

## Ocular Adverse Reactions of Systemic Drugs

Len V Koh PhD OD FAAO

Midwestern University Arizona College of Optometry

"All substances are poisons: there is none which is not a poison. The right dose differentiates a poison and a remedy." Paracelsus (1493-1541)

- Over 2 million serious ADRs yearly
- 100, 000 Deaths yearly
- 4<sup>th</sup> leading cause of death

Why is the drug not safe?

### **Alendronate (Fosamax)**

- Bisphosphonate derivative
- Osteoporosis, Paget's disease
- Inhibits bone resorption
- ADRs:
- **<1%: Episcleritis, scleritis, uveitis**

### **Amiodarone (Cordarone)**

- Antiarrhythmic agent, Class III
  - Recurrent ventricular fibrillation
  - Hemodynamically-unstable ventricular tachycardia
- ADRs:
- **Corneal deposits (>90%; causes visual disturbance in <10%), photophobia**
- **May cause optic neuropathy and/or optic neuritis → visual impairment.**

### **Bimatoprost (Lumigan, Latisse)**

- Prostaglandin analogues
  - Elevated intraocular pressure
  - Hypotrichosis of the eyelashes
- Prostaglandin-Associated Periorbitopathy (PAP)

### **Digoxin (Lanoxin)**

- Antiarrhythmic Agent
  - Heart failure
  - Atrial fibrillation
- Inhibition of the sodium/potassium ATPase pump

- Ocular: Visual disturbances (blurred or yellow vision)

### **Ethambutol (Myambutol)**

- Antitubercular Agent
  - Tuberculosis
- ADRs:
- Ocular: Optic neuritis (1-5%); color blindness, or visual defects (usually reversible with discontinuation)

### **Hydroxychloroquine (Plaquenil)**

- Aminoquinoline (antimalarial)
  - Malaria
  - Rheumatoid arthritis, lupus erythematosus
- Ophthalmic effects: loss of visual acuity, macular pigmentary changes, and loss of foveal reflex.
  - Risk factors include daily doses >6.5 mg/kg lean body weight.

### **Interferons**

- Interferon Retinopathy
- a baseline funduscopic examination at initiation
- a follow-up examination at least every 3 months thereafter?
- Isotretinoin (Accutane)
- Acne Products, Antineoplastic Agent
  - Acne, severe recalcitrant nodular
  - Neuroblastoma, high-risk
- Reduces sebum production
- Ocular: Conjunctivitis (4%), blepharitis (1%), chalazion (1%), hordeolum (1%), night vision decreased, photophobia.
- Pseudotumor cerebri especially in children

### **Thioridazine (Mellaril)**

- First Generation (Typical) Antipsychotic
  - Schizophrenia/psychosis
- blocks postsynaptic mesolimbic dopaminergic receptors
- Ocular: Pigmentary retinopathy, blurred vision, cornea and lens changes

### **Chlorpromazine (Thorazine)**

- Antimanic Agent; First Generation (Typical) Antipsychotic
- psychotic disorders

- Ophthalmic: Blurred vision, corneal changes, epithelial keratopathy, retinitis pigmentosa
- Ocular examination (yearly in patients >40 years; every 2 years in younger patients)

### **Prednisone**

- Corticosteroid, Systemic
- Acute asthma, COPD, gout, antineoplastic, RHA
- *Ophthalmic conditions:*
- Allergic conjunctivitis, keratitis, allergic corneal marginal ulcers, herpes zoster ophthalmicus, iritis and iridocyclitis, chorioretinitis, anterior segment inflammation, diffuse posterior uveitis and choroiditis, optic neuritis

### **Sildenafil (Revatio, Viagra)**

- Phosphodiesterase-5 Enzyme Inhibitor
  - Erectile dysfunction
  - Pulmonary arterial hypertension
- ADRs:
- Flushing (10-19%), headache (16-46%), dyspepsia (3-17%)
- Ophthalmic: Visual disturbance (2% to 11%; including vision color changes, blurred vision, and photophobia; dose related)

### **Tamsulosin (Flomax)**

- Alpha<sub>1A</sub> Blocker
- ADR >10%
  - Headache (19% to 21%),
  - Dizziness (15% to 17%)
  - Ejaculation failure (8% to 18%)
- Intraoperative floppy iris syndrome (<1%)
- Blurred vision (≤2%)

### **Topiramate (Topamax)**

- Anticonvulsant
  - Epilepsy
  - Migraine prophylaxis
  - Multiple off-label uses
- Blocks neuronal voltage-dependent sodium channels
- Acute myopia and secondary angle-closure glaucoma in adults and children, typically within 1 month of initiation
- Discontinue in patients with acute onset of decreased visual acuity and/or ocular pain.

**Tamoxifen (Soltamox)**

- Antineoplastic Agent, Estrogen Receptor Antagonist; Selective Estrogen Receptor Modulator (SERM)
- Breast cancer treatment and risk reduction
  - Competitively binds to estrogen receptors on tumors and other tissue targets
- Cataract (7%)
- (<1%): Decreased visual acuity, retinal vein thrombosis, retinopathy, corneal changes, and color perception changes.
- Tamoxifen keratopathy; Tamoxifen maculopathy

**Vigabatrin (Sabril)**

- Anticonvulsant
  - Refractory complex partial seizures
- Inhibits gamma-aminobutyric acid transaminase (GABA-T)
- Dose: 1.5g twice daily
- Visual field constriction ( $\geq 30\%$ ), nystagmus (13% to 15%), blurred vision (11% to 13%), Diplopia (3% to 7%)
- [www.SABRIL.net](http://www.SABRIL.net) for more info

**Conclusions**

- Many drugs have potential ocular adverse drug reactions
- All structure of the eyes can be affected
- Multiple medications can lead to a single clinical manifestation
- A single medication can lead to multiple ocular disorders
- Some of the ophthalmic ADRs are irreversible
- Pharmacovigilant and comanagement are essential

**References**

- Miguel A. et al. Ophthalmic adverse drug reactions to systemic drugs: a systematic review. *pharmacoepidemiology and drug safety* 2014; 23: 221–233
- <https://dailymed.nlm.nih.gov/dailymed/>
- <http://www.fda.gov/Safety/MedWatch/>
- <https://www.lowestmed.com/>
- <http://www.goodrx.com/>