Essential Topical Ophthalmic Drugs

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Course Goal
To provide current and accurate information about key topical drugs that are used to treat eye diseases.

Introduction to Ocular Pharmacotherapy
- Antibiotics
- Corticosteroids
- Combination Medications
- Non-Steroidal Anti-Inflammatory Medications
- Anti-Viral Medications
- Glaucoma Medications
- Ocular Allergy Medications
- Dry Eye Treatments

My Dandy Dozen!

Our Dozen “Go-to” Drugs

- Prednisolone Acetate 1%
- Loteprednol .5%
- Nepafenac .1%
- Tobramycin .3% + Dexamethasone .1%
- Cyclosporine .05%
- Moxifloxacin .5%
- Tobramycin .3%
- Olopatadine HCL .2% or .1%
- Travoprost-Z .004%
- Timolol .25% or .5%
- Doxycycline
- Acyclovir
- Prednisone
Local (Ocular) Side Effects of Topical Medications

- Posterior Subcapsular Cataract
- Glaucoma

Systemic Side Effects of Topical Medications

- Keep in mind the patient's medical history and current medications
  - Polypharmacy
- Keep in mind "special" populations
  - Pregnant or lactating women
  - Geriatric population
  - Pediatric population
  - Immuno-compromised patients
  - Patients with systemic disease
  - Exceptional patients
  - Visually impaired patients

Instillation of Medications: Eye Drops

Proper technique can significantly increase efficacy!

Pharmacotherapy of Anterior Uveitis

What is your ocular treatment plan?
Corticosteroids

- Topical steroids are used to treat ocular inflammatory conditions
- Choosing which medication to use depends on the severity and location of the ocular inflammation

Moderate to Severe Inflammation

- Prednisolone acetate 1% (Econopred-Plus, Pred Forte)
  - ophthalmic suspension
  - greatest anti-inflammatory efficacy
  - the acetate suspension facilitates corneal penetration to provide increased concentrations in the anterior chamber
  - effective for treating a host of ocular inflammations especially anterior uveitis and severe episcleritis

Newer Steroid

- Difluprednate .05% emulsion (Sirion/Alcon)
  - No shaking
  - Less frequent dosing
  - BAK-free
  - Derived from prednisolone
  - FDA indication for post-Sx. inflam, pain
  - IOP rise *

Difluprednate Molecule

- Fluorination increases specificity for glucocorticoid receptor
- Addition of the acetate ester enhances tissue penetration

Corticosteroids

- Possible ocular side effects
  - Steroid-induced glaucoma
    - prolonged use (3-5 weeks) may cause an increase in intraocular pressure
  - cataract formation
  - decreased healing
  - promotion of certain viral and fungal infections
    - Herpes Simplex Virus

Mild-Moderate Inflammation

- Loteprednol etabonate 0.5% (Lotemax)
  - ophthalmic suspension
  - effective against moderate ocular inflammation
  - effective in treating post-operative inflammation
  - relatively small tendency to increase IOP
  - frequently used “off-label” in DES
Mild-Moderate Inflammation

- Loteprednol etabonate 0.5% (Lotemax)
  - ophthalmic suspension
  - post-operative
  - small tendency to increase IOP
  - used “off-label” in DES

Loteprednol ointment .5%

What if there is IOP rise?

Handle it.

Taper Appropriately

- When?
  - Need at least a 2-step reduction in cell
- How?
  - Cut dose by 1 for each given time interval
  - If dosing q.i.d. for five days, taper to t.i.d. for five days, then b.i.d. for five days, 1xd x 5d, then D/C
  - The longer the treatment period, the longer the taper.

Inflammation/Infection

- Phlyctenulosis
  - Small, white limbal nodules with surrounding redness as response to Staph.
  - Associated with tuberculosis
  - Good response to topical AB/steroid such as tobramycin/dexamethasone
  - does qid x 5-7 days

Steroid-Antibiotic Combinations

- Dexamethasone alcohol .1% with tobramycin .3%
  - (Tobradex)
  - moderate to severe conditions with inflammation and risk of infection
Steroid-Antibiotic Combinations
- These medications are **steroids** and therefore cause the same side effects
- **Primary use** is for control of inflammation
- Provides antibacterial prophylaxis while treating the ocular inflammation
- Examples:
  - Adenoviral KC w/sig epi staining
  - Marginal K infiltrate --->

Steroid-Antibiotic Combinations
- Loteprednol etab. 0.5% with tobramycin 0.3% (Zylet)
  - Mild-moderate inflammation and risk of infection

What’s New?
- **TobraDex ST** (tobramycin/dexamethasone ophthalmic suspension) 0.3/0.05%.
- Indicated for inflammatory ocular conditions for which a corticosteroid is indicated and where bacterial infection or risk for infection exists.
- Formulated with a new vehicle to enhance bioavailability to targeted tissues.
- Useful for blepharitis/MGD

Irvine-Gass Syndrome
- Post-operative Cystoid Macular Edema (CME)

Fundus Evaluation
- DFE shows macular detail obscuration
- “Honeycomb” lesion w/cystic spaces
- Macular elevation

Optical Coherence Tomography
Adverse Events Associated with Conventional NSAID Therapy

- Mild/Moderate corneal side effects¹:
  - Burning and irritation
  - Superficial punctate keratitis
  - Delayed wound healing
- Severe corneal issues²:
  - Thinning
  - Perforation due to melts

² Mah et al. ASCRS 2000.

“New” (and old) NSAID

- Acuvail™ (Allergan)
  - Ketorolac tromethamine 0.45%
  - New formation of Acular 0.5%
  - Preservative-free
  - FDA approved for pain, post-cataract Sx
- Dosage is bid

NSAIDs: What’s new?

- BROMDAY™
- ISTA
- bromfenac ophthalmic solution 0.09%
- Once-a-day dosing

Objective Findings

- VA: c SRx OD 20/25 OS 20/80 PH NI
- Pupils: (-)APD, PERRLA
- EOMS: Smooth / Full
- CF: Full OD/OS
- Lens, Vitreous: Clear OD/OS
- IOP: 13 mm Hg OD, 12 mmHg OS
Topical Antibiotics

- First-line agents for Bacterial Infections
  - Fluoroquinolones eradicate a wide variety of ocular pathogens
  - Aminoglycosides provide broad spectrum coverage, slightly more effective against gram-negative bacteria
  - Polymyxin B combinations provide broad spectrum coverage
  - Macrolides provide broad spectrum coverage

Fluoroquinolones

- Ciloxan (ciprofloxacin 0.3%, Alcon)
- Iquix (levofloxacin 1.5%, Vistakon)
- Ocuflox (ofloxacin 0.3%, Allergan)
- Quixin (levofloxacin 0.5%, Vistakon)
- Vigamox (moxifloxacin 0.5%, Alcon)
- Zymar (gatifloxacin 0.3%, Allergan)
Fourth Generation FQs
- levofloxacin 0.5%, 1.5%
- moxifloxacin 0.5%
- gatifloxacin 0.3%
- All interfere w/enzymes DNA gyrase, topoisomerase IV, which are needed for the synthesis of bacterial DNA
- Thus, two separate mutations needed for resistance.

Inflammation/Infection (Cont’d)
Corneal ulcers
- May be bacterial, viral, fungal, other bugs
- Edema: accumulation of fluid within the tissue, can be diffuse or microcystic
- Ulceration: epithelial break accompanied by infiltration, may involve deeper corneal layers
- Contact lens wearers at higher risk, specially extended-wear patients
- Neovascularization: new blood vessels as response to hypoxia
- Infiltrate formation: immune response

Inflammation/Infection (Cont’d)
Corneal ulcers
- If culturing same day, do not use any eye drops b/f, may interfere with process
- If bacterial, must be treated aggressively with topical AB
- If HSV, use topical/po antivirals
- If suspect fungal or acanthamoeba, co-manage w/corneal specialist

New Fluorquinolone
- Besifloxacin 0.6% susp
- FDA indication for bact. conj.
- Durasite vehicle
  - Lengthens ocular surface contact time

Besivance and MRSA
- Minimum inhibitory concentrations for besifloxacin were at least 2-4X lower than other antibiotics tested
- No systemic counterpart decreases resistance

What’s new in the Tx. of bacterial conjunctivitis?
WHAT’S NEW?
- Zymaxid (gatifloxacin .5%)
- Allergan increased conc. of Zymar (.3%)
- Approved for > 1 year old
- Approved for bact. conj.
- Well-suited for Bacterial Keratitis

Case
- A 25 year old male states that he has hayfever in the spring and has been congested recently. He complains of itchy, red, watery eyes.
- DVA OD: 20/20
  OS: 20/20
- Ocular assessment of the conjunctiva is remarkable for mild redness and a watery discharge, no corneal staining

Case
- Diagnosis? Management?
- Ocular allergy
- Since he is symptomatic and reported seasonal recurrence, then an antihistamine with some mast cell stabilizing properties would provide both immediate relief as well as long term relief with continued use

Allergic Eye Disease
- Common symptoms: Itching, mucous discharge, occasional swelling and redness.
- Patients often report a history of allergies and concurrent rhinitis.
- Common signs: chemosis, hyperemia, papillae, mucous.
Allergic Conjunctivitis

TREATMENT
- Reassurance
- No rubbing!!!
- Avoidance
- Cold compresses
- Artificial tears
- Olopatadine
- Ketotifen fumarate
- Loteprednol

Allergies

- Olopatadine .1 %
- Combo drug: Antihistamine/Mast Cell Stabilizer
- Very safe
- Very comfortable
- BID dosing or qd (Pataday .2%)

What’s new in the treatment of allergic conjunctivitis?

Bepreve (ISTA Pharm)

- Bepotastine besilate ophthalmic solution 1.5%
- H-1 receptor antagonist
- Inhibitor of the release of histamine from mast cells.
- Bid dosing
- Pregnancy Category C
- Approved for children >2 y/o

POAG OS > OD

NFL
**Prostaglandins**
- latanoprost
- travoprost
- bimatoprost

**Prostaglandins**
- MECHANISM
  - ENHANCES UVEOSCLERAL OUTFLOW
  - LUMIGAN MAY AID CONVENTIONAL TM OUTFLOW
- EFFICACY
  - 27-34% REDUCTION OF IOP
  - IOP REDUCTION STARTS IN 3-4 HOURS
  - MAXIMUM IOP EFFECT AFTER 8-12 HOURS
- DOSING
  - ONCE A DAY

**SIDE EFFECTS**

**Want longer lashes?**

LATISSE solution is a prescription treatment for hypotrichosis
**PG CONTRAINDICATIONS**

**IS THERE A DIFFERENCE?**

**WHAT’S NEW?**

- Lumigan .01%
  - Optimized formulation with a reduced concentration of bimatoprost.

**IS THERE A DIFFERENCE?**

**WHAT’S NEW?**

- TRAVOPROST-Z .004% (2006)
  - NO BENZALKONIUM CHLORIDE (BAK)
  - SoEs
  - LESS HYPEREMIA
  - LESS CORNEAL TOXICITY
  - STATISTICALLY EQUIVALENT IOP
- INSTILLATION AIDS
- FUTURE USE IN COMBOS

**QUESTION**

- What is your preferred class to use as adjunctive therapy when the target IOP is not reached or progression is noted w/1 med?
  - NON-SELECTIVE BETA-BLOCKER
  - CARDIOSELECTIVE BETA-BLOCKER
  - ALPHA-AGONIST
  - TOPICAL CARBONIC ANHYDRASE INHIBITOR
  - MIOTICS
2006 SURVEY DATA

Nonselective Beta-Blockers

- Timolols
  - timolol hemi-hydrate 0.25% or 0.5%
  - Levobunolol
    - 0.25% or 0.5%

WHAT'S NEW?

- Non-preserved Timolol maleate
  - .25%, .5%

Combinations

- COMBIGAN
  - Brimonidine/Timolol
  - Bid dosing
- COSOPT
  - Dorzolamide/Timolol
  - Bid dosing
- The Future?
  - A PG/BB combo

Non-Selective Beta Blockers

- 0.25 vs 0.5 timolol
- Qd vs bid
- Depends upon iris color
- Recommendation
  - Lowest concentration once a day
  - Check for efficacy

Dry Eye Treatment

- Artificial tears is the mainstay of initial topical treatment
  - preservative free vs. preserved
  - low viscosity (thinner consistency)
  - medium viscosity (medium consistency)
  - high viscosity (thick consistency)
  - ointments
Soothe XP Emollient
- Restoryl
- Meta-stable emulsion
- Increases lipid layer
- Highly purified mineral oils
  - Drakeol-15
  - Drakeol-35
- Polyhexamethylene biguanide-preserved

WHAT’S NEW?
- Systane Balance (Alcon)
- For evaporative dry eye secondary to MGD
- Enhancement of lipid layer
- Propylene Glycol 0.6%
- Mineral oils
- Oil in water emulsion
- LipiTech System and demulcent.

Dry Eye Treatment
- Cyclosporine 0.05% (Restasis)
  - Ophthalmic emulsion
  - Provides anti-inflammatory effects for ocular surface tissues and lacrimal glands
  - Requires 3-4 months of continuous use to reach clinically significant effects and up to 6 months to achieve full therapeutic effects

Omega-3s
- Decrease inflammation
- Decrease apoptosis
- Increase tear secretion

Questions and Comments?

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