Ocular Adverse Drug Reactions to Systemic Medications

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Disclosure Statement

- Alcon
- Allergan
- Bausch & Lomb Pharmaceuticals
- PHARMAKON Group
- United States Pharmacopeia
- Vision Service Plan

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“The remedy often times proves worse than the disease”

-- William Penn (1693)
WHO Causality Assessment of Suspected Adverse Drug Reactions
- Certain
- Probable/Likely
- Possible
- Unlikely
- Conditional/Unclassified
- Unable to Assess/Unclassifiable

Drugs Affecting the Cornea

Drugs Affecting The Cornea
- Chloroquine and hydroxychloroquine
- Chlorpromazine
- Gold salts
- Amiodarone

Chloroquine and Hydroxychloroquine

Clinical Signs
- Diffuse punctate deposits in corneal epithelium
- Curved lines converging below central cornea
- Green-yellow pigmented lines in whorl pattern
Symptoms

- Halos around lights
- Glare
- Photophobia
- Symptoms and signs disappear on discontinuation of therapy

Epidemiology

- At 400 mg daily dosage of hydroxychloroquine, no keratopathy occurs
- At 800 mg daily dosage, 6% develop keratopathy in 6 months, increasing to 100% in 4 years

Mechanism

- Reversible drug binding to intracellular nucleoproteins
- Changes are limited to corneal epithelium
- Individual susceptibility

Management

- Baseline examination
- Differential diagnosis includes Hudson Stähli lines and Fabry’s keratopathy
- Does not contraindicate continued treatment

Chlorpromazine

- Occur only in patients with concomitant heavy lens opacities
- Corneal pigmentation is white, yellow-white, brown or black
- Occurs at level of endothelium and Descemet’s membrane in interpalpebral fissure area
- Irreversible
Symptoms

- Glare
- Halos around lights
- Hazy vision

Clinical Signs

- Numerous minute gold particles appear as yellow-brown to violet and red deposits in stroma
- Deposits localize to posterior one-third of stroma

Symptoms

- No visual disturbances or other symptoms
Mechanism

- Gold is deposited in lens and cornea by circulation in aqueous

Epidemiology

- Occurs in 45-97% of patients receiving 1-7 grams total dosage
- No correlation between density of deposits and total dosage
- Positive correlation between duration of treatment and density of deposits

Management

- Gold therapy does not need to be reduced or discontinued
- Deposits often disappear within 3-6 months following discontinuation of chrysotherapy

Amiodarone

Clinical Signs

- Keratopathy begins 1-3 months after drug therapy is begun
- Prevalence is virtually 100% after 3 months

Amiodarone Keratopathy

- Faint, horizontal line in lower third of cornea
- Grade 2 occurs within six months
- Superior extension produces whorl pattern
- Grade 4 consists of irregular, round clumps of deposits
- Resolves within 6-18 months following discontinuation of drug
- Blurred vision
- Glare
- Halos around lights
- Light sensitivity

- Binds to polar lipids and accumulates within lysosomes
- Drug-induced lipid storage disease

- Drug dosage should be reduced or discontinued if visual symptoms are annoying or incapacitating
- Systemic symptoms may necessitate drug withdrawal

- Aspirin, Coumadin, Pradaxa, Plavix, Vitamin E, or Ginkgo biloba
Drugs Affecting the Lens

- Gold salts
- Corticosteroids
- Phenothiazines

Appearance of Steroid-Induced Cataract

- Posterior subcapsular
- Cannot be differentiated from early complicated cataract, radiation cataract or age-related posterior subcapsular cataract

Chlorpromazine Cataract

- Anterior subcapsular
- Stellate
Drugs Affecting the Pupil

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

Drugs Affecting the Retina

Drugs Causing Miosis
- Anticholinesterases
- Morphine
- $\alpha_1$-Adrenoceptor Antagonists
  - IFIS syndrome

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

The presence of POAG does not contraindicate the use of drugs that dilate the pupil!
Drugs Affecting Retinal Function

- Hydroxychloroquine
- Thioridazine
- Talc
- Cardiac glycosides
- Clomiphene
- Sildenafil
- Tamoxifen
- Aspirin

Phenothiazine Retinopathy

- Thioridazine dose should not exceed 800 mg/day
- Toxicity occurs within 30-60 days
- Toxicity may be reversible
- Pigmentary retinopathy, retinal edema, reduced night vision, loss of visual acuity

Talc Retinopathy

- First described in 1972 in 17 drug addicts who had injected methylphenidate (Ritalin) intravenously
- Associated with heroine, methadone, codeine, meperidine, and pentazocine
- Talc (magnesium silicate) and corn starch are fillers and binders
- Injection of at least 9,000 pills of methadone is required

Ophthalmoscopic Appearance

- Posterior polar location
- Tiny, glistening, yellow crystals within arterioles of perifoveal arcade
- Peripheral retinal neovascularization can lead to disc neovascularization, vitreous hemorrhage, or retinal detachment
Cardiac Glycosides (Digitoxin and Digoxin)

- Dyschromatopsia (yellow or blue tinge)
- Snowy, hazy, or blurred vision
- Dimming of vision
- Flickering or flashes of light
- Glare

Tamoxifen Retinopathy

- Macular edema
- White refractile opacities in macular and paramacular area
- Onset of ocular signs is 17-27 months
- Total toxic dose is 108-230 grams
- Progressive?

Oral Contraceptives

- *No* increased risk of
  - Dry eye, conjunctivitis, keratitis, uveitis, strabismus, cataract, glaucoma, retinal detachment
- Significant increased risk of retinal vascular lesions
  - Vascular occlusion, vein thrombosis, and retinal hemorrhage

Oral Contraceptive-Related Disc and Vitreous Hemorrhage
Drugs Affecting the Optic Nerve

- Ethambutol
- Isoniazid
- Corticosteroids
- Tetracyclines
- Amiodarone

Antitubercular Drugs

- Ethambutol
- Isoniazid
- Red-green color deficiency and visual field loss secondary to optic neuritis

Amiodarone

- Optic neuropathy occurs in 2%
- Disc swelling with or without peripapillary hemorrhages
- Characteristics
  - Insidious onset
  - Slow progression
  - Bilateral vision loss
  - Distinguish from NAION

Amiodarone Optic Atrophy
Reporting Adverse Drug Reactions

- www.who-umc.org
- www.eyedrugregistry.com
- www.fda.gov/medwatch/index.html

Reference Source