University of Anbar
College of pharmacy
Therapeutic I, 5th stage
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Glaucoma

Glaucoma is an ocular disorder that lead to an optic neuropathy characterized by changes in the optic nerve head (optic disc) that is associated with loss of visual sensitivity and field.

Pathophysiology

There are two major types of glaucoma:

A: primary open-angle glaucoma (POAG) or ocular hypertension, which accounts for most cases

B: closed-angle glaucoma (CAG). Either type can be a primary inherited disorder, congenital, or secondary to disease, trauma, or drugs

- In POAG, the specific cause of optic neuropathy is unknown. **Increased intraocular pressure (IOP)** was historically considered to be the sole cause.
- Additional contributing factors include increased susceptibility of the optic nerve **to ischemia**, **excitotoxicity**, **autoimmune reactions**, and other abnormal physiologic processes.
- Although IOP is a poor predictor of which patients will have visual field loss, the risk of visual field loss increases with increasing IOP.
- IOP **is not constant**; it changes with **pulse**, **blood pressure**, **forced expiration** or **coughing**, **neck compression**, and **posture**.
- IOP demonstrates **diurnal variation** with a minimum pressure around 6 pm and a maximum pressure upon awakening.
- The **balance** between the inflow and outflow of aqueous humor determines IOP.

- Inflow is **increased** by β-adrenergic agents and **decreased** by α2- and β-adrenergic blockers, dopamine blockers, carbonic anhydrase inhibitors (CAIs), and adenylate cyclase stimulators.
- Outflow is increased by cholinergic agents, which **contract the ciliary muscle** and open the trabecular meshwork, and by prostaglandin analogues and β- and α2-adrenergic agonists, which affect **uveoscleral outflow.**

Secondary Glaucomas has many causes, including trauma, uveitis, chronic steroid use, diabetic retinopathy, ocular vascular occlusion.

Treatment

Goal of Treatment: The goal is to **preserve visual function by reducing IOP to a level at which no further optic nerve damage occurs.**

Treat ocular hypertension if the patient has a significant risk factor such as

- IOP greater than 25 mm Hg.
- family history of glaucoma,
- severe myopia
- presence of only one eye.

Initiate drug therapy in a stepwise manner, starting with **lower concentrations** of a single well-tolerated topical agent. Historically**, β-blockers (eg, timolol)** were the treatment of choice provided no contraindications existed.

Treatment of closed-Angle Glaucoma

Acute CAG with high IOP requires rapid reduction in IOP. **Iridectomy** is the definitive treatment producing a hole in the iris that permits aqueous humor flow to move directly from the posterior to the anterior chamber.

Osmotic agents are used to rapidly decrease IOP. Examples **include glycerin**, 1 to 2 g/kg orally, and **mannitol**, 1 to 2 g/kg IV.

Once IOP is controlled, **pilocarpine** should be given every 6 hours until iridectomy is performed.

Practice approach

Lower IOP By:

1. Decreasing Production of Aqueous Humor

2. Increasing Outflow of Aqueous Humor

Drugs that Decrease Aqueous Production

Beta-Blockers [levobunolol, timolol, carteolol, betaxolol]

Mechanism: Act on ciliary body to **decrease** production of aqueous humor .

Administration: Topical drops to avoid systemic effects

Side Effects: Cardiovascular (bradycardia, asystole, syncope), bronchoconstriction (avoid **with b1-selective betaxolol**), depression

2. **Alpha-2 Adrenergic Agonists** [apraclonidine, brimonidine]

Mechanism: Decrease production of aqueous humor

Administration: Topical drops

Side Effects: Lethargy, fatigue, dry mouth [apraclonidine is a derivative of clonidine (antihypertensive) which cannot cross BBB to cause systemic hypotension]

3. **Carbonic Anhydrase Inhibitors** [acetazolamide, dorzolamide]

Mechanism: Blocks CAII enzyme production of bicarbonate ions (transported to posterior chamber, carrying osmotic water flow), thus decrease production of aqueous humor

Administration: Oral, topical

Side Effects: **malaise, kidney stones**, possible (rare) aplastic anemia

Drugs that Increase Aqueous Outflow

1. Nonspecific Adrenergic Agonists [epinephrine, dipivefrin]

Mechanism: uveoscleral outflow of aqueous humor

Administration: Topical drops

Side Effects: Can precipitate acute attack in patients **with narrow iris-corneal angle**, headaches, cardiovascular arrhythmia, tachycardia

2. **Parasympathomimetics** [pilocarpine, carbachol, echothiophate]

Mechanism: increase contractile force of ciliary body muscle, increase outflow via TM .

Administration: Topical drops or gel, (slow-release plastic insert)

Side Effects: **Headache, induced myopia**.

3. Prostaglandins [latanoprost]

Mechanism: May increase uveoscleral outflow by relaxing ciliary body muscle

Administration: Topical drops

Side Effects: **Iris colour change**

Additional Considerations

1. No single medication can be used in all patients

2. Compliance

    Critical: Rx often requires several agents, multiple times a day, everyday , so there is an important role of slow-release drug delivery devices

3. Effectiveness of Rx measured by ability to lower IOP, but other factors may be (more) important, like neuroprotection and increased blood flow to optic nerve

4.Non-pharmacological ways to lower IOP:

A- Laser (argon laser trabeculoplasty) : Increase aqueous outflow, but it may lose effectiveness over time

B- Surgical (trabeculectomy) :

- Creates alternative path for aqueous outflow
- Only definitive therapy for closed angle