PHARMACY BULLETIN

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FAQ: Which Systemic Drug for Glaucoma is safest in renal impairment?

Glaucoma and Intraocular pressure

Pathological intraocular pressure (IOP) elevation is a major risk factor for glaucoma as it can damage the optic nerve and cause vision loss. Hence, lowering eye pressure can help slow down the progression of vision loss from glaucoma.[1]
There are 6 main pharmacologic classes of anti-glaucoma medications which can be used as monotherapy or in combination therapy. They are: prostaglandin analogues (Latanoprost), beta-blockers (Timolol), adrenergic agonists (Brimonidine), carbonic anhydrase inhibitors (Brinzolamide, Acetazolamide), cholinergic agents (Pilocarpine) and osmotic agents (Glycerol & Mannitol). For this bulletin, we will be focusing on mainly the systemic glaucoma drugs available in HCTM.

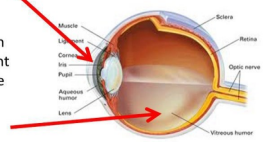
Carbonic Anhydrase Inhibitor (Acetazolamide) → Suppress aqueous humour production at ciliary bodies → Reduce Intraocular Pressure

Osmotic agents (Glycerol & IV Mannitol) → Create an osmotic gradient between the blood & vitreous humour that draws water from the vitreous cavity → Reduce Intraocular Pressure

Aqueous Humour and Vitreous Humour

Aqueous Humour
- Jelly-like material at the front of the eye behind the cornea; supplies cornea with nutrients, bends light and maintains shape

Vitreous Humour
- Bends light and gives the eye structure



Used as an adjunctive therapy as well as monotherapy in selected cases. Long term use is not advisable due to serious SEs

Carbonic Anhydrase Inhibitor

Used in acute situations when rapid IOP reduction is desired

Osmotic agents

Drug	Acetazolamide	Glycerol	Mannitol
Formulations available	Injection 0.5g/vial, Tab 250mg	Glycerin BP/Glycerol 99.9%, 0.85-1g/mL	IV Infusion (500ml) 10% (0.1g/mL), 20% (0.2g/mL)
Route	IV push/IV infusion or Oral	Oral	IV (for infusion)
Pharmacokinetics	Onset of action: *Oral* 1-1.5 hours, *IV* 2-10 minutes Duration: *Oral* 8-12 hours, *IV* 4-5 hours Half-life: 2.4-5.8 hr, *HD:* 26-60.8 hr	Onset of action: 10-30 minutes Duration: 4-6 hours Half-life: 10mins—1 hour	Onset of action: 15-30 minutes, *Diuresis*: 1-3 hours Duration: Approximately 6 hours Half-life: ~ 2 hrs, *AKI/ESRF:*~ 36 hrs, *HD:* 6hrs, *PD:* 21 hrs
Monitoring & Precautions	Intraocular pressure (30 to 60 mins after administration for acute angle-closure glaucoma), serum electrolytes; periodic CBC with differential; monitor growth in pediatric patients. [3]	Avoid in diabetics because the increased caloric load can cause ketoacidosis. [4]	When giving mannitol, monitor cardiac function as the fluid shifts can precipitate heart failure. Additional electrolytes, including sodium, potassium, and osmolality: The clinician should stop mannitol if significant electrolyte abnormalities develop or the osmolality reaches 320 mOsm or higher. Urine output: If output declines, consider discontinuation of mannitol therapy.[5]

Abbreviations and their meaning :
AKI: Acute Kidney Injury ESRF: End Stage Renal Failure HD: Hemodialysis PD: Peritoneal Dialysis

Continuation from the previous page...

Drug	Acetazolamide	Glycerol	Mannitol
Adult Dose	Adjunct in open-angle glaucoma, Preoperative management of angle-closure glaucoma[6] Adult: [IV/Oral] 250-1,000 mg daily, may be given in divided doses for amounts over 250 mg daily Glaucoma following surgery; Prophylaxis[6] 500mg orally 1 hour preoperatively (off-label dosage)	*Oral* 1-1.5g/kg as a single dose. May go up to 2g/kg. Additional dose of 500mg/kg may be administered at approx. 6-hour intervals, if necessary.	Reduction of intraocular pressure 0.25-2g/kg (usual dose: 1.5g/kg) of a 20% w/v solution (1.25-10ml/kg) or as a 10% w/v solution (1.7-13ml/kg) as a single dose IV over *30-60 mins*, repeated if necessary 1 or 2 times after 4-8 hours When used preoperatively administer 60-90 mins prior to surgery to achieve maximum reduction of pressure before surgery
Renal Adjustment	CrCl (mL/min):[5,6,10] ≥ *50* No need dose adjustment 30-49 250mg BD 10-29 Avoid use, if essential, 125mg BD with close monitoring *< 10* Avoid use, if essential, use 125mg OD with close monitoring. In HD 250mg BD In PD 125mg OD	Not much data available. MIMS: Patients must be evaluated for kidney or heart disease prior to administration of hyperosmotics; glycerol may alter blood glucose levels and should not be given to diabetes mellitus (DM) patients	In AKI: minimize AKI by keeping the dose below 0.25 g/kg q 4 hours (1.5 g/kg daily). Patients who develop AKI may recover kidney function (within 24 hours) if treated with 1-2 hemodialysis sessions to remove the excess mannitol; by contrast, patients managed without dialysis may recover kidney function more slowly (7 to 10 days). Severe renal impairment (GFR< 30mL/min): Use a test dose of 0.2g/kg via infusion over *3-5 mins* to produce a urine flow of at least 30-50mL/hr over the next 2-3 hours. If urine flow does not increase, a second dose of 0.2g/kg may be given; but if there is inadequate response, the patient should be re-evaluated and Mannitol should not be used.[6,8] In Anuria : Contraindicated because of the inability to excrete Mannitol
Notes	The product's labeling contraindicates use in severe kidney impairment, but use may be considered after careful assessment of risks vs benefits along with close monitoring for adverse effects.	-	Total dose of 100g Mannitol in 24 hours should only be exceeded if there is at least 100mL/hr of urine output.

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