Case Report – Asthma Patient

- 62-year-old white female with POAG
- Early nasal step in one eye only; other visual field is normal
- Taking prostaglandin analog once daily at bedtime with excellent adherence
- IOPs are consistently low (16 to 18mm Hg) but occasionally rise to the mid-20s
- Why??
What We Will Cover Today

• Drugs that impact the ocular surface
• Drugs that increase IOP
• Drugs that lower IOP
• Drugs that may cause angle closure
• Drugs that may cause optic neuropathy
• Adverse drug interactions

DRUGS THAT IMPACT THE OCULAR SURFACE

Why Is This A Potential Problem For Our Glaucoma Patients?

• May decrease tolerability of topical medications
• May decrease compliance/adherence with therapy
• May increase potential for BAK toxicity
• May increase risk of ocular surface infection
• May impact results of functional tests

Drug-Induced Dry Eyes

Drugs Causing Dry Eye

• Anticholinergics
• Antihistamines
• Phenothiazines
• Anti-anxiety agents
• Tricyclic antidepressants
• Vitamin A analogs
Parasympathetic (Cholinergic) Innervation of Lacrimal Gland

Anticholinergics
- 1-2 mg oral atropine reduces aqueous tear secretion from 15 µl/min to 3 µl/min
- 1-2 mg oral scopolamine reduces tear secretion from 5 µl/min to 0.8 µl/min

Anticholinergic Agents
- Sominex (diphenhydramine)
- Lomotil (diphenoxylate and atropine)
- Detrol LA (tolterodine)

Pulmonary Drugs with Anticholinergic Activity
- Atrovent (ipratropium)
- Spiriva (tiotropium)

Oxybutynin (Oxytrol) Transdermal (Rx to OTC January 25, 2013)

Antihistamines
- H1 blockers reduce both aqueous and mucin production
- As little as 4 mg daily of chlorpheniramine maleate can produce positive Schirmer test
- Four days of once-daily loratadine (Claritin) can induce dry eye and corneal staining
- Can aggravate underlying condition of dry eye
Case Report

Antidepressants Causing Dry Eye
- Celexa
- Cymbalta
- Effexor XR
- Lexapro
- Nardil
- Paxil
- Prozac
- Sinequan
- Wellbutrin
- Zoloft

Descriptive Words in Package Insert Suggesting “Dry Eye”
- Anticholinergic
- Cholinergic antagonist
- Antimuscarinic
- Muscarinic antagonist
- Parasympatholytic

So Where Do I Find Package Inserts?
“What If I Don’t Have Time For All That?!!”

DRUGS THAT CAN INCREASE IOP
Drugs That Can Increase IOP

**Open Angle**
- Corticosteroids
- Topiramate

**Narrow Angle**
- Anticholinergics
- Antihistamines
- Phenothiazines
- Antidepressants
- Decongestants
- Bronchodilators

Drugs Causing Mydriasis

- Cholinergic antagonists
  - Anticholinergics
  - Antihistamines
  - Phenothiazines
- Adrenergic agonists
  - Amphetamines
  - $\alpha_1$-Adrenoceptor Agonists

Etiology

- Mydriasis can produce pupillary block and precipitate acute or subacute angle-closure glaucoma
- Weak cycloplegic effect may increase IOP even in open-angle glaucoma patients
- Relaxation of ciliary muscle may decrease traction on trabecular meshwork and increase resistance to aqueous outflow

Adrenergic Agonists

- Bronchodilators
  - Epinephrine (Primatene Mist)
  - Ephedrine (Primatene Tablet)
- Cold/hay fever decongestants
  - Pseudoephedrine (Sudafed)
  - Phenylephrine

Etiology

- Pupillary block occurs only in susceptible individuals
- Small eyes
- Hyperopia
- Steep corneal and lens curvatures
- Narrow angles
Drugs That Can Increase IOP (Open Angle)

Corticosteroids
Topiramate

Corticosteroids

- Can elevate IOP via all routes of administration
  - Oral
  - Intravenous
  - Topical ophthalmic
  - Periocular
  - Inhalation
  - Intranasal

Interesting Facts

- In steroid responders, oral steroids produce about 60% the increase in IOP as compared with topical agents
- In POAG patients, response rate is 46 to 92% compared with 18 to 36% in normal population
- Risk factors include increasing age, diabetes, high myopia, connective tissue diseases, and a first-degree relative with open-angle glaucoma

Interesting Facts

- In steroid responders, onset of IOP elevation occurs after about two weeks of topical use
- Time of onset often longer for systemic steroids
- Complex pathophysiologic factors result in increased resistance to aqueous outflow
**Patient Management**

- Monitor glaucoma patients carefully when they are taking systemic steroids.
- IOP normally returns to pretreatment levels within 2 to 4 weeks of steroid taper or discontinuation.
- The use of low to medium-dosage inhaled steroids and nasal steroids appears to have little risk.

**Drugs That Can Cause Secondary Angle Closure**

- Sulfonamides
- Diuretics
- Carbonic anhydrase inhibitors
- Isotretinoin
- Topiramate (Topamax)
  - Also a component of Qsymia (weight loss drug FDA-approved on July 18, 2012)

**Topiramate**

- Used to treat seizures, migraine headache, bipolar disorders.
- 85% of cases of mostly bilateral, acute angle-closure glaucoma occur within the first two weeks of treatment.
- Acute myopia, secondary angle-closure glaucoma, suprachoroidal effusions.

**Mechanism**

**Treatment of Topiramate-Induced Angle-Closure Glaucoma**

- Cycloplegic, NOT miotic
- Topical aqueous suppressants
  - β blocker
  - CAI
  - α2 agonist
- Topical steroids
New Weight-Loss Drug Containing Topiramate

DRUGS THAT CAN DECREASE IOP (Open Angle)

Drugs That Can Decrease IOP
- Beta-blockers
- Cannabinoids
- Cardiac glycosides
- Ethyl alcohol

Beta Blockers
- Used extensively for treatment of systemic hypertension
- Atenolol, metoprolol, nadolol, pindolol, propranolol, and timolol have been documented to produce dose-dependent reduction in IOP
- Ocular hypotensive effect comparable to that achieved with topically applied timolol

Mechanism
- Decreased aqueous formation via an action linked to predominantly beta-2 receptors on nonpigmented ciliary epithelium
- Nonselective oral beta blockers have particularly effective ocular hypotensive effects
- Topical beta blockers often produce little additional IOP reduction when administered concomitantly with oral beta blockers
Management

• Reduction in IOP may confuse the diagnosis of open-angle glaucoma
• Patients with glaucomatous optic neuropathy may be diagnosed incorrectly as having NTG
• Adding a topical beta blocker may be unproductive except in patients receiving a beta-1 selective oral agent
• Discontinuation of oral beta blocker therapy may result in substantially higher IOP

Bottom Line

• Although oral beta blockers are not approved as ocular hypotensive agents, the IOP lowering activity of these drugs may have a beneficial effect in the glaucoma patient
• In general, it is best to avoid topical beta blockers in patients taking oral beta blockers

Cannabinoids

• Have been administered orally, topically, and by inhalation as a means of reducing IOP
• Smoking and ingesting marijuana significantly reduces IOP
• After smoking a single marijuana cigarette, maximal ocular hypotensive response occurs 60 to 90 min. after inhalation and lasts approximately 4 hours

Classification of β Blockers

Cannabinoids

Welcome to COLORADO

Side Effects

• Postural hypotension
• Tachycardia
• Anxiety
• Drowsiness
• Euphoria
• Hunger
Cardiac Glycosides

- Systemic digoxin therapy reduces IOP by 14% in patients with POAG
- Physiologic effects are produced by inhibiting Na^+K^-ATPase
- This reduces active transport of sodium, a process necessary for aqueous formation

Management

- Systemic administration of cardiac glycosides may reduce IOP but would be inadequate to control IOP when maximal medical therapy has failed
- These drugs have low therapeutic index (low margin of safety)
- Side effects include GI disturbances, fatigue, and visual complaints
- Cardiac toxicity is not uncommon

Ethyl Alcohol (Ethanol)

- Reduces IOP by increasing serum osmolarity and functioning as a short-acting hyperosmotic agent
- Reduces IOP in both normal and glaucomatous eyes
- Maximal ocular hypotensive effect occurs 1 to 2 hours after consumption

DRUGS THAT MAY CAUSE OPTIC NEUROPATHY
Drugs (Confounders) Causing Optic Neuropathy

- Ethambutol
- Amiodarone
- Sildenafil

Several dozen published cases of optic neuropathy

Etiology for NAION with ED drugs is controversial and unproven

NAION associated with sildenafil is considered “possible” by WHO causality classification

Sildenafil (Viagra)

- Mild, transient, dose-related impairment of color vision
- Peak effect is 30 min to 2 hr after ingestion
- Visual side effects occur in 3-10% of users
- Bluish-tinged, pink-tinged, or yellowish-tinged vision
- Symptoms last several min to several hours
- Effects are due to inhibition of PDE-6, involved in retinal phototransduction
Look Out for Non-FDA Approved Generics of Viagra, Levitra, and Cialis

(These are sold OTC!)

OTC ED Food “Supplements”

Look Out for Non-FDA Approved Generics of Viagra, Levitra, and Cialis

(These are sold OTC!)

Other Products with Undeclared ED Components

ADVERSE DRUG INTERACTIONS

Drug-Drug Interactions

<table>
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<td>Cardiac glycosides</td>
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<td>Quinidine</td>
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<td>Xanthines</td>
<td>β Blockers</td>
<td>Bronchoospasm</td>
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Identifying Drugs with Interaction Potential

- Mobile programs (e.g., ePocratesRx from www.epocrates.com)

- Drug Interactions
  - With ePocrates check for interactions among up to 30 drugs at one time