Principles of Medical Therapy and Management

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Management goals

- preserve visual function while maintaining the best possible quality of life

- This goal can be achieved by preventing or slowing the progression of glaucomatous damage by lowering IOP to a level at which further damage is minimal.

- To avoid unnecessary treatment, physicians must decide whether treatment is really indicated.

Management goals

When elevated IOP is present without glaucomatous damage (i.e., ocular hypertension), the physician must evaluate the risk factors for progression to glaucoma before deciding whether to treat.

When the patient presents with established glaucomatous damage or dangerously high IOP, the indication to initiate treatment is usually clear.

How to Start

- Initiating treatment involves

- establishing the target IOP or IOP range,
- selecting the appropriate medication,
- educating and instructing the patient,
- and establishing the efficacy and safety of the treatment at follow-up evaluations.

Establishing the Target Pressure

- no single pressure value is appropriate for all patients
- The IOP target is based on the status of the optic nerve head and other risk factors for progression
- reducing the IOP by 20% to 30% from baseline is recommended,

Establishing the Target Pressure

- which should result in:

- target IOP in the middle to high teens for eyes with minimal damage
- low to middle teens for eyes with moderate damage
- high single digits to low teens for eyes with advanced damage

Establishing the Target Pressure

- The less the initial pretreatment IOP, the more advanced the optic nerve damage
- the older the patient, the lower the target pressure should be set.

- The currently available approaches to lower IOP:
- Medical therapy,
- laser trabeculoplasty,
- filtering surgery,
- cyclodestructive procedures

- Unfortunately, there is no ideal treatment for glaucoma.

PRINCIPLES OF INITIATION OF THERAPY

- Prior to the initiation of therapy in any patient, it is important to establish a baseline for future comparisons.

- The IOP of most people who do not have glaucoma varies by <4 mm Hg
- If the IOP is not dangerously high on the initial visit, it may be useful to obtain another IOP measurement on a separate visit or obtain the patient's diurnal IOP variation prior to starting therapy.

- optic disc appearance and visual field

PRINCIPLES OF INITIATION OF THERAPY

- Once therapy is indicated, the initial target IOP reduction should be at least 25% of pretreatment level.

- The suggestion that an IOP of 21 mm Hg, 17 mm Hg, and 14 mm Hg or less prevents further glaucomatous damage was based on population statistics

- some patients continue to develop progressive glaucomatous disease at IOP below this level, requiring adjustment of target IOP throughout the course of care.

Medical Treatment

- Medical treatment is the most common initial intervention to lower IOP.

- Topical medication classes include
- miotics,
- beta-blockers,
- epinephrine derivatives,
- carbonic anhydrase inhibitors,
- alpha-agonists,
- prostaglandin analogues.

Mechanism of action

- IOP
- Proudction
  - A: a-adrenergic
  - B: beta blockers
  - C: CAI
- drainage
  - P: PG
  - P:pilocarpine

Beta- Blockers

with the mean peak IOP lowered by 25% and the mean trough lowered by 20% using nonselective agents.

Evidence suggests that this occurs only during the day and not during sleep.

None of the beta-blockers should be used more than twice daily.

Contraindications to beta-blocker

asthma,
severe chronic obstructive pulmonary disease,
bradycardia,
second- or third-degree heart block,
congestive heart failure

Beta- Blockers

- Peak effect in 2hrs
- Reduces pressure 20-25%
- Decrease efficiency overtime(after 12 menthes) because of downregulation of receptors ➡ beta blocker HOLIDAYS(for a month)

Alpha-Adrenergic Agonists

Brimonidine 0.5% prevents the rise in postoperative IOP after laser trabeculoplasty.

Brimonidine is approved for use three times a day (TID) but is commonly used twice daily (BID) because at the morning trough, there is no difference in IOP between the two regimens.

Chronic use of apraclonidine is limited by the risk for allergic reaction

Brimonidine is generally contraindicated in children under 2 years old because of the risk of side effects, such as bradycardia, hypotension, hypothermia, hypotonia, lethargy, and apnea.

Carbonic Anhydrase Inhibitors

- aqueous production is decreased approximately 50% or more
- Dorzolamide 2%,, Brinzolamide 1%, Oral acetazolamide, 500 mg BID,
- Topical carbonic anhydrase inhibitors are a reasonable choice for concomitant therapy or as monotherapy when other more effective agents cannot be used
- Carbonic anhydrase inhibitors lower IOP very effectively; however, their use in the chronic treatment of glaucoma is limited by the frequency and severity of side effects.
- Metabolic acidosis may occur in patients who have severe hepatic or renal disease. Sickle cell crisis may be exacerbated by the acidosis as well

Miotics

- Miotics are parasympathomimetic agents whose action increases the contractile force of the longitudinal muscle of the ciliary body on its insertion into the scleral spur. This results in an increased facility of outflow of aqueous through the effects on the trabecular meshwork.

- Miotics were the earliest drugs used for glaucoma, and they lower IOP by 20%–30%.

- Such effects are often dose related. Pseudo-cholinesterase inhibitors are cataractogenic in adults and cause iris pigment epithelial cysts in children, although the latter effect may be prevented with concomitant use of topical phenylephrine.

- Useless if the IOP is >>40 mmhg

Prostaglandin Analogues

latanoprost reduced IOP by 25%–34% and was statistically more effective than timolol.

The peak effect occurs approximately 12 hours after instillation.

In a 6-month trial comparing latanoprost and bimatoprost, there was a statistically significant greater IOP reduction with bimatoprost than latanoprost at all time points

conjunctival hyperemia burning and stinging blurred vision ,itching ,foreign body sensation tearing and eye pain

THE ONLY EYE DROP THAT FDA APPROVED

Prostaglandin Analogues

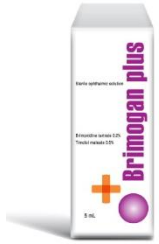
- Latanoprost resulted in increased iris pigmentation in 11%–23% of patients
- There is a theoretical risk that PG analogues may break down the blood–aqueous barrier potentially worsening or reactivating uveitis, cystoid macular edema (CME) and herpes infections.

FIXED COMBINATION MEDICATIONS

Common formulations Include:

timolol/dorzolamide 

timolol/brimonidine

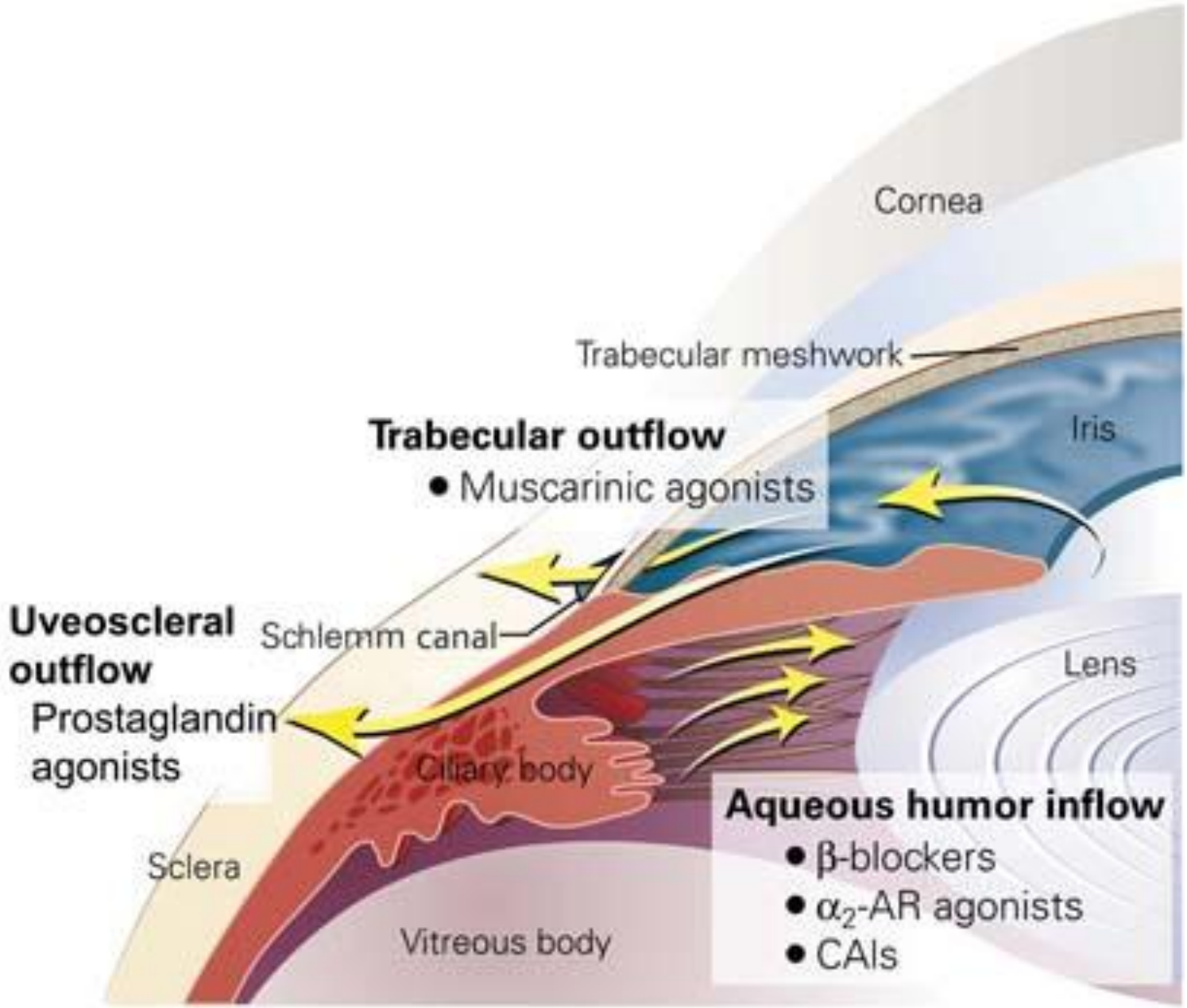
brinzolamide/brimonidine 

Data show that the fixed combinations are more effective than either component alone.

because of the minimal further IOP reduction provided by the addition of timolol to the prostaglandin analogs,

TABLE 10.24.1 Drugs Used to Manage Glaucoma

Drug	Example	Mechanism of Action	Efficacy	Side Effects
Beta-blockers nonselective	Timolol Levobunolol Carteolol Metipranolol	Decreased aqueous production (waking hours only)	+++	Pulmonary: bronchoconstriction Cardiovascular: bradycardia/heart block Exacerbation of CCF Depression Impotence Death
Adrenergic agents nonselective	Epinephrine Dipivefrin	Outflow enhancement	+ (+)	External eye: toxic reaction
Alpha-adrenergic agents	Apraclonidine	Decreased aqueous production	++ (+)	External eye: allergic reaction
	Brimonidine	Also, uveoscleral outflow increase with brimonidine		Lethargy Dry mouth Allergic reaction
Miotics	Carbachol Pilocarpine Echothiophate	Increased conventional aqueous outflow	+++	Eye ache Headache Dim vision
Carbonic anhydrase inhibitors				
Systemic	Acetazolamide	Decreased aqueous production	++++	Malaise Blood dyscrasia Kidney stones
	Methazolamide			Depression Weight loss
Topical	Dorzolamide Brinzolamide		++	Metallic taste
				Eye irritation
Lipids (Prostaglandin analogues, prostamides, decosanoids)	Latanoprost Travoprost Bimatoprost Tafluprost	Enhanced aqueous outflow (conventional and unconventional)	++++	Iris color change Hyperemia Periocular skin pigmentation Orbitopathy


Cornea
Trabecular meshwork
Iris
Trabecular outflow
• Muscarinic agonists
Uveoscleral outflow
Prostaglandin agonists
Schlemm canal
Lens
Ciliary body
Aqueous humor inflow
• β-blockers
• α2-AR agonists
• CAIs
Sclera
Vitreous body

Follow these **5 steps** to ensure you use your eye drops **correctly**

1

Wash your hands. Tilt your head back and look at the ceiling.*

2

Using your index finger, gently pull down your lower eyelid to form a pocket

3

Gently squeeze 1 drop into the pocket. Do not let the bottle tip touch your eye, your fingers, or anything else.

4

Gently close your eyes and lightly press on the inside corners of your eyes.

5

Then carefully blot away any excess liquid that may be on your skin.

* With certain glaucoma eye drops, first you will need to remove your contact lenses, if you wear them. Wait 15 minutes after using your eye drops before you put your contact lenses back into your eyes.

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Wash out period

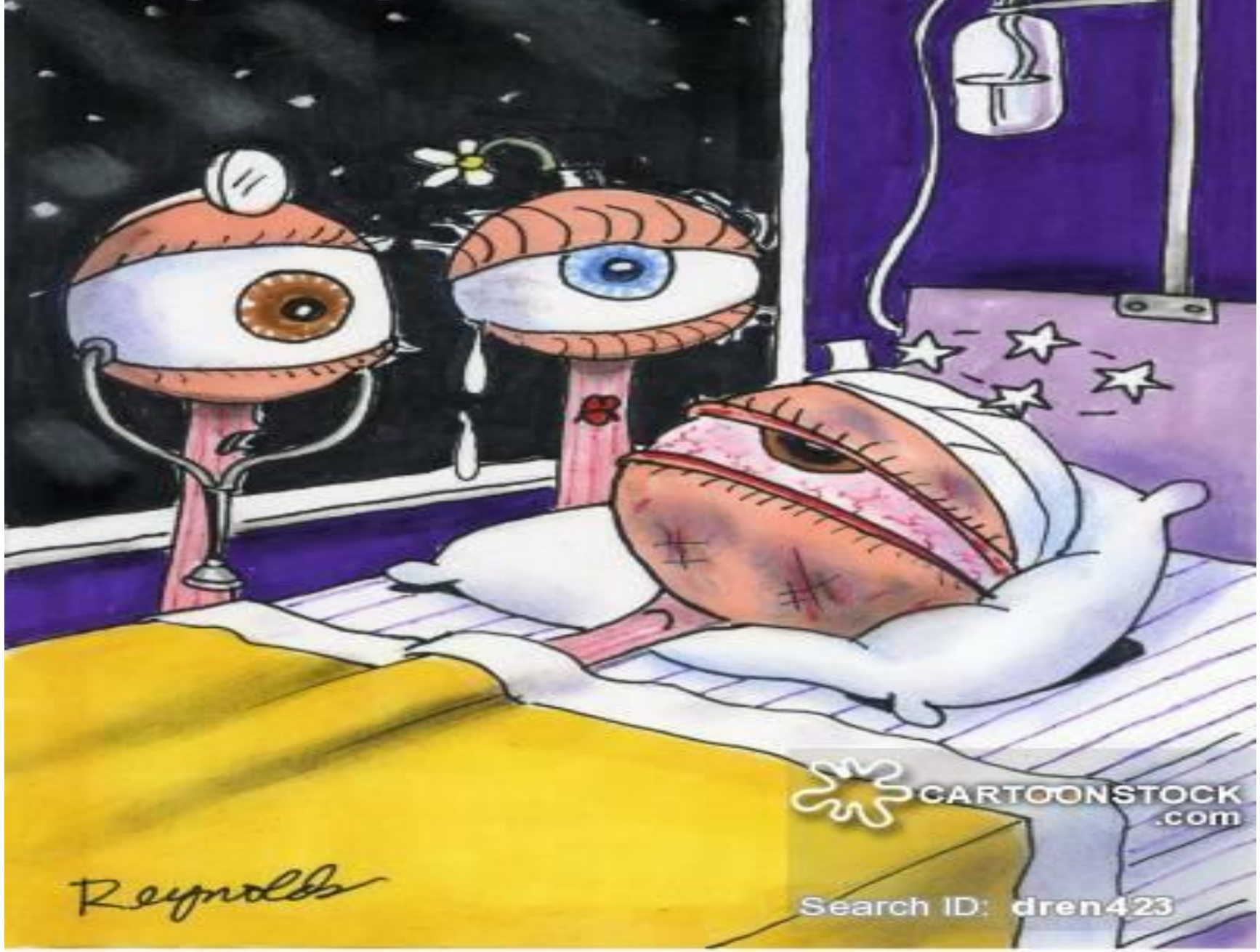
DRUG	Wash out period
Miotics	1-3 days
Beta blockers	2-5 days
CAI	1 week
PG	4-6 weeks

Hyperosmotic agents

- lower intraocular pressure by creating an osmotic gradient between the blood and the ocular fluids
- The amount of this fall in pressure is dependent upon the degree of its elevation and the osmotic gradient induced.
- Hyperosmotic agents currently used are effective at a dose in the range of 1 to 2 Gm. per kilogram over 30-60 minutes

Hyperosmotic agents

- Dehydration
- Nausea and vomiting
- Vertigo, chills
- Agitation and disorientation
- Chest pain, congestive failure, pulmonary edema
- Diuresis—urinary retention
- Vitamin K deficiency
- Subdural hematoma



"We're hopeful the built up pressure will subside, but right now he's still in a glau**coma**."

Thank you