A GUIDE TO

deprescribing

phn TASMANIA
An Australian Government Initiative

primary health TASMANIA

CPS Experts in Medicines
CONSULTANT PHARMACY SERVICES

GLAUCOMA EYE DROPS

KEY POINTS

Glaucoma treatment is generally considered lifelong, however review may be warranted in some patients.

Consider discontinuation in patients who have significant difficulty with medication administration and whose life expectancy may be limited.

Patients on treatment for mild glaucoma or ocular hypertension would be at minimal risk for vision loss if medications are ceased in the short to medium term.

For a patient with no visual field loss (or who has a mild, asymptomatic visual field defect) from glaucoma, it would take some time before they would experience symptomatic vision loss even without treatment - unless the pressure is very high.

Symptomatic vision loss from glaucoma (i.e. the patient is aware that vision is fading) indicates the glaucoma is advanced, and IOP-lowering medications should be continued

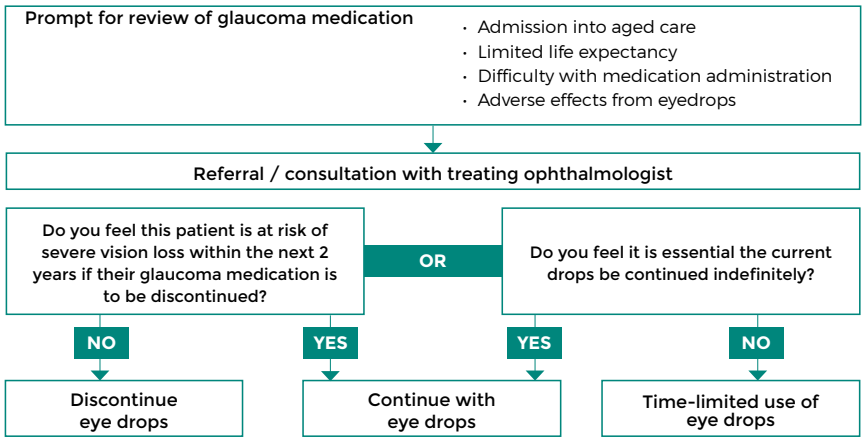
CONTEXT

This guide considers the deprescribing of topical ophthalmic agents for open-angle glaucoma, particularly in patients with a limited life expectancy and those with difficulties relating to administration of eye drops (e.g. severe dementia).

RECOMMENDED DEPRESCRIBING STRATEGY

The treating ophthalmologist should be actively consulted in the process of considering deprescribing of glaucoma treatment.

DEPRESCRIBING ALGORITHM



BACKGROUND

Glaucoma is the most common neurodegenerative disease of the optic nerve, with Glaucoma Australia estimating over 300,000 Australians impacted, with around 50% unaware they have the disease.[1]

The Glaucomas are characterised by optic neuropathy, optic disc changes and irreversible, progressive visual field loss caused by progressive degeneration of retinal ganglion cells. Degeneration results in cupping, a characteristic appearance of the optic disc and visual loss.[2] Increased intraocular pressure (IOP) or ocular hypertension (although not a defining characteristic) is the only modifiable risk factor for glaucoma.

INTRAOCULAR PRESSURE REDUCTION

A target IOP for treatment is determined based upon the patient's severity of disease which can be determined by a variety of factors, including a patient's risk factors for glaucoma progression, the extent of optic nerve damage and rate of deterioration. Other factors should be considered, such as life expectancy, and potential for adverse effects from treatment. In general, the initial target aims for 20% to 50% reduction in the IOP; however, the target pressure needs to be continuously reassessed during patient follow-up, depending on the evolution of the disease. The maintenance of IOPs in the low to mid teens (<15mmHg) may be the goal for advanced primary open angle glaucoma.[4]

RISK FACTORS

The risk of glaucoma is highest when examination reveals an increased cup-disk ratio (CDR), CDR asymmetry, disc haemorrhage, or elevated intraocular pressure. Other risk factors that may warrant referral to optometry / ophthalmological review include the following:[3]

- Older age
- Family history of glaucoma
- Black race
- Use of systemic or topical corticosteroids
- High intraocular pressure

These patients require greater reduction in IOP. It is worth noting that in a recent NHMRC review of the diagnosis and management of glaucoma it was concluded, "There is a paucity of information regarding the management of glaucoma in elderly patients such as those in nursing homes and aged care facilities. For example, ß-blockers have been shown to increase the risk of falls in the elderly, more research may be available to inform subsequent revisions of this guideline."[4] Although elevated IOP is a risk factor for glaucoma, a significant proportion of people with glaucoma have IOPs that are not elevated and some people with elevated IOP may never develop glaucoma. The presence of characteristic visual field defects can confirm the diagnosis, but as many as 30-50% of retinal ganglion cells may be lost before defects are detectable by standard visual field testing.[5]

EFFICACY

Topical drugs are first-line treatment (either alone or in combination). They reduce IOP by decreasing production of aqueous humour and/or by increasing its outflow. The ultimate objective of glaucoma treatments is to preserve the remaining visual field (i.e., to stop visual field defect progression).

EARLY TREATMENT

The Ocular Hypertension Treatment Study randomized patients with ocular hypertension (high IOP but no clinical signs of glaucomatous damage to the optic nerve or visual field) to treatment vs no treatment. At the end of 5 years of follow-up, 4.4% of patients in the medication group vs 9.5% in the untreated group developed signs of glaucoma.[5] The Early Manifest Glaucoma Trial also randomized patients to treatment vs no treatment; with all patients having a clear diagnosis of glaucoma at the baseline visit. After a median follow-up of 6 years, progression was less frequent in the treatment group (45%) than in the control group (62%).[6] This however highlights that progression can be slow for some individuals and that review of medication treatment is appropriate in individuals whose life expectancy might be limited, or in whom adverse effects or difficulty with eye drop administration may be a problem.

The target IOP should be achieved with the fewest medications and minimum adverse effects. Several different classes of pressure-lowering medications are available. Medication choice may be influenced by cost, adverse effects, and dosing schedules. In general, prostaglandin analogues are the first line of medical therapy. These drugs reduce IOP by reducing outflow resistance resulting in increased aqueous humour flow through the uveoscleral pathway.

Other classes of topical medications (e.g. ß-blockers, alpha2 agonists) are less effective in lowering IOP than prostaglandin analogues. They are used as second-line agents or when there is a contraindication or intolerance to the use of prostaglandin analogues. Laser or surgical interventions are considered if drug treatment is inadequate or intolerable.

LONG TERM TREATMENT

Generally, glaucoma treatment is considered life-long (with the aim of slowing the progression of the disease and delaying visual field loss) unless there are changes to an individual's circumstances that prompt review (see recommended deprescribing strategy). Some patients will be on multiple topical therapies, either individually or as combination preparations. Cessation of treatment will cause an increase in IOP, the extent of which will differ depending on the individual. The time from cessation of treatment (and subsequent increases in IOP) to lead to significant progression of disease is variable.

Evidence indicates that factors associated with greater risk of glaucoma progression include [7]

- Elevated/ fluctuating IOP,
- Optic disc haemorrhage,
- An increased CDR or CDR asymmetry,
- Increased severity of glaucomatous disc damage and
- Very low blood pressure.

ADVERSE EFFECTS

The prostaglandin analogues are administered once daily, preferably at night and generally have few systemic adverse effects. However, they can cause local adverse effects such as conjunctival hyperemia, elongation and darkening of eyelashes, darkening of the iris, loss of orbital fat (so-called prostaglandin-associated periorbitopathy) and periocular skin pigmentation. They often exacerbate dry eye, ocular surface disease and blepharitis which can be a common ocular comorbidity. Some of the other agents, such as ß- blockers, may have significant systemic adverse effects and can be contraindicated in patients with history of asthma, bradycardia or use of other rate-limiting medications due to additive effects.

Eye drops contain the therapeutic agents, along with various additives, including preservatives. It is worth noting that as opposed to benzalkonium, purite and polyquad preservative are considered less irritant to the eye. Most preservatives also act as surfactants which destabilize bacterial cell membranes. This causes destruction of the cell membrane, inhibition of cell growth, and reduction of cell adhesiveness. However, preservatives also exert these effects on normal corneal and conjunctival cells, resulting in ocular surface disorders. These include superficial punctate keratitis, corneal erosion, conjunctival allergy, conjunctival injection, and anterior chamber inflammation.[7]

Correct instillation technique has been identified as a problem for patients using glaucoma medications. Many patients do not wait a sufficient time between instilling their different drops, with an approximate 5 minute gap considered necessary to reduce the risk of displacement. Over-administration of drops can also become a problem when multiple attempts are needed to deliver one drop to each eye. One study revealed that more than 37% of patients instilled more than two drops per eye, when the intent was to instil just one. In the same study, more than 20% of patients instilled more than three drops per eye.[8] Over-administration of eyedrops can result in overflow of drops, that may flow down the cheek and result in wastage and increased costs (e.g. needing to purchase eyedrops more frequently).

FACTORS TO CONSIDER

The rate of ganglion cell loss and subsequent functional decline can vary. As shown in **Figure 1**, Line A represents the reduction in visual function due to the normal ageing process. Older patients, that are diagnosed with glaucoma later in life, may experience a moderate rate of decline and therefore carry a lower risk of developing severe functional impairment (Line B) than a younger patient with the same extent of decline and rate of progression (Line C). In some cases, a gradual rate of functional decline may be tolerated by the patient and treatment may remain unchanged (Line D). In other cases, a rapid rate of decline will require a lower target IOP, likely resulting in more extensive treatment (Line E).[9]

Review of medication treatment may be appropriate in individuals whose life expectancy might be limited, or in whom adverse effects or difficulty with medication administration may be a problem.

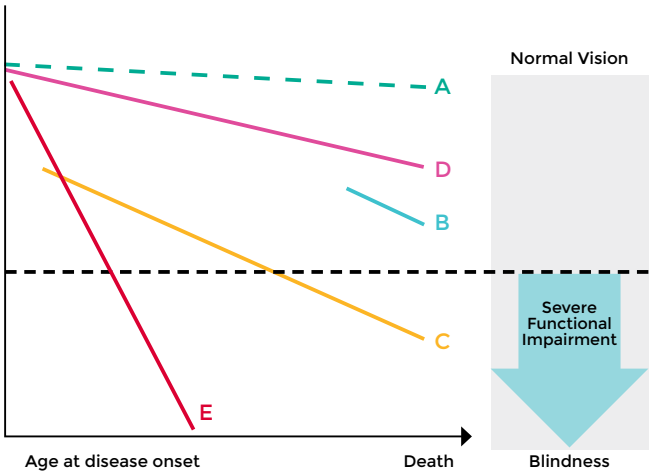


Figure 1: Variation in Functional Decline due to Glaucoma (Adapted from Reference 9)

CONSEQUENCES OF CESSATION OF EYEDROPS

The IOP will increase soon after stopping the drops, however what impact this will have on the patient's vision depends on how advanced the glaucoma is. There is a risk that patients with advanced glaucoma will lose vision over time. However, although it is possible to slow the rate of visual field loss with treatment, this loss may still occur despite ongoing treatment in some patients.

IN FAVOUR OF DEPRESCRIBING

Factors in favour of continuing glaucoma medication:

- Individuals whose life expectancy is limited
- Patients who have mild glaucoma or ocular hypertension, who would be at minimal risk of clinical significant deterioration of vision after cessation of treatment
- Patients who are admitted to residential aged care and monitoring their IOP becomes difficult (e.g. unable to attend ophthalmological examinations and appointments) and/or where their other medical conditions become more of a priority.

AGAINST DEPRESCRIBING

Factors against deprescribing glaucoma medication:

- advanced disc cupping as documented by ophthalmologist
- advanced visual field loss (MD on humphrey static perimetry less than or equal to -15 dB)
- visual field defect involving the central part of the vision in one or both eyes
- loss of vision in one eye from glaucoma already
- known very high pre-treatment IOP (over 35mmHg)
- patient is still reading or performing tasks that improve their quality of life

DISCONTINUATION SYNDROMES

Glaucoma medications can be stopped abruptly without the need for tapering. Any subsequent increases in IOP would likely be asymptomatic and would not result in pain, though some patients (e.g. those with dementia) may have difficulty with expressing concerns regarding any changes to their vision.

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AUTHORSHIP

This guide was prepared for Primary Health Tasmania by Xenia Jak and reviewed by Angus Thompson, Pharmacist Clinical Editor, Primary Health Tasmania and the Deprescribing Project Advisory Group. Dr Shane Jackson, Dr Mark Naunton and Dr David Wechsler were involved with earlier versions of this document.

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DECEMBER 2022