Ocular side effects of systemic medication

Introduction

- After a drug molecule enters the systemic circulation, it can reach ocular tissues through uveal or retinal circulations.
- The choroid, sclera and ciliary body have thin, fenestrated walls for drug molecules to pass.
- Small, lipid soluble molecules pass freely into the aqueous humor, and can further diffuse into avascular structures such as the lens, cornea, and trabecular meshwork
- Drug molecules that enter by means of the uveal circulation exit the eye from the Canal of Schlemm, ciliary body or may diffuse into adjacent anatomical structures.
- Drugs from the retinal circulation can re-enter the systemic circulation, diffuse into the vitreous and anatomical structures, or get actively transported out.

Ocular Accumulation Sites

- Three major accumulation sites- cornea, lens and vitreous. The duration of drug in the eye is prolonged if deposited, increasing chances for toxicity.
- The cornea has a permeable endothelium, and the stromal glycosaminoglycans (GAGs) can bind drug molecules, leading to edema and decreased transparency.
- Drug molecules can also bind to lens protein, and photosensitize the lens to ultraviolet (UV) radiation.
- Lastly, drug molecules tend to accumulate in the vitreous due to the slow rate of fluid exchange.

MELANIN BINDING

- Melanin absorbs light and damage results from the free- radical nature of melanin in structures such as the uveal tract and the RPE.

- Chloroquine and chlorpromazine have a high affinity to melanin and tend to affect ocular tissues

DRUG METABOLISM

- In patients with hepatic and renal disease, there is a decreased rate of excretion, which allows drug molecules to accumulate to toxic levels.

PHOTOSENSITIZERS

- Exposed lens proteins, when UV photosensitized by bound drug molecules, may denature, opacify and accumulate leading to cataract formation.

PHOTOSENSITIZERS

- UV radiation can potentially affect the retina in aphakic and pseudophakic patients, because UV can penetrate without the normal absorptive lens barrier.
- Well-known photosensitizers that cause anterior subcapsular lens changes-
  - allopurinol,
  - phenothiazine,
  - amiodarone, and
  - chloroquine

Drugs Affecting Cornea

Causes:

a. Antimalarial

- Chloroquine (Nivaquine, Avlocor)
- Hydroxychloroquine (Plaquenil)

- INDICATIONS: malaria; certain rheumatological disorders
- Unlike retinopathy, keratopathy bears no relationship to dosage or duration of treatment.
- reversible on cessation of therapy.

b. Amiodarone

- INDICATIONS: atrial fibrillation; ventricular tachycardia
- Keratopathy - slowly reversible on discontinuation of medication.
- Higher dose/ longer duration of administration → more advanced the corneal deposits.
- Keratopathy does not affect vision- discontinuation not indicated.
- Other toxic effects-
- anterior subcapsular lens deposits
- Optic neuropathy

Drug affecting the lens:

1. Steroids wither topical systemic or nasal → Cataract (PSc tope) Posterior subcapsular Cataract
2. Chlorpromazine
3. Busulfan for leukemia
4. Cold for R.A

Drugs affecting retina

ANTIMALARIALS: Drugs

- Antimalarial-melanotropic drugs
  - **Chloroquine** retinotoxicity - related to the total cumulative dose (>300g) , Rx duration > 3y
  - **Hydroxychloroquine** - much safer than chloroquine the risk of toxicity is increased if a daily dose over 6.5 mg/kg is administered for longer than 5 years, although even then the risk is still very small.