GLAUCOMA

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CLASSIFICATION

- Drugs which increases outflow of aqueous humor
  - Cholinomimetics – Pilocarpine
  - Anticholinesterases – Physostigmine, Demacarium, Ecothiophate
  - Prostaglandin analogues – Latanoprost, Unoprost
- Drugs which decreases secretion of aqueous humor in ciliary muscle
  - β-blockers – Timolol, Betaxolol, Levobunolol
  - α-agonists – Dipivefrine, adrenaline, phenylephrine, clonidine, apraclonidine, brominidine
  - Carbonic anhydrase inhibitors
    - Topical – Brinzolamide, Dorzolamide
    - Systemic – Acetazolamide, Methazolamide

Treatment in Angle closure (narrow angle, acute congestive) Glaucoma

- The i.o.t. rises rapidly to very high values (40–60 mmHg).
- It is an emergent condition with marked congestion of eyes and severe headache.
- Failure to lower i.o.t. quickly may result in loss of sight.
- *Hypertonic mannitol (20%) 1.5–2 g/kg or glycerol (10%): infused i.v. decongest the eye* by osmotic action.
- A retention enema of 50% glycerine is also some times used.
- Acetazolamide: *0.5 g i.v. followed by oral twice* daily is started concurrently.
- *Topical β blocker: Timolol 0.5% is instilled* 12 hourly in addition.

- *Miotic: Once the i.o.t. starts falling due to the* above i.v. therapy, pilocarpine 1–4% is instilled every 10 min initially and then at longer intervals.
- Contraction of sphincter pupillae changes the direction of forces in the iris to lessen its contact with the lens and spreads the iris mass centrally → pupillary block is removed and iridocorneal angle is freed.
- However, when i.o.t. is very high, the iris muscle fails to respond to miotics.
- *Apraclonidine (1%)/latanoprost 0.005%* instillation may be added.
- Drugs are used only to terminate the attack of angle closure glaucoma.
- Definitive treatment is surgical or laser iridotomy.

- **Treatment in Open angle (wide angle, chronic simple) glaucoma**
- **β Adrenergic blockers:**
- Topical β blockers have been the first line drugs till recently, but PG F2α analogues are the preferred drugs now.
- Acts by lowering i.o.t. by reducing aqueous formation.
- This is due to down regulation of adenylyl cyclase due to β2 receptor blockade in the ciliary epithelium and a secondary effect due to reduction in ocular blood flow.
- They are as effective as miotics; produce less ocular side effects.
- Ocular β blockers are lipophilic with high ocular capture and have no/ weak local anaesthetic activity.
- ***Ocular side effects of β blockers:*** *These are* generally mild and infrequent—stinging, redness and dryness of eye, corneal hypoesthesia, allergic blepharo-conjunctivitis and blurred vision.

- ***Systemic adverse effects:*** Bradycardia, accentuation of heart block and CHF.
- *These are the major* limitations in the use of ocular β blockers, and occur due to absorption through nasolacrimal duct.
- Life-threatening bronchospasm has been reported in asthmatic and COPD patients.

Timolol:

- It is the prototype of ocular β blockers; nonselective (β1 + β2) and has no local anaesthetic or intrinsic sympathomimetic activity.
- Ocular hypotensive action (20–35% fall in i.o.t.) becomes evident within 1 hr and lasts for ~12 hrs.
- Some effect on i.o.t. persists for 1–2 weeks following discontinuation.
- High level of clinical safety, i.e. 1 or 2 missed doses will not affect i.o.t. control.
- May need additional medication along with timolol.
- **DOSE:** 0.25% and 0.5% eye drops; start with 0.25% drops BD, change to 0.5% drops in case of inadequate response.

- **Betaxolol:**
- It is β1 selective blocker offering the advantage of less broncho-pulmonary and probably less cardiac, central and metabolic side effects.
- It appears to exert a protective effect on retinal neurones independent of i.o.t. lowering, by blocking some Ca2+ channels and reducing Na+/Ca2+ influx.
- This action is more prominent in betaxolol than in timolol.
- However, betaxolol is less efficacious in lowering i.o.t. than timolol, because ocular β receptors are predominantly of the β2 subtype.
- Transient stinging and burning in the eye is more common with it.
- Most ophthalmologists prefer to start with betaxolol and change over to timolol (or a similar drug) only if i.o.t. control is insufficient or there is local intolerance to betaxolol.
- **DOSE:** 0.5% eye drops; 1 drop in each eye BD.

- **α Adrenergic agonists**
- **Dipivefrine:**
- It is a prodrug of Adrenaline; penetrates cornea and is hydrolysed by the esterases present there into Adrenaline, which itself has poor corneal penetration.
- **MOA:** The released Adrenaline lowers i.o.t. by augmenting uveoscleral outflow, β2 receptor mediated increase in hydraulic conductivity of trabecular filtering cells, as well as by reducing aqueous formation (α1 + α2 receptor mediated).
- Though better tolerated and longer acting than Adrenaline, dipivefrine still produces significant ocular burning and other side effects.
- It is infrequently used for add on therapy.
- **DOSE:** 0.1% eye drop; 1 drop in each eye BD.

- **Apraclonidine:**
- It is a polar clonidine congener which does not cross blood-brain barrier, but applied topically (0.5–1%) it lowers i.o.t. by ~25%.
- It decreases aqueous production by primary α2 and subsidiary α1 action in the ciliary body.
- **ADVERSE EFFECTS:** Itching
- lid dermatitis, follicular conjunctivitis, mydriasis, eyelid retraction, dryness of mouth and nose.
- Its use is restricted to short term control of spikes of i.o.t. after laser trabeculoplasty or iridotomy.
- **DOSE:** 1% eyedrops

Prostaglandin analogues (High cost is a disadvantage)

- Low concentration of PGF2α was found to lower i.o.t without inducing ocular inflammation.
- Acts by increasing uveoscleral outflow, by increasing permeability of tissues in ciliary muscle.

LATANOPROST:

- Instilled in the eye, this PGF2α derivative has shown efficacy similar to timolol (i.o.t. reduction by 25–35%) and the effect is well sustained over long-term.
- It reduces i.o.t. in normal pressure glaucoma also.
- Ocular irritation and pain are relatively frequent; no systemic side effects.
- Blurring of vision, increased iris pigmentation, thickening and darkening of eyelashes have occurred in some cases.
- Because of good efficacy, once daily application is preferred.
- PG analogues have become the first choice drugs for open angle glaucoma.
- **DOSE:** 0.005% eye drops, one drop in each eye OD in the evening.

- **Carbonic anhydrase inhibitors:**
- **Acetazolamide:**
- *Oral treatment* with acetazolamide (0.25 g 6–12 hourly) reduces aqueous formation by limiting generation of bicarbonate ion in the ciliary epithelium.
- It is used to supplement ocular hypotensive drugs for short term indications like angle closure, before and after ocular surgery/laser therapy.
- Systemic side effects—paresthesia, anorexia, hypokalaemia, acidosis, malaise and depression restrict long-term use.
- **Dorzolamide (2% eyedrops BD-TDS):**
- It is a topically useful carbonic anhydrase inhibitor developed to circumvent systemic side effects of acetazolamide.
- It lowers i.o.t. by ~20%; somewhat less efficacious than timolol.
- **ADR:** Ocular stinging, burning, itching, corneal edema and bitter taste
- Dorzolamide is used only as add on drug to topical β blockers/PG analogues, or when these drugs are contraindicated.

Miotics:

- Till the 1970s topical pilocarpine and/or antiChEs were the standard anti-glaucoma drugs.
- *However, because of several* drawbacks*, they are now* used only as the last option.
- In open angle glaucoma, they lower i.o.t. by increasing ciliary muscle tone thereby improving patency of trabeculae.
- ***The current approach to treatment of open* angle glaucoma can be summarized as;**
- Start monotherapy with latanoprost or a topical β blocker;
- If target i.o.t. is not attained, either change over to the alternative drug or use both the above concurrently
- Brimonidine/dorzolamide (occasionally dipivefrine) are used only when there are contraindications to PG analogues and/or β blockers, or to supplement their action.
- Topical miotics and oral acetazolamide are added only as the last choice.