**OCULAR PHARMACOLOGY II**

Miotics, Glaucoma Meds, Antibiotics, Corticosteroids, NSAIDS Antivirals, Antihistamines

Christopher J. McDevitt, M.D.

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**CHOLINERGIC AND ANTICHOLINERGIC MEDS**

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**CHOLINERGIC DRUGS**

- Direct agonists
- Indirect agonist
- Antagonist

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**CHOLINERGIC AGONISTS**

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**CHOLINERGIC NEURON**

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**CHOLINERGIC DRUGS**

- Direct agonist:
  - Miosis, accommodation
  - Increase aqueous outflow decrease IOP
- Acetylcholine 1% carbachol 0.01% intracameral use constrict pupil anterior segment surgery
- Acetylcholine rapid effect but short lived
- Carbachol 100 times more effective longer lasting 24 hours and decreases IOP
CHOLINERGIC DRUGS DIRECT AGONIST

- Pilocarpine:
  - Lowers IOP by increasing outflow
  - Open angle glaucoma treatment

- Side effects:
  - Miosis older patients with cataract difficulty in scotopic conditions
  - Cataractogenesis
  - Induced myopia and accommodation problems for younger patients; slow dissolving pilocarpine gel at bedtime

CHOLINERGIC DRUGS: INDIRECT AGONIST CHOLINERSTERASE INHIBITORS

- Phospholine iodide
  - No longer available for ophthalmic use in US
  - More potent than direct acting use twice a day

- Physostigmine, neostigmine, edrophonium

CHOLINERGIC ANTAGONISTS

- Atropine: post-synaptic blockage of acetylcholine
  - Pupil dilatation, cycloplegia for iritis, accurate cycloplegic refraction
  - Treat malignant glaucoma
  - Systemic atropine given during ophthalmic surgery involving EOM manipulation to block oculocardiac reflex and prevent bradycardia and hypotension

- Side effects of systemic absorption of atropine eye drops:
  - Side effects treated with physostigmine
  - Other antagonists: tropicamide, cyclopentolate, homatropine, scopolamine, flushing, tachycardia, constipation, urinary retention, delirium.

INDIRECT ACTING ANTAGONIST

- Edrophonium test: increases acetylcholine at neuromuscular junction
- Myasthenia gravis: antibodies to acetylcholine receptor resulting in generalized weakness, ptosis and diplopia
- Edrophonium used to diagnose myasthenia gravis
- Neostigmine can be given IM for the same purpose and has a longer duration of activity
- Allows clinician more time to make orthoptic measurement for desired endpoint

NEUROMUSCULAR BLOCKADE FOR GENERAL ANESTHESIA

- Globe laceration repair under general anesthetic
- Use of neuromuscular blocking drugs by anesthetist; i.e. succinylcholine is a “depolarizing” neuromuscular blocker and can cause contraction of EOMs on induction of general anesthetic and should not be used
- Exert force on open globe
- Increase IOP in other cases where pressure measurement is desired such as in an examination under anesthesia

MYDRIATICS AND CYCLOPLEGICS

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Norepinephrine (NE) is a transmitter.
- Alpha and beta receptors for NE
  - Direct agonists
  - Indirect agonists
  - Antagonists

Alpha-1 phenylephrine: Mydriasis stimulates iridial muscle.
- Nephrotoxic: decongestant with rebound vasodilation and hyperemia
- Elevate systemic blood pressure
- Caution: using 10% phenylephrine topically (5mg per drop), MI, stroke, cardiac arrest risks
- Systemic “pressor” dose bolus IV 50-100ug

Apraclonidine (Iopidine):
- Pre and post YAG cap and SLT, cataract extraction to manage increased IOP
- Prevents NE release decrease pupil size
- Decreases aqueous production and increases outflow
- Topical sensitivity 40% and tachyphylaxis limit long-term use

Brimonidine (Alphagan):
- Topical sensitivity 15%
- 0.2% with BAK
- 0.15% with polyquad
- 0.1% with sodium chlorite preservative (Alphagan-P)
- Avoid in infants less than 2 years: hypotension, hypothermia, bradycardia
- CNS effects resulting from medication crossing the blood-brain barrier

Cocaine 4% or 10%
- Hydroxyamphetamine 1%
- Office diagnostic testing to confirm Horner syndrome
- Available through compounding pharmacies
**BETA-ADRENERGIC AGONISTS**

- Epinephrine not available for glaucoma treatment
- Dipiveprin (Propine) 0.1% available as generic
- Reduce aqueous production and increase trabecular outflow
- Reduced effectiveness over time

**BETA-ADRENERGIC ANTAGONIST: BETA BLOCKERS**

- Reduce aqueous production by up to 80%
- Inhibit the normal physiological responses of increasing pulse and BP with exertion: may be poorly tolerated in active or elderly with routine activities
- Reduce bronchoospasm in asthma and COPD patients

- 6 drugs:
  - Betaxolol: selective $\beta_1$ inhibitor; less irritating
  - Carvedilol (Coreg): nonselective
  - Levobunolol (Betagan): nonselective $\beta$ blockers
  - Metipranolol (Optipranolol)
  - Timolol maleate (Timoptic)
  - Timolol hemihydrate (Betimol)

**BETA-ADRENERGIC ANTAGONISTS**

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**CARBONIC ANHYDRASE INHIBITORS**

- Carbonic anhydrase is enzyme involving the production of aqueous humor in the ciliary body
- Topical preparations for Glaucoma treatment
- Acetazolamide (Diamox) oral in the management of pseudotumor cerebri

**CARBONIC ANHYDRASE INHIBITORS**

- Topical:
  - Dorzolamide (Trusopt); In combination with Timolol (Cosopt)
  - Brinzolamide (Azopt)

- Systemic:
  - Acetazolamide 4 times daily
  - Methazolamide twice daily
  - Side-effect is a systemic metabolic acidosis
  - Low potassium may also result
  - Renal stone formation 11 times higher
  - Numbness and tingling hands and feet, weight loss from anorexia
  - Skin rash
**Prostaglandin Analouges**

- Latanoprost (Xalatan)
- Bimatoprost (Lumigan)
- Travoprost (Travatan)
- Tafluprost (Zioptan)
- Unoprostone (Rescula)

**Ocular side effects:**
- Darkening of iris and periorcular skin
- Hypertrichosis of eyelashes
- Cystoid macular edema (CME)
- Conjunctival hyperemia
- Uveitis
- Reactivation of HSV keratitis
- Use with caution in pregnant patients since uterine contractions are mediated by prostaglandin

**Routes of Administration**
- Local injection
- Ocular implantation
- Topical
- Systemically

**Categories**
- Glucocorticoids
- Non-steroidal anti-inflammatory drugs
- Mast cell stabilizers
- Antihistamines
- Antifibrotics

**Anti-Inflammatory Drugs**

**Corticosteroids and Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)**

**Ocular Anti-Inflammatory Drugs**

**Routes of Administration**
- Local injection
- Ocular implantation
- Topical
- Systemically

**Categories**
- Glucocorticoids
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**Glucocorticoids/Steroids**

- **Most important effect** is inhibition of arachidonic acid (AA)
- AA is converted into potent mediators of inflammation:
  - prostaglandins
  - endoperoxidases
  - leukotrienes
  - thromboxanes
- **Adverse ocular effects** from topical steroids:
  - Glaucoma
  - Posterior subcapsular cataract
  - Bacterial, viral infections
  - Uveitis
  - Ptosis
  - Scleral melt
  - Eyelid skin atrophy
STEROIDS ADVERSE EFFECTS: SYSTEMIC ADMINISTRATION

- Suppression of pituitary–adrenal axis
- Hyperglycemia, muscle-wasting, osteoporosis
- Redistribution of fat from periphery to trunk
- Euphoria
- Insomnias
- Aseptic necrosis of the hip
- Peptic ulcer
- Diabetes mellitus
- Psychosis

4% develop an IOP > 31 mm Hg after 6 weeks
- Reduce aqueous outflow is cause of IOP rise
- Dexamethasone > prednisolone > FML
- Reversible upon discontinuation of the drug if use is less than one year
- Permanent elevations of IOP if used more than 18 months
- Loteprednol 0.2%, 0.5% have lower incidences of increased IOP
- Fluocinolone implant for chronic uveitis
- Triamcinolone 40mg/ml preservative free for intravitreal use: increased rates of cataract and need for glaucoma treatment

NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS)

- Flurbiprofen 0.3% (Ocufen) first available topical NSAID used pre-op to reduce intraoperative miosis for cataract surgery
- Diclofenac 0.1% (Voltaren) prophylaxis and treatment of post-op inflammation and CME
- Ketorolac (Acular) post-op inflammation and allergic conjunctivitis treatment
- Nepafenac (Novanac), Bromfenac (Kibrom) twice daily dosing treating postop cataract and retinal surgery inflammation
- NSAIDs have topical anesthetic properties: useful in short term management of corneal abrasion, anterior segment procedures and refractive surgery

MAST CELL STABILIZERS, ANTIHISTAMINES

- Human eye has approximately 50 million mast cells containing granules containing chemical mediators
- Immediate hypersensitivity reaction triggered when antigens combine with IgE on the surface of mast cells
- Mast cells release histamine and other factors
- Histamine increases capillary dilation, conjunctival swelling and injection
- Safer than steroids for chronic use
**MAST CELL STABILIZERS, ANTIHISTAMINES**

- **H1 antagonist**: emedastine (Emadine), azelastine (Optivar)
- **Mast cell stabilizers**: cromylin (Crolom), lodoxamide (Alomide), pemirolast (Alamast), nedocromil (Alocril) take days to weeks to reach peak efficacy
- **Mixed H1 antagonists/mast cell stabilizers**: olopatadine (Patanol), ketotifen (Zaditor, Alaway), epinastine (Elestat), azelastine (Optivar)

**OPHTHALMIC ANTIBIOTICS**

**OPHTHALMIC ANTIBACTERIALS**

**OPHTHALMIC ANTIBIOTICS FLUOROQUINOLONES**

- Fluoroquinolones:
  - ofloxacin, levofloxacin, ciprofloxacin, moxifloxacin, gatifloxacin, besifloxacin
  - Broad spectrum: gram-positive and gram-negative
  - Older generation have good potency with gram-negative
  - Newer meds have expanding gram-positive coverage
  - Treat corneal ulcers, conjunctivitis
  - High rate of intraocular penetration

**OPHTHALMIC ANTIBIOTICS SULFA DRUGS**

- Sulfonamides: sulfacetamide ophthalmic solution and ointment
- Sensitivity reactions 5% incidence
- More effective when combined with trimethoprim or pyrimethamine
- Cross allergenicity with non-antibiotic sulfonamides is unlikely based on chemical differences but is theoretically possible
- No cross-allergenicity between sulfonamide and sulfates

**OPHTHALMIC ANTIBIOTICS AMINOGLYCOSIDE; IODINE**

- Aminoglycosides: gentamicin, tobramycin
- Neomycin 8% of patients (maxitrol) develop allergy
- Erythromycin, clarithromycin, azithromycin
- Bacitracin alone or in combination with polymyxin, neomycin
- Polymyxin/trimethoprim (Polytrim) may be used in sulfa allergic patients
- Iodine:
  - Topical povidone-iodine 5% solution: prepare surgical field and is important in prophylaxis against endophthalmitis
  - Povidine iodine scrub damages corneal epithelium
  - Iodine allergic patients do not use. Allergic to contrast media or seafood allergic probably OK to use
COMBINATION ANTI-INFLAMMATORY, ANTIBIOTIC DRUGS

ANTI-VIRAL MEDICATIONS

ANTIVIRAL DRUGS

- Trifluridine (Viroptic) herpes simplex keratitis
- Acyclovir 3% ointment not available in US. 5% dermatological ointment not approved for ophthalmic use
- Ganciclovir gel 0.15% (Zirgan) approved for treatment of HSV keratitis

ANTIVIRAL DRUGS SYSTEMIC

- Acyclovir (Zovirax) used to treat ocular HSV and HZV; 400mg twice daily prevents recurrence of epithelial and stromal keratitis
- Valacyclovir (Valtrex) HZV but not HSV infections
- Famciclovir (Famvir) HZV reduces duration of post herpetic neuralgia
- Ganciclovir CMV retinitis intravitreal insert release drug over 5-8 month period