Adverse ocular reactions to topical ocular drug therapy
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Route of penetration

Topical drugs – route of penetration
  Cornea
  Conjunctiva
  Sclera
NB. The vast majority of all topical drugs penetrate via the cornea

Practical aspects of topical ocular medication:

Cul de sac & tear film
  Normally 7-10 microlitres volume
  Expands transiently to 30 microlitres
  However, topical drop size typically 40-70 microlitres

Elimination of Drug from the eye
  Initial overflow and loss
  1. Cul de sac expands transiently to 30 microlitres
  2. Average ophthalmic drop approx. 50 microlitres

Therefore excess volume of drug:
  a) drains via naso-lacrimal duct within 15 seconds
  b) or overflows lid margin onto cheek

Elimination – naso-lacrimal flow
  Approximately 80% of the applied drop leaves via naso-lacrimal system without entering the eye!
  2-3 rather than a single drop does not increase ocular dose but does increase systemic dose

Toxicity of topical agents

Ocular toxicity
  Anaesthetics
  Adrenaline type drugs
  Neomycin & aminoglycosides
  Preservatives

Systemic toxicity
  Topical beta-blockers:
    Respiratory and cardiac depression
  Topical Atropine:
    Fatal adult dose is 100mg, however, for 4Kg baby, dose is 10mg (20 drops 1%)
Specific drug group side-effects

**G Timolol (0.25 - 0.50%)**

- Foreign body sensation
- Dry eye symptoms
- Decreased corneal sensitivity
- Hypersensitivity to components
- Pseudopemphigoid

**G Timolol (0.25 - 0.50%) Systemic side effects**

**Cardiovascular**
- Bradycardia
- Arrhythmia
- Heart block
- Hypotension
- Worsening angina

**Respiratory**
- Bronchospasm
- Dyspnoea
- Respiratory failure

**Central nervous system**
- Insomnia
- Depression
- Nightmares
- Confusion
- Paraesthesia

**G Atropine 1%**
- Extreme care with children

**Prostaglandin analogues G Xalatan, Travatan, Lumigan**

- 5-15% of patients have adverse events
- Burning & Stinging
- Hyperaemia (redness)
- FB sensation
- Punctate epitheliopathy

**Prostaglandin analogues G Xalatan, Travatan, Lumigan**

- Increased eyelash length & thickness
- Iris pigmentation
- Iritis / uveitis
- Cystoid macular oedema
- Reactivation of HSV
**Brimonidine 0.2%**

10-20% have adverse ocular events
- Allergic follicular conjunctivitis
- Hyperaemia
- Burning sensation
- Rarely – corneal erosions

**Systemic effects**
- Allergic lid reaction
- Altered taste
- Dry mouth
- Nasal drying
- Hypertension

**Combined medications**
*e.g. G. Combigan or G Cosopt*
- Combined drugs
- Combined side effects

**Summary: Local and systemic side effects**

These are relatively common with topical agents
- Take careful patient history
- Refer to data sheet before Rx

**Lecture 2: Adverse ocular reactions to systemic drug therapy**

**How important are side-effects?**

**Background**
- OTC medicines 40% >60 year olds
- Prescription medicines
- Likelihood of side effects depends on:
  - Prevalence of the treated condition
    - eg. Hypertension vs malaria
- Prescribing habits
- Therapeutic index (lethal vs effective dose)

**Causes of ocular effects include:**
- Cyclospasm
- Cycloplegia
- Corneal edema
- Media changes
- Optic neuritis
- Retinal changes
Common ocular effects
- ↓ tolerance to CL
- Cataract
- ↓ accommodation +/- mydriasis
- ↑ IOP
- Diplopia

Corticosteroids: established SE.
- Steroid induced glaucoma/hypertension
- Posterior sub-capsular cataract
- Increased risk of infections
- Rx Routes
- Oral
- Inhaled
- Applied to skin

Alimentary tract
Drugs act locally in the gut & do not require absorption for intended effect
- Examples:
  - Hyoscine (Buscopan)
  - Ocular effects:
    - Mydriasis
    - Cycloplegia (mild & transient)
    - Closed angle glaucoma (rare)

Cardiovascular system
Direct ocular effect
- Indirect effect – through BP & blood flow
Examples
- Cardiotonic eg Digoxin
- Toxic effect on Retina
- ↓ Colour vision
- Glare phenomenon

Cardiovascular/Renal systems
- β-blockers
- Oculo-mucocutaneous syndrome
- Similar to:
  - Stevens Johnson Syndrome
  - Sulphonamides
**Cardiovascular system**
Anti-arrhythmics eg Amiodarone
- Vortex keratopathy
- Optic neuropathy

**Respiratory system**
- Treatment usually local (inhalers)
- Limited side effects
Examples
- Ventolin (Salbutamol)
  - Mydriasis
  - Tachycardia

**Central Nervous system**
Affects ocular tissue or brain centres controlling eye movements
Examples
- Hypnotics eg benzodiazepines
  - Blurred vision (↓ accommodation, abn EOM)
- Antipsychotics eg Chlorpromazine
  - Pigmentary deposits
    (lens, iris, Descemet's membrane)
  - Corneal deposits
- Anticonvulsants
  - Nystagmus & diplopia (overdose)

**Rx Infectious Diseases**
Antibiotics eg Tetracycline
- Transient myopia
- Colour vision defects
- Stains soft CL
Anti-tuberculosis eg Ethambutol, Isoniazid
- Toxic optic neuropathy

**Rx Endocrine system**
- Corticosteroids
- Cataract (posterior subcapsular)
  ▲ IOP
- Corneal thinning

**Always consider the full soma - Viagra (Sildenafil citrate)!**
- Pharmacology
- Inhibits vascular-associated enzyme phosphodiesterase 5 (PDE5)
- Lesser but definite inhibitory effect on PDE6, located in the retina
- Ocular effects
  - Transient, mild impairment of color discrimination (blue-green spectrum) at peak plasma levels
- No significant effects on IOP
- No long-term effects on visual function