2010

Non-Steroidal Anti-Inflammatory Drugs

- Inhibition of prostaglandin synthesis is the mechanism of action.
- They specifically inhibit the action of cyclooxygenase, an enzyme vital to prostaglandin synthesis.
- Prostaglandins are powerful mediators of inflammation.
  - Acular (Ketorolac 0.5%) by Allergan and generic
  - Acular LS (Ketorolac 0.4%) - Allergan
  - Acuvail (Ketorolac PF 0.45%) - Allergan
  - Ocufen (Flurbiprofen 0.03%) - Allergan and generic
  - Profen (Suprofen 1%) by Alcon and generic
  - Voltaren (Diclofenac 0.1%) by Novartis and generic
  - Bromday (Bromfenac 0.09%) by B+L
  - Nevanac (Napafenac 0.1%) by Alcon
### Nepafenac Ophthalmic Suspensions

- **Nevanac 0.1% AND Ilevro 0.3%**
- **Indication:** Treatment of pain and inflammation associated with cataract surgery
- **Nevanac** is dosed tid; **Ilevro**, once daily
- **Ilevro** is to be prescribed the day before surgery, the day of surgery and then 14 more days
- **BAK 0.005%, pH 6.8, pregnancy category C,** pediatric use down to age 10
- Marketed by Alcon as Ilevro 0.3% ophthalmic suspension 1.7 ml in a 4 ml bottle

### Bromfenac Ophthalmic Solutions

- **Bromday 0.09% and Prolensa 0.07%** (22% less concentration)
- **Indication:** Treatment of pain and inflammation associated with cataract surgery
- Both are dosed once daily
- Both are prescribed the day before surgery, the day of surgery and then 14 more days
- **BAK 0.005% BAK pH 7.8, pregnancy category C,** pediatric use down to age 18
- Marketed by B&L at Prolensa 0.07% ophthalmic solution 1.6 ml and 3 ml in a 7.5 ml bottle

### Hydroxychloroquine Retinotoxicity

- **Risk Factors:**
  - Daily dosage exceeding 6.5mg/kl (400mg/135 lbs)
  - Obesity (HCQ is not absorbed into adipose tissue)
  - Duration of use longer than 5 years
  - Renal or hepatic function impairment
  - Age greater than 60 years
  - Pre-existing retinal disease

Reference: Archives of Ophthalmology, January 2011

### Pearls Regarding Hydroxychloroquine

- Patient education and proper follow-up is essential to prevention
- Toxicity can develop despite daily dosing below the recommended maximum dosage
- Macula can appear normal even with profound VF abnormalities
- Lean body weight should be established for obese patients
- Beyond 10-2 VF testing, consider SD-OCT looking for thinning of the paramacular retina

Reference: Archives of Ophthalmology, January 2011

### American Academy of Ophthalmology 2011 Revised Recommendations

- Risk depends more on “cumulative exposure” and is independent of daily dose or dose per weight
- Daily dosing greater than 6.5 mg/kg (400mg/135 lbs) hastens the accumulation of HCQ and may enhance the rate and degree of tissue damage.
- Intermediate dosing can be “easily achieved”: “300mg daily results from taking 200 mg and 400 mg on alternate days”

Reference: Ophthalmology, February 2011

### Perspective on Hydroxychloroquine Screening

- “advises strongly that 10-2 VF’s be supplemented with ... SD-OCT”
- Routine (non-high risk) patients: Exam at baseline, and begin annual screening 5 years later
- Clearance of HCQ from the body can take many months after it is stopped
- Risk “increases sharply” after 5 to 7 years to approximately 1%

Reference: Ophthalmology, February 2011
American Academy of Ophthalmology 2011 Revised Recommendations

- Fundus photography: used to document any baseline macular abnormalities but has no role for screening
- Focus on 10-2 “pattern deviation display”. An abnormal 10-2 should be repeated to verify defect producibility
- Obtain SD-OCT to corroborate any functional (10-2) defects
- 10-2 may be less sensitive than SD-OCT

Reference: Ophthalmology, February 2011