Pharmacology for the Para

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Disclosures
- Allergan Pharmaceuticals Speaker’s Bureau
- Bio-Tissue
- BioDLogics, LLC
- Katena/IOP
- Seed Biotech
- Johnson and Johnson Vision Care, Inc.

Agenda
- Review of common topical medications
- Ocular side effects of medications
- Off Label Uses of Common Medications
- Name That Medication

Common Topical Medications
- Allergy
  - Hallmark symptom of ocular allergies?
  - Up to 30% of US population affected by seasonal allergy symptoms
  - 1/3 of world’s population affected
  - 70-80% of those exhibit itching
- Seasonal Allergic Conjunctivitis (SAC)
  - Grasses, pollens, ragweed, cottonwood
- Perennial Allergic Conjunctivitis (PAC)
  - Mold, mildew, dust mites, animal dander

Name That Medication
Hallmark symptom of ocular allergies?
Up to 30% of US population affected by seasonal allergy symptoms
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Mold, mildew, dust mites, animal dander

Seasonal Allergic Conjunctivitis (SAC)
Perennial Allergic Conjunctivitis (PAC)
Anti-allergy

- Lastacaft (Allergan): One drop daily
- Bepreve (B&L): One drop 2x/day
- Patanol (Alcon): One drop 2x/day
- Pataday (Alcon): One drop daily
- Pazeo (Alcon): One drop daily

What causes the itch?
- Allergen enters the eye
- Release of chemicals by mast cells
  - Histamine

Treatment of allergies
- Anti-histamines
- Mast cell stabilizers

Indications:
- A lubricant indicated for the treatment of moderate to severe dry eye

Contraindications:
- In patients with known severe hypersensitivity to any of the ingredients in the formulation

Supplied in 15 ml bottles

Dosage
- 1 or 2 drops in affected eye(s) as needed

Safe for CL wearers

Prescription Only

Treats all 3 tear film layers
- Lipid layer: Amisol
- Aqueous layer
- Mucin layer

Has a high oncotic pressure
- Re-establishes integrity of epithelium
- Reduces microcystic edema
- Prevents recurrent damage

Behind the Counter (BTC)

Over the Counter (OTC)
Ocular Side Effects of Systemic Medications

**Case Study**
- 59 year old female starting new medication
- Ocular Hx: Unremarkable
- Medical Hx: Multiple Sclerosis
- Baseline Exam: 20/20 OD, OS

**Case Study - Baseline**

**Case Study – 8 Months Later**
- 20/40

**Gilenya (fingolimod)**
- **Indications**
  - for the treatment of patients with relapsing forms of multiple sclerosis to reduce the frequency of clinical exacerbations and to delay the accumulation of physical disability
- **Contraindications**
  - None

**Ophthalmic Concerns**
- Macular edema (0.4%)
- Can occur with or without visual symptoms
- Ophthalmologic evaluation should be performed before starting
- Repeat 3-4 months after treatment initiation
- Monitor visual acuity at baseline and during routine evaluations of patients
- OCT recommended
**Topamax**
- Indicated for treatment of migraines or seizures
- Potential side effects
  - Acute myopia
  - Shallowing of anterior chamber
  - Angle closure glaucoma
  - Maculopathy

**Flomax (Tamsulosin)**
- Strong association with IFIS first reported in 2005
  - Iris billowing and floppiness
  - Iris prolapse to main and side incisions
  - Progressive miosis
- Classified:
  - Mild (17%)
  - Moderate (30%)
  - Severe (43%)
- Important to make surgeon and patient aware

**Flomax (Tamsulosin)**
- Most widely prescribed treatment worldwide for BPH
  - $1.9 billion 2009
- Systemic Alpha1 antagonist
  - Highly selective for A1a receptor
- Relaxes smooth muscles
  - Bladder neck and prostate
  - Permitting more complete emptying
  - Iris dilator smooth muscle

**Flomax (Tamsulosin)**
- IFIS can occur more than 1 year after Flomax has been discontinued
  - Eventually produce a permanent atrophic change in the iris dilator muscle that is not reversed by discontinuation
  - IFIS has occurred within 3 – 7 days of initiating treatment
  - Stopping pre-operatively is of unpredictable and questionable value

**Plaquesnil**
- Indicated for the prevention or treatment of malaria infections
- Also can be used to treat auto-immune diseases
  - Lupus
  - Rheumatoid Arthritis
- Recommended testing every 6-12 months
  - Baseline photos prior to initiation of therapy
  - OCT
  - HVF 10-2 White on White
**Plaquinil**

- Potential for changes to cornea or optic nerve
- Potential for deposition in macular region
  - More common
  - Toxic maculopathy
  - Changes can be noted on DFE, OCT, and HVF

**Plaquinil**

- Recommended testing every 6-12 months
  - Baseline photos prior to initiation of therapy
  - OCT
  - HVF 10-2 White on White
  - Co-manage with rheumatologist

**Queen Ann’s Lace**

- Slang term for marijuana

**Queen Ann’s Lace**

Alaska
Arizona
California
Colorado
Connecticut
District of Columbia
Delaware
Hawaii
Illinois
Maine
Maryland
Massachusetts
Michigan
Minnesota
Montana
Nevada
New Hampshire
New Jersey
New Mexico
New York
Oregon
Rhode Island
Vermont
Washington

23 States and Washington DC have legalized medical marijuana
Queen Ann’s Lace

- Binds to cannabinoid receptors in brain
  - Highest density in areas responsible for influencing
    - Pleasure
    - Memory
    - Thinking
    - Concentrating
    - Sensory and time perception
    - Coordinated movement

Potential systemic effects
- Cardiac arrhythmias
- Coronary insufficiency
- Myocardial infarction

Potential ocular effects
- Decreased tracking
- Dilated pupils
- IOP lowering capabilities
  - The high dose of marijuana necessary to produce a clinically relevant effect on IOP in the short term requires constant inhalation, as much as every three hours.
  - Glaucoma Research Foundation

Appropriate medical uses (NIH)
- Stimulate appetite and alleviate cachexia
- Control nausea and vomiting associated with cancer chemotherapy
- Decrease intraocular pressure
- Analgesia
- Neurological and movement disorders

Off Label Use of Common Medications

Once a drug has been approved for marketing, a physician may prescribe it for uses or in treatment regimens or patient populations that are not included in approved labeling. Such “unapproved” or, more precisely, “unlabeled” uses may be appropriate and rational in certain circumstances, and may, in fact, reflect approaches to drug therapy that have been extensively reported in medical literature.

Off Label Use

Use of a medication or product for a different indication, age group, dosage or administration than approved by the FDA.

FDA Recommendations
- Good medical practice and the best interests of the patient require that physicians use legally available drugs according to their best knowledge and judgment

Off Label Use
- Responsible to be well-informed about product
- Base its use on firm scientific rationale and on sound medical evidence
- Maintain records of product’s use and effects
### Restasis

**Indications**
- Topical immuno-modulator indicated to increase tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca

**Contraindications**
- In patients with known or suspected hypersensitivity to any of the ingredients in the formulation

**Dosage**
- 1 gtt in affected eye Q12H

### Off Label Uses - Restasis

**Vernal keratoconjunctivitis (VKC)**
- A seasonal form of allergic conjunctivitis
- Severe itching, redness, sensitivity to light, and discharge
- VKC has the potential to lead to corneal ulcers, keratoconus, and permanent vision loss
- Histopathological studies showed T-lymphocytes in the conjunctival papillae

**Herpes Stromal Keratitis**
- Not active viral infection but viral antigens initiating a T-lymphocytic destruction of the stroma
- Studies show topical steroids effective
- Concerns?
  - May limit herpetic reactivation

**Corneal transplantation**
- Reduces inflammation, does not increase the susceptibility to infection
- Eliminates the issues surrounding the potential for a steroid response

**Meibomian Gland Dysfunction**

**Recurrent Corneal Erosions**
- Improves tear film
- Controls MGD
Off Label Uses - Restasis
- Atopic Keratoconjunctivitis
- Graft vs. Host Disease
- Ocular Rosacea
- Thygeson’s Superficial Punctate Keratitis
- Superior Limbic Keratoconjunctivitis
- Pterygium Recurrence Prevention

Bottom Line
- Topical cyclosporine is an excellent and safe alternative to topical corticosteroids
- Useful where patients may require long term or high dose topical steroids
- No impact on IOP or viral replication
- Does not slow wound healing or cause cataracts

Other Off Label Uses
- Prostaglandins
  - Refractive fluctuations thought to be due to IOP
  - Minimal in intact cornea
  - Once daily dosing may stabilize or maintain IOP

- Alpha-agonists (Alphagan P)
  - Post-surgical glare/halos (RK, LASIK, multi-focal implants)
  - Inhibits sphincter dilator muscle
  - Dosed 30-60 minutes before night time driving

Topical Antibiotics
- Ciloxan
- Vigamox/Moxeza
- Zymaxid
- Besivance
- Tobradex ST
- AzaSite

Topical Fluoroquinolones
- Vigamox/Moxeza
  - moxifloxacin HCl 0.5%
  - Indications
  - Treatment of bacterial conjunctivitis by susceptible organisms
  - Vigamox: TID x 7 days
  - Moxeza: BID x 7 days

- Zymaxid
  - gatifloxacin 0.5%
  - Indications
  - Treatment of bacterial conjunctivitis by susceptible organisms
  - Instill one drop every two hours in the affected eye(s) while awake, up to 8 times on Day 1
  - Instill one drop two to four times daily in the affected eye(s) while awake on Days 2 through 7

Besivance
- besofloxacin 0.6% ophthalmic suspension
- Indications
  - Treatment of bacterial conjunctivitis by susceptible organisms
- Developed specifically for topical ophthalmic use
  - No widespread systemic, agriculture, or animal feed usage
  - Greatly reducing chance for resistance
  - Research shows some potential anti-inflammatory properties
Off Label Uses
- Corneal ulcers
- Corneal abrasions
- Empirical treatment of non-cultured ulcer
- Surgical prophylaxis of infection

Name The Medication
- Can be used with certain surgical procedures
- Can be used for glaucoma patients
- Several different formulations
  - 1%, 2%, 4% drop
  - 4% gel
- Has a green cap

Name the Medication
- Is used during cataract surgery
- Can be used to reduce inflammation
- Several different formulations
  - 0.25%, 0.5%, 1%, 2%, 5% drops
  - 1% gel
- Has a red cap

Cycloplegics vs. Mydriatics
- Tropicamide and Cyclopentolate
  - Mostly mydriatic effects
  - Not considered therapeutic
- Risks
  - Acute angle closure
- Adverse Effects
  - Blur, photophobia
**Name the Medication**
- Can be used for allergies
- Can be used after surgical procedures
- Can be used for inflammation
- Supplied as drops, ointment, or emulsion
- Usually has a pink or white cap

**Topical Corticosteroids**
- Indicated for the treatment of pain and inflammation
- Concerns over long term use?
  - Increased IOP
  - Increased risk of infection
  - Increased incidence of cataracts

**American Academy of Ophthalmology Color Code**
- Created by Academy’s Committee on Drugs
- Cooperation of FDA, pharmaceutical companies
- Aimed at safety of patient

**Topical Medication**
- Beta-blockers
  - Used in treatment of_________
  - Lower IOP by decreasing aqueous humor production
  - Timolol, Istralol, Betimol

**Topical Medication**
- Beta-blocker combination
  - Lower IOP by decreasing aqueous humor production and increases outflow
  - Combigan

**Topical Medication**
- Carbonic Anhydrase Inhibitors (CAI)
  - Lower IOP by decreasing aqueous humor production
  - Azopt
Topical Medication

- Anti-infectives
  - Antibiotics
  - Anti-virals
  - Anti-fungals

Concerns

- Pigmentation
  - Pigmentation of the iris, periorbital tissue (eyelid) and eyelashes can occur. Iris pigmentation is likely to be permanent.

- Eyelash Changes
  - Gradual change to eyelashes including increased length, thickness and number of lashes. Usually reversible.

Topical Medication

- NSAID (Non-Steroidal Anti-Inflammatory)
  - Reduce pain and inflammation without side effects of steroids
  - Commonly used after cataract surgery

Topical Medication

- Prostaglandin Analogs
  - Increase uveo-scleral outflow

Topical Medication

- Adrenergic agonists
  - Decrease aqueous humor production and increase outflow

Review

- Adrenergic Agonists
- Beta Blockers
- Anti-infectives
- Mydriatics/Cycloplegics
- NSAIDs
- Miotics
- Corticosteroids
- Beta Blocker Combo
- Carbonic Anhydrase Inhibitors
- Prostaglandin Analogs

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Conclusion

- All medications will have side effects
- It’s safe and appropriate to use off label meds
- Use technology to your advantage

Thank you

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