Glaucoma: Topical Treatment Tips & Comparison Chart

The RxFiles

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The RxFiles Academic Detailing Program
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Glaucoma can be defined as "a group of ocular disorders that are responsible for excavation and atrophy of the optic disc and gradual loss of the visual field."[1] It is the second leading cause of blindness in Canada in people older than 50 and the number one cause of irreversible blindness worldwide. Primary open angle glaucoma (**POAG**) represents 90% of all cases and will be the focus of this discussion.[2]

The eye continuously produces aqueous humour to maintain ocular integrity. It also provides nutrition and waste disposal in the anterior segment structure. In a normal eye, this fluid flows through the trabecular meshwork, and the canal of Schlemm, eventually reaching venous drainage. In POAG, flow is impaired due to obstruction or dysfunction in the drainage system. This increases intraocular pressure (**IOP**) and can lead to damage of the optic nerve and eventual loss of visual field. The goals in treating POAG are to preserve visual function and prevent blindness. Therapeutic options include drug therapy, laser treatment and surgical management, all of which are aimed at decreasing IOP. Drug therapy reduces IOP by increasing outflow of aqueous humour or decreasing its production. **See Comparison Chart Pg 2**.

Eyeing your patient's technique...

Eyedrops must be administered correctly to lower IOP. In a SCH study, several criteria were used to evaluate eyedrop administration technique in ambulatory glaucoma patients. The criteria were evaluated before and after pharmacist demonstration. All patients who completed a follow-up visit (n=17) had improved technique after pharmacist intervention. (Table I)

Table I: Subjects who met study criteria for proper drop instillation

Step	**Subjects performing step correctly:**	
	Initial visit (n=20)	**Follow-up** (n=17)
Tilted head back	12 (60%)	14 (82%)
Formed a pouch	16 (80%)	17 (100%)
Instilled correct number of drops	11 (55%)	17 (100%)
Did not touch dropper to eye area	10 (50%)	10 (59%)
Closed eye gently after instillation (without blinking/rubbing/squeezing)	0 (0%)	17 (100%)
Applied pressure-lacrimal punctae	1 (5%)	16 (94%)

EYEDROP ADMINISTRATION - PROBLEM AREAS

•45% of patients, at the initial visit, failed to instill any drops into their eye at all. None were aware that they had missed!
•45% of patients using more than one drop to treat glaucoma, did **not** wait at least 5 minutes between administration of drops therefore the second drop virtually washes the first one out of the eye
•0% of patients performed the punctal pinch method at initial visit

Nasolacrimal Duct Occlusion: Eighty-five per cent of a 50 µL dose of ophthalmic solution will flow into the nasolacrimal drainage apparatus. The nasolacrimal duct drains into the rhinopharyngeal mucosa where much of the drug will be absorbed into the systemic circulation. It is estimated that 30-80% of a drug administered topically to the eye will be absorbed into the systemic circulation.[3] By gently closing the eye and occluding the nasolacrimal duct after instillation (the punctal pinch method), the amount of drug absorbed into the systemic circulation is decreased, and efficacy is enhanced due to increased contact time with the eye.

Potential Risks with Improper Eyedrop Administration:

- Deterioration of eyesight due to uncontrolled glaucoma
- Development of systemic side effects (↑ risk if: elderly, suffering from concomitant disease states)
- ↑ cost due to addition of unnecessary adjunctive agents
- Eye infections due to contamination of the bottle during administration
- ↑ cost due to drop wastage

Teaching patients proper administration technique is essential for successful topical therapy of glaucoma. This should include: a physical demonstration by a health care professional, observation of patient technique at initiation of therapy, after any adjunctive agents have been added, and periodically throughout therapy.

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References available on request or online

TOPICAL OPHTHALMICS FOR POAG : COMPARISON CHART[4,5,6]

Prepared by Carolyn Anderson BSP – **www.sdh.sk.ca/RxFiles** - **July/01**

Name Brand Name (Dosage forms)	Dose Frequency	Cost for 1 mo. of tx	Comments *remove contact lenses prior to instilling any eyedrops *occlude the lacrimal punctae for at least 1 min after instillation * all suspensions must be shaken prior to use *wait at least 5 minutes between consecutive drops *allergies to preservatives possible
β-Blockers: ↓ aqueous production via sympathetic receptor blockade in the ciliary body *(~20-40% ↓ in IOP)*			**β**-blockers are usually the **first line** of therapy for POAG **if no CI exists** (asthma, COPD, bradycardia, heart block, overt CHF, cardiogenic shock) **Systemic side effects (up to 10% incidence)**: ↓HR, ↓BP, CHF, cold extremities, bronchospasm, ↓ symptoms of hypoglycemia, ↓ libido, itchy red skin, alopecia, CNS SE's (H/A, depression, fatigue, weakness etc.), tolerance to IOP ↓'ing effect may occur with prolonged therapy -systemic side effects are more likely to occur with timolol & levobunolol (non-selective β1β2 antagonism) vs betaxolol (β1-selective) **Topical side effects**: **(up to 10% incidence)** stinging, dry eyes, foreign body sensation, photophobia, blurred vision, ↓ visual acuity, eyelash crusting -allergic reaction has been reported (no cross-reactivity between agents, therefore may switch within the class) **Drug interactions**: caution with other drugs that ↓ HR/BP
Betaxolol BETOPTIC S 0.25% susp	1 gtt q12h	$34 (10ml)	
Levobunolol BETAGAN 0.25, **0.5**% soln	1 gtt q12-**24**h	$25 (5,10ml)	
Timolol TIMOPTIC **0.25**,0.5% soln	1 gtt q**12**-24h	$25 (10ml)	
TIMOPTICXE **0.25**,0.5%gelsoln	1 gtt q24h	$25 (5ml)	
α/β agonist: ↑ outflow via trabecular meshwork and ↓ production of aqueous humour *(~20-25% ↓IOP)*			Note: Brimonidine may also ↑ uveoscleral outflow Dipivefrin is a prodrug of epinephrine therefore ↑ potency & ↑ tolerability vs. epinephrine ophthalmic drops Apraclonidine for perioperative control of IOP (1%) and as short-term adjunctive therapy in POAG (0.5%) (2nd-3rd line tx) -may not provide ↑ benefit when given with **β**-blockers or carbonic anhydrase inhibitors because they have common MOA's -usually only short-term therapy b/c tachyphylaxis develops (apraclonidine>brimonidine) and topical side effects **Systemic side effects**: **(up to 10% incidence)** dry mouth/nose, arrhythmias, H/A, ↓ HR, anxiety, sleep disturbances,↓ BP, lethargy, fatigue, drowsiness -CNS SE's more common with brimonidine (>10%) (vs. apraclonidine) due to ↑'d lipophilicity **Topical side efects:** (**up to 10% incidence)** burning/stinging, photophobia, blurred vision, mydriasis (dipivefrin), blanching , eyelid elevation. Allergic reaction with apraclonidine (incidence as high as 50%): hyperemia, pruritis, discomfort, edema & ++tearing **Drug interactions:** ↑ effect of CNS depressants (eg. alcohol, benzodiazepines, etc.), MAOI's contraindicated with apraclonidine, other drugs that ↓BP
Dipivefrin PROPINE 0.1% soln	1 gtt q12h	$26 (10ml)	
α2 agonists: ↓ aqueous production via local α2 agonist action *(~18-27% ↓IOP)*			
Apraclonidine IOPIDINE **0.5**%, 1% soln	1 gtt q**8**-12h	$32 (5ml)	
Brimonidine ALPHAGAN 0.2% soln	1 gtt q8-12h	$46 (10ml)	
PNS agents: (Direct and Indirect) ↑ outflow via trabecular meshwork *(~20-30% ↓IOP)*			Pilocarpine has similar efficacy to β-blockers in terms of IOP reduction but not as well tolerated (2nd line tx) -2% soln 1 gtt q6-12h produces desired response in most patients (patients with darkly pigmented eyes may require higher doses of pilocarpine) Cholinesterase inhibitor reserved for those who don't respond to other agents (3rd or 4th line tx) due to their high incidence of ocular and systemic side effects -miosis occurs within 10-30 min of echothiophate administration and can last up to 4 weeks -Refrigerate echothiophate until reconstituted, then stable for 1 month at room temp or 3 months if kept in the refrigerator **Systemic side effects: (up to 10% incidence)** headache/browache, nervousness, polyuria, hypersensitivity reactions -H/A, sweating, tremor, salivation, N/V, diarrhea, cramps, ↓ BP/HR (more likely with AchE inhibitors) (<1%) **Topical side effects: (up to 10% incidence)** local burning and stinging, photophobia, myopia leading to decreased vision at night, fixed small pupils. Cataracts can occur especially with echothiophate, and its prolonged use may cause formation of rounded nodules (cysts) of the pigmentary epithelium which may interfere with vision (usually reversible if discontinue drug). **Drug interactions:** Stop echothiophate prior to surgery because prolonged apnea with general anaesthetic
Direct acting agonists:			
Pilocarpine 0.5,**1**,2,4,6,(10χ) % soln;	1 gtt q4-**12**h	$10 (10ml)	
4% gel PILOPINE-HS	½ " at HS	$23 (5g)	
Indirect Acting agonist (AchE inhibitor):			
Echothiophate soln PHOSPHOLINE IODIDE	**Summer 2001 - D/C by Co**		
Carbonic Anhydrase Inhibitors: ↓ secretion of aqueous humour by 40-60% *(~15-25% ↓IOP)*			Well tolerated and can be used as both monotherapy (q8h) or as adjunct treatment (q12h) **Caution**: in diseases that may induce acidosis (COPD, DM, hepatic/renal insufficiency), if Creatinine Cl < 30mL/min (eliminated renally) & possible cross-sensitivity with sulfonamides **Systemic side effects: (up to 10% incidence)** bitter taste (25%), H/A, nausea, fatigue -possible blood dyscrasias (as seen with PO acetazolamide: rare, non-dose-dependent effect) **Topical side effects: (up to 10% incidence)** immediate ocular discomfort (33% with dorzolamide, **improved with brinzolamide**), superficial punctate keratitis (10-15% with dorzolamide), blurred vision, allergy **Drug interactions:** salicylates have caused accumulation of oral acetazolamide (=CNS toxicity, metabolic acidosis); never been shown with eyedrops but it is possible, as ophthalmic CAInh's are absorbed systemically
Brinzolamide AZOPT 1% susp	1 gtt q**8**-12h	$26 (5ml)	
Dorzolamide TRUSOPT **2**% soln	1 gtt q**8**-12h	$26 (5ml)	
Prostaglandin F2α analogue: active metabolite (latanoprost acid) ↑'s outflow via uveoscleral route *(~25-35% ↓IOP)*			**Monotherapy or can be used as an adjunctive agent** (additive ↓ IOP with β-blockers, dipivefrin, and CAInh (po or topical)) Refrigerate prior to opening; once opened: cool place/ refrigerate for a max of 6 weeks Well-tolerated, fewer systemic side effects and better night-time control of IOP vs. timolol but more ocular reactions occur **Systemic side effects: (up to 10% incidence)**, skin reaction (toxic epidermal necrolysis possible), upper respiratory tract infection/cold/flu (4%), chest pain, muscle & joint pain (1-2%) **Topical side effects: (up to 15% incidence)** altered iris pigmentation (7-22%) (especially in patients with mixed pigmentation), foreign body sensation, blurred vision, and burning on instillation (>10%), mild conjuctival hyperemia (improves after 2-4weeks), dry eye, tearing, pain, photophobia, edema, darkening, thickening, and lengthening of the eyelashes, darkening of the eyelid (these are especially NB for pt if tx is in one eye only) **Drug Interactions**: any eyedrop with thimerosol as preservative→immediate precipitate will form (thus administer >5 minutes apart)
Latanoprost XALATAN 0.005% soln	1 gtt q hs -1 study showed hs better than am dosing -no advantage of >1 gtt/day	$36 (2.5ml)	

Combination Therapies: multiple mechanisms of action (synergy)	Sig	Cost#	
Dorzolamide/ Timolol : COSOPT (2%/0.5%) soln -bottle/Ocumeter Plus	1 gtt q12h	$35 (5,10ml)	Timolol and pilocarpine have additive effects on IOP (i.e. ~↓ 40-70%) Dorzolamide and timolol have additive effects on IOP (i.e. ~↓ 35-65%) Combination products may offer both **cost & convenience** advantages over same agents given separately
Timolol/ Pilocarpine: TIMPILO 2 (0.5%/2%) & TIMPILO 4 (0.5/4%) susp	1 gtt q12h	$24 (5ml)	
Levobunolol/Dipivefrin: PROBETA (0.5%/0.1%) soln	1 gtt q12h	$23 (5,10ml)	

Notes: **POAG**= primary open angle glaucoma; **IOP**= intraocular pressure; **Cost #** per~month of therapy Rx in SK including mark-up and dispensing fee (when multiple strengths/intervals exist, **bolded strength/interval** used to calculate cost)

χ = non-formulary; AchE=acetylcholinesterase; BP=blood pressure;CAInh= carbonic anhydrase inhibitors; CI= contraindication;CNS=central nervous system;H/A=headache;MOA= mechanism of action;PNS= Parasympathetic nervous system;SE=side effects.

References: *RxFiles* - Glaucoma

[1] Elolia R, Stokes J. Monograph series on aging-related diseases: X1. Glaucoma. *Chronic Diseases in Canada* 1998; 157-69.
[2] Alward, WLM. Medical management of glaucoma. *New Engl J Med* 1998; 339: 1298-1307.
[3] Diamond JP. Systemic adverse effects of topical ophthalmic agents. Implications for older patients. *Drugs Aging* 1997; 11:352-360.
[4] Dipiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey LM. *Pharmacotherapy: a pathophysiologic approach*. Fourth ed. Stamford, CT: Appleton and Lange; 1999:1470-75.
[5]Boucher M. Glaucoma: Keeping a close eye on your patients. *Pharmacy Practice* 2000; 16(2): 61-66
[6] Tsao S. The use of drugs in glaucoma patients. *CPJ* 2000; 133(7): 30-34.