Glaucoma Medical Therapy

Hassan Eisa Swify
FRCS Ed (Ophthamology)

Mohamed Farouk Kamel
MRCS Ed (Ophthamology)

Declaration

- We have no financial interset in any of the products.
- We have nothing to declare.
- We use drug commercial name & drugs of the same group are considered the same regarding efficacy unless stated otherwise.

The goal of glaucoma therapy

- is to preserve visual function by lowering IOP below a level that is likely to produce further damage to the optic nerve.
- The treatment regimen that achieves this goal with the lowest risk, fewest side effects and least disruption of the patient's life, taking into account the coast implications of treatment should be the one employed.
- Tow decisions arise in choosing appropriate glaucoma therapy :

When to treat? and How to treat?

Factors to consider in glaucoma management include:

- Initial IOP
- Life expectancy
- Ethnicity
- Extent of optic nerve damage
- Compliance

- A **target** IOP should be determined. This represents the IOP aimed for following therapy. For example, a patient with advanced glaucomatous optic neuropathy may require a target IOP of 12 mmHg.

Ocular hypotensive agents

- They are divided into several groups based on chemical structure and pharmacologic action .

- The groups of agents in common clinical use include:
  - Beta-Adrenergic antagonists (**selective and non-selective**)
  - Carbonic Anhydrase Inhibitors (**systemic and topical**)
  - Hypotensive Lipids (**Prostaglandin analogs, Prostamides, Decosonoids**)
  - Adrenergic Agonists (**selective & non-selective Alpha 2 agonist**)
  - Parasympathomimetics (**cholinergic and Anticholine esterase**)
  - Hyperosmotic agents.
  - Combination medications.

Effectiveness in lowering IOP

Class	IOP reduction	Examples
Class I	30 %	B-blockers (non selective) Hyypotensive Lipids (Latanoprost, Unoprostone) α2 - agonists (Brimonidine)
Class II	20%	Pilocarpine CAIs (Dorzolamide, Brinzolamide) α - agonists (Aprachlonidine) B1- blockers
Class III	10%	Propine Other older alpha agonists

Beta Blockers

Generic Name/ Trade name	Mechanism of action	Dosage	IOP decrease	Side effects
Timolol *(Timolol)*	Decrease aqueous production 20-50%.	Every 12 hours	20-30%	**Ocular side effects:** Burning, irritation, corneal anesthesia, punctate keratitis and allergy. **Systemic side effects:** Bradychardia, heart block, bronchospasm, decreased libido, CNS depression and mood swings.
Levobunolol *(Betagan)*				
Betaxolol *(Betoptic)*			15-20%	Fewer pulmonary complications due to selective Beta blockage

Carbonic Anhydrase Inhibitors (CAIs):

Topical agents: Dorzolamide and Brinzolamide.

Systemic agents: Acetazolamide and Methazolamide.

Generic Name/ Trade name	Mechanism of action	Dosage	IOP decrease	Side effects
Dorzolamide *(Trusopt)*	Decrease aqueous production	Every 8–12 hours	15-20%	Eye irritation, bitter taste, blurred vision and punctate keratopathy.
Brinzolamide *(Azopt)*		Every 8–12 hours	15-20%	
Acetazolamide *(Diamox)*		62.5- 250 mg / every 6–12 hours	15-20%	malaise, weight loss, kidney stones, paresthesia of fingers or toes, anorexia, diarrhea, loss of libido, impotence, mental depression.

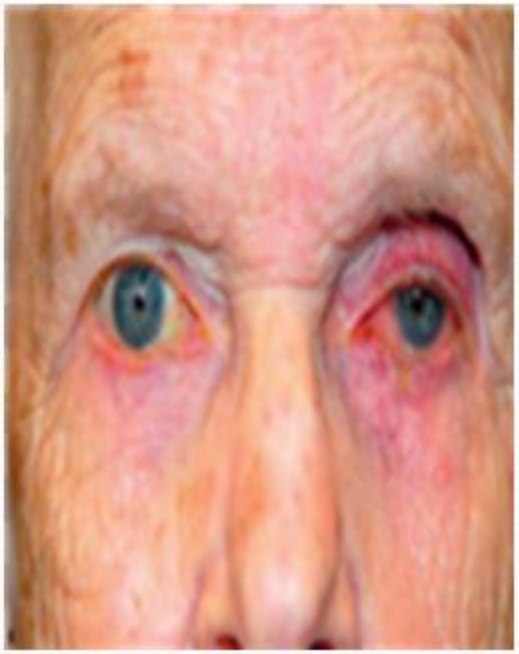
Hypotensive Lipids:

- **Prostaglandin analogs:** Travoprost and Latanoprost.
- **Prostamide:** Bimatoprost.
- **Decosanoid:** Unoprostone Isopropyle.

Generic Name/ Trade name	Mechanism of action	Dosage	IOP decrease	Side effects
Latanoprost *(Xalatan)*	Increased USO (uveoscleral outflow)	Once daily	25-32%	• darkening of the iris and periocular skin • conjunctival hyperemia. •Hypertrichosis • exacerbation of underlying Herpes keratitis, CME & uveitis.
Bimatoprost *(Lumigan)*				
Travoprost *(Travatan)*				

Prostaglandin Associated Periorbetopathy (PAP)

- Upper lid ptosis.
- Deepening of upper lid sulcus.
- Involution of dermatochalasia.
- Orbital fat atrophy.
- Mild enophthalmos.
- Inferior scleral show.
- Increased prominence of lid vessels.
- Tight orbits.



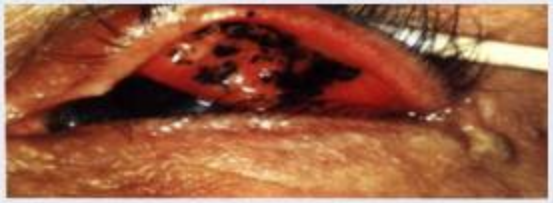
Parasympathomimetics (Miotics):

- **Direct-acting cholinergic agonists: Pilocarpine and Carbachol.**
- **Indirect-acting Anticholinesterase agents: Echothiophate iodide.**

Generic Name/ Trade name	Mechanism of action	Dosage	IOP decrease	Side effects
Pilocarpine *(Isoptocarpine)* *(Ocucarpine)* *1,2,3,4%*	Increase trabecular outflow	Every 6-12 hours	15-25%	posterior synechia, keratitis, miosis, brow ache, cataract, myopia, retinal tear, dermatitis, increased salivation

Adrenergic agents:

- **Non-selective adrenergic agonists:** Epinephrine and Dipivefrin (propine).
- **Alpha$_2$-Adrenergic Agonists:** Brimonidine and Apraclonidine.

Generic Name/ Trade name	Mechanism of action	Dosage	IOP decrease	Side effects
Apraclonidine **0.5%,1.0%** ***(Iopidine)***	•Decreases aqueous production (prevents severe elevation of IOP following laser procedures)	•Maximum effect in 4–5 hours •Duration of effect: 8–12 hours	20-30%	High rate of allergy limits use of apraclonidine for chronic treatmen 
Brimonidine 0.2% ***(Alphagan)***	•Decrease aqueous production. • increase USO •neuroprotection	Every 8-12 hours TID if monotherapy BID if adjunctive therapy	20-30%	Tachyphylaxis, Headache, increased BP, tachycardia, arrhthmia and nervousness . Locally: pupillary dilatation, allergic blepharoconjunctivitis and cystoid macular oedema in aphakic and pseudophakic eyes without intact posterior capsule.
Brimonidine 0.15% Alphagan-p				

Hyperosmotic Agents

- Used to control acute episodes of elevated IOP.
- Oral glycerin and IV Manittol.
- Side effects: headache, mental confusion, back ache, acute congestive heart failure and myocardial infarction.

Possible additive effects between different classes of antiglaucoma drugs

- Not recommended

+ Partially additive
++ May be additive, but not invariably
+++ Fully additive

	Beta blockers	Lipid-receptor agonists	Alpha$_2$ agonists	Topical CAIs*	Systemic CAIs*	Miotics	Adrenergics
Beta blockers	+++	+++	+++	+++	+++	+	-
Adrenergics	-	-	+++	+++	+++	-	+
Miotics	++	+++	+++	+++	_	+++	+++
Systemic CAIs*	+++	+++	-	-	+++	+++	+++
Topical CAIs*	+++	+++	-	-	+++	+++	+++
Alpha$_2$ agonists	+++	-	+++	+++	+++	-	+++
Lipid-receptor agonists	-	+++	+++	+++	++	-	+++

Combined medications

- Potential benefits of improved efficacy, convenience and compliance.
- Timolol + Dorzolamide → Cosopt, Xolamol, Twinzol, Episopt
- Timolol + Prinzolamide → Azarga
- Timolol + Latanaprost → Xalacom
- Timolol + Travoprost → Duotrav
- Timolol + Alphagan → Combigan

Concomitant therapy with Cosopt and Cidamex is not useful

•Although the β-blocker and the topical (CAI) both act by decreased Aq production, they are almost completely additive in their effects on aqueous humour flow.

•Thus, the combination product Cosopt has a powerful (IOP) lowering effect of 32.7% at peak moment

• Similar effects on aqueous humour flow and IOP were observed with timolol and the oral CAI acetazolamide (Diamox) taken together.

•When a maximal IOP lowering effect is needed, it can be useful to switch from Cosopt® to [Diamox + a topical β-blocker].

• Diamox is more effective as a suppressor of aqueous humour flow than Dorzolamide.

•Dorzolamide has no additive effects in subjects already taking Diamox

DO NOT USE :

- Acetazolamide in :
  - Renal impairment. In the elderly and diabetics check urea and electrolytes.
  - Adrenal failure.
  - Liver cirrhosis .
  - Pulmonary obstruction or emphysema.
  - Sulphonamide sensetivity.

- Alpha2 Agonists in:
  - ***Should be avoided in infants and young adults***.
  - Should be used with caution in patients on Mono Amine oxidase inhibitors and Tricyclic Antidepressants.

DO NOT USE :

- ***Beta-Blockers:***
  - ***Bronchial asthma.***
  - ***Slow pulse rate or more than 1st degree heart block.***
  - ***Myasthenia gravis.***

- ***Drug interactions:***
  - Acetazolamide + Aspirin → Severe acidosis and CNS disturbence.

Recommendations:

- A monocular therapeutic trial should be considered when first initiating the medical therapy, as the other eye's IOP can be used as a baseline control to gauge effect of a medication (particularly useful in patients with a widely fluctuating diurnal curve).
- A difference of more than 4 mm Hg between the 2 eyes post treatment is strongly suggestive of a clinical effect.
- However, some agents (especially beta-blockers) may have crossover effects on the other eye even with monocular treatment(70% reduction), so clinical correlation must be kept in mind.
- If monocular therapy is found to be effective, then initiation of binocular therapy may be considered.

Recommendations:

Once a medicine has been initiated:

- Initial follow-up care should be performed 3-4 weeks after the beginning of therapy.
- IOP should be rechecked at the drug's peak and trough times to see if the target IOP has been reached and is maintained throughout the day.
- Look for signs of allergy (eg, hyperemia, skin rash, follicular reaction).
- Inform the patient of systemic adverse effects and symptoms that may occur.
- Treatment should be continued if a therapeutic trial has shown effective lowering of IOP without adverse effects.
- Reevaluation should be performed 2-4 months later depending on the clinical picture.

Recommendations:

- Some medications (eg, latanoprost, brimonidine) may have an effect that plateaus at 6-8 weeks in certain patients; keep this effect in mind when scheduling further follow-up examinations.
- Other patients will be nonresponders to some therapies. If this occurs, the medication should be discontinued and a new drug initiated.

Recommendations:

- While discontinuing or changing therapies, keep in mind that many drugs have a wash-out period of up to 2-4 weeks (especially beta-blockers), during which they may still have some IOP-lowering effect or residual systemic response.

- If one medication is not adequate in reaching the target pressure, a second medication should be chosen that has a different mechanism of action, so that the 2 drug therapies will have an additive effect. (Usually, no additive effect is seen if 2 medications from the same drug class are used.)

Recommendations:

- The use of gel vehicle decreases the plasma concentration of the drug (b-blockers).
- B-blockers are better used early in the morning to avoid early morning pressure rise while minimizing systemic hypotension during sleep.
- Apraclonidine is effective for short term therapy e.g Argon laser iridectomy; trabeculoplasty, Nd-YAG capsulotomy and cataract extraction.

Recommendations:

Chronic miotics can be helpful in case of plateau iris configuration

- useful in case of plateau iris configuration
- It works by thinning the iris& can prevent formation of peripheral anterior synechiae (PAS) and chronic-angle closure in the long-term.
- In order to minimize side-effects, a dilution of the pilocarpine up to a 0.1% solution can be tried, and the patient can be advised to briefly interrupt the treatment from time to time to avoid posterior synechiae.
- In case of intolerance to pilocarpine or residual appositional closure, argon laser peripheral iridoplasty can be used to shrink and flatten the peripheral iris, but follow-up with periodic gonioscopy remains mandatory as retreatment may be necessary1,2


THANK
YOU