GLAUCOMA

who to refer for testing and how to manage their treatment

Glaucoma is the leading cause of preventable blindness in New Zealand and it is estimated that half of the people affected by it are undetected.[1] To improve detection rates every person should ideally have an assessment of their optic nerve before age 45 years, and people with risk factors, e.g. a family history of glaucoma, examined earlier. Topically administered intraocular pressure-lowering medicines are the mainstay of glaucoma prevention and treatment. However, systemic absorption of these medicines does occur, which can result in adverse interactions with other treatments, e.g. antihypertensive medicines, or exacerbations of underlying conditions. Adherence to glaucoma treatment is a problem for many patients as the condition is often asymptomatic until it is relatively advanced.

Glaucoma: the sneak-thief of sight

The term glaucoma describes a group of progressive conditions characterised by damage to the optic nerve and a reduction in the visual field. The neural damage that occurs is currently irreparable and all forms of glaucoma can lead to an irreversible loss of vision.[2] Chronic glaucoma is usually asymptomatic until it is advanced, therefore detection largely relies on Optometrists testing people who are at increased risk, e.g. people aged over 45 years or who have a family history of glaucoma, and then referring those with signs of glaucoma to an Ophthalmologist for treatment initiation. Glaucoma treatment is not curative; however, it does slow the progressive visual loss. On average, patients receiving treatment for the most common type of glaucoma (primary open-angle glaucoma – Page 28) will increase the amount of time until they lose their vision by more than 50%.[3]

Raised intraocular pressure is not a defining feature of glaucoma

Ocular hypertension (intraocular pressure [IOP] > 21 mmHg) is no longer considered a defining characteristic of glaucoma.[2] A large study found that over one-third of patients aged over 55 years who were diagnosed with glaucoma had an IOP < 21 mmHg.[4] Therefore glaucoma is best thought of as an optic neuropathy for which ocular hypertension is the most important risk factor.

Reducing IOP is the only pharmacological strategy for slowing glaucoma progression; IOP-lowering treatment has been shown to be effective in multiple trials, including in patients with IOP levels within the "normal" range.[5]

Patients who are diagnosed with ocular hypertension and have major risk factors (Page 29) for developing glaucoma are also generally treated with IOP-lowering medicines to reduce their risk of developing glaucoma.

The pathophysiology of glaucoma

In a glaucomatous eye ganglion cell axons are damaged at the optic nerve head, which is the most anterior section of the optic nerve, visible on ophthalmoscopy. This damage results in a characteristic "cupped" appearance of the optic nerve head and a typical pattern of visual field loss, usually an arcuate scotoma (Figure 1). Often chronic glaucoma will affect eyes asymmetrically.[1] Genetic mutations in multiple genes appear to increase the risk of people developing the most common

Figure 1: Normal vision (left) and an arcuate scotoma (right) in a patient in the advanced stages of primary open-angle glaucoma

form of glaucoma. More than 30 mutations of the myocilin gene have so far been linked to glaucoma in different ethnic groups.[6]

The optic nerve itself is made up of 1.2 million ganglion cell axons, whose cell bodies lie in the retina and transmit axon potentials from the retina to the lateral geniculate nucleus, where the visual pathway continues to the visual cortex. When a person has elevated intraocular pressure, damage to the ganglion cell axons is thought to occur due to mechanical stress and/or impaired vascular perfusion from increased pressure. In people with glaucoma without ocular hypertension, other factors are also likely to be involved, such as microvascular insufficiency and neurodegenerative processes.

The classification of glaucoma

Glaucoma is classified according to the morphology of the angle of the anterior chamber, between the iris and the cornea, where the aqueous humour drains through the trabecular meshwork (Figure 2). In patients with open-angle glaucoma the iris does not block the flow of fluid. In patients with angle-closure glaucoma there is contact between the iris and the trabecular meshwork which causes the two structures to adhere to each other (synechia), obstructing the drainage of aqueous humour and causing IOP to rise.[3]

The same medicines (mostly topical) are used to treat patients with open-angle or angle-closure glaucoma, however, patients with angle-closure glaucoma also generally benefit from laser iridotomy. Both open-angle and angle-closure glaucoma can be further classified as primary or secondary.

Open-angle glaucoma

Open-angle glaucoma occurs when the trabecular meshwork becomes blocked over time or the tissues around it harden preventing the drainage of aqueous humour from the anterior chamber of the eye.[8]

Primary open-angle glaucoma is the most common form of glaucoma and accounts for 90% of cases in developed countries.[1] If open-angle glaucoma occurs in a patient with an IOP within the normal range this is termed "normal tension glaucoma". Many glaucoma experts now regard normal tension glaucoma and primary open-angle glaucoma to be at opposite ends of the same disease spectrum.

The physiology of intraocular pressure

Aqueous humour supplies nutrients to structures in the eye and removes waste products. It is produced by the ciliary body in the posterior chamber of the eye (Figure 2). Aqueous humour circulates from the posterior chamber, through the pupil and into the anterior chamber where it exits, mainly through the trabecular meshwork and into venous circulation. A smaller quantity also leaves the eye through the secondary uveoscleral drainage pathway. The balance between the production and drainage of aqueous humour in the eye determines IOP. The average IOP in "normal" eyes is 15 – 16 mmHg, with a range of 10 to 21 mmHg, skewed to the high end.[1] Diurnal variations in IOP can occur, typically of 3 – 6 mmHg, with a peak in the morning and a trough in the evening.[3]

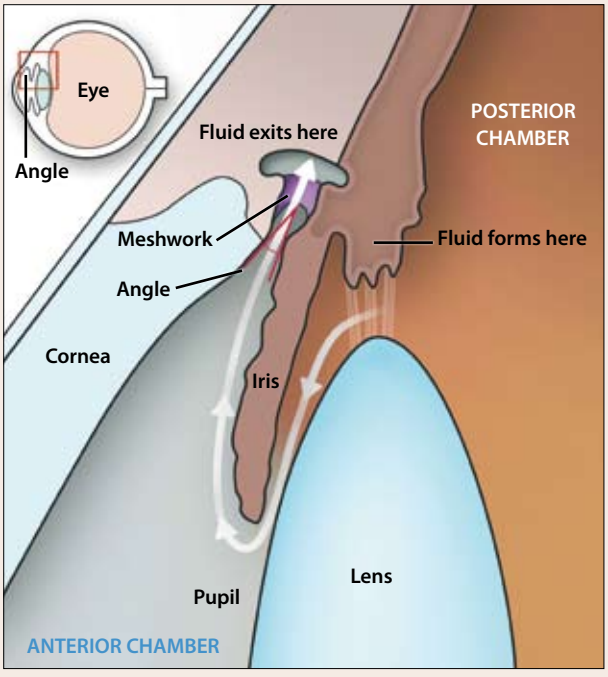

Figure 2: The production and drainage of aqueous humour. Adapted from Yumori and Cadogan, 2011[7]

Secondary open-angle glaucoma is most often caused by pseudoexfoliation (PFX) syndrome, although not everyone with PFX syndrome will develop glaucoma.[9] PFX syndrome is a systemic condition which mainly affects the eyes and is characterised by the deposition of flaky, white protein fibres within the anterior segment of the eye resulting in the trabecular meshwork becoming blocked. There is likely to be a genetic component to the development of PFX syndrome, although ultraviolet light, oxidative stress, infection and inflammation have also been linked to the condition.[10] PFX syndrome is more common with increasing age and is estimated to affect approximately 25% of people aged over 60 years.[10]

Patients with glaucoma due to PFX syndrome are generally managed in the same way as those with primary open-angle glaucoma, although the topical treatments used to lower IOP are often less effective.[11] Some patients require laser trabeculoplasty to alter the drainage tissue of the eye or surgical interventions.

Eye trauma can cause neovascular open-angle glaucoma which may develop immediately after blunt or penetrating eye trauma, or years later.[6] Corticosteroids raise IOP when administered by oral, nasal or ocular routes and this is the most common cause of medicine-induced glaucoma.[6]

Angle-closure glaucoma

There are several different angle-closure conditions. Unlike open-angle forms of glaucoma they are all generally treated by laser iridotomy once IOP and any inflammation have been stabilised.[3]

Acute angle-closure crisis is a medical emergency and the patient should be discussed with an Ophthalmologist immediately. This condition is rare and occurs in people who have a narrow ocular drainage angle, a thicker lens or a thinner iris, which are factors that increase the likelihood of blockage. IOP can be elevated to approximately 70 mmHg during acute angle-closure crisis which may cause permanent damage to ganglion cells in days to weeks, rather than the much slower progression of typical glaucoma.[12] Often acute angle-closure crisis will occur when the pupil is dilated, e.g. watching TV or in dim lighting, during periods of acute stress or excitement or as an adverse effect of atropine following surgery.[12] The most common symptoms of acute angle-closure glaucoma include intense deep eye pain, blurred vision, headache, nausea and vomiting. Ciliary injection, a fixed mid-dilated pupil, a hazy cornea and decreased visual acuity are all features suggestive of acute-angle closure glaucoma. Acute angle-closure crisis usually occurs only in one eye, but in a small number of cases, it will occur in both eyes simultaneously.[12] People who have had acute angle-closure crisis in one eye have an increased risk of developing the same condition in the other eye in the future.[12]

For further information see: "Causes, complications and treatment of a red eye", BPJ 54 (Aug, 2013).

Intermittent angle-closure glaucoma occurs in patients who have a series of minor acute angle-closure episodes due to the angle of drainage becoming partially or intermittently blocked.[3]

Chronic angle-closure glaucoma occurs when the drainage meshwork is occluded by iris synechiae gradually without the acute symptoms of angle-closure crisis. This condition mimics primary open-angle glaucoma and is diagnosed by an Ophthalmologist or Optometrist.[3]

Increased ocular pressure is the most important risk factor

An increase in IOP is the most significant risk factor for open-angle glaucoma. Ten percent of people with ocular hypertension develop open-angle glaucoma within five years.[6] This risk can be reduced by intervention with the same IOP-lowering medicines used for the treatment of glaucoma. There is strong evidence supporting the treatment of people with ocular hypertension and major risk factors for glaucoma.[6] Several trials have demonstrated that for every 1 mmHg increase in mean IOP there is an associated 10% increased risk of progression to glaucoma.[13] Other major risk factors for open-angle glaucoma include:[1, 3, 14]

- Advanced age – The prevalence of open-angle glaucoma is estimated to be 1% in people of European descent aged under 40 years and as high as 5% in European people aged over 75 years
- A family history of glaucoma – The incidence of glaucoma in first-degree relatives is three to five times higher than in the general population
- Myopia requiring optical correction – It is thought that the stronger the myopia, the higher likelihood that the patient will develop glaucoma. There may be genetic linkage between glaucoma and myopia
- Diabetes – People with diabetes have almost twice the risk of developing open-angle glaucoma than people without diabetes
- African descent – People of African descent are reported to have a greater than four-fold increased risk of developing open-angle glaucoma compared with people of European descent

The use of corticosteroids can result in substantially increased expression of the myocilin gene and the long-term use of corticosteroids by any route of administration increases the risk of glaucoma.[3, 15] In general, patients taking long-term, high-dose corticosteroids (> 10 mg prednisone equivalent) for periods of greater than two months should be considered for referral to an Optometrist or Ophthalmologist for an eye assessment. Patients who are taking high-dose prednisone for longer periods are likely to require regular follow-up examinations.

Other risk factors for open-angle glaucoma include: hypertension, smoking, hypothyroidism, peripheral vasospasm, migraine and sleep apnoea, although these associations are thought to be less strong.[1, 6] Low systemic blood pressure may be a risk factor for normal tension glaucoma.[6] A low incidence of glaucoma in Māori has been noted in the literature but there is currently no explanation for this.[16]

The principal risk factors for angle-closure glaucoma are having an eye that is anatomically predisposed to aqueous humour blockage or being of Asian descent.[3, 8]

Glaucoma is usually diagnosed by an Ophthalmologist or Optometrist

Optic nerve head pathology is reported to be over 90% sensitive and specific for glaucoma.[1] This generally involves an Ophthalmologist or Optometrist using a slitlamp and other specialised equipment to perform IOP measurements and automated field testing, as well as objective measurements of the volume of ganglion cell axons. Confrontational visual field testing in primary care is not sensitive or specific enough to be used for the diagnosis of glaucoma. New technologies are now available that allow IOP measurement using simple hand-held devices, some of which do not require topical anaesthesia, and these may become more prevalent in general practices over time.

Ophthalmoscopy has a limited role in diagnosing glaucoma as it only allows viewing of structures of the eye in two dimensions and is limited to single optic nerve assessment, one eye at a time. However, direct visualisation of the optic nerve head by ophthalmoscope can detect some features which should increase the suspicion of glaucoma:

- An increased cup-to-disk ratio (vertical ratio 0.6 or more)
- Thinning and/or notching of the neuroretinal rim
- Flame-shaped disk haemorrhage

An example of optic cupping viewed by ophthalmoscope, and the resulting increased cup-to-disk ratio, can be seen here (Figure 2 "Glaucomatous excavation of the optic nerve"): **www.ncbi.nlm.nih.gov/pmc/articles/PMC1479464/**

Ideally by age 45 years every person should have an eye examination, repeated five-yearly from age 45 years and then three-yearly from age 60 years.[8] First-degree relatives, e.g. siblings or children, of people with glaucoma are recommended to have their first eye examination five to ten years earlier than when their relative developed the condition.[6] For patients with multiple risk factors the monitoring frequency is increased. Early eye examinations can also help identify people who are susceptible to angle-closure glaucoma.

Referral of patients at risk of glaucoma

In most situations patients at risk, or suspected of having glaucoma, should be referred to an Optometrist. This is because it is difficult to gather sufficient clinical detail in primary care to allow triage into a public eye clinic. However, General Practitioners are able to refer patients to an Ophthalmologist for a publicly funded eye examination, e.g. if the patient has suspected cupping of the optic disc on ophthalmoscopy or visual field loss, if cost is a barrier.

Managing ocular hypertension and glaucoma

Reducing IOP is the focus of glaucoma treatment and prevention. IOP-lowering topical medicines are generally effective at slowing the progression of glaucoma and should be started before there are clear signs of the condition. However, there is a substantial variability in individual response.[6] In general, patients who are diagnosed with glaucoma late in its course are more likely to lose their vision, and a larger reduction in IOP will be required to reduce the likelihood of this occurring.[6] Treatment can still provide benefit to patients with advanced glaucoma.

IOP-lowering treatment is most often initiated by an Ophthalmologist, however, from July, 2014, it is expected that Optometrists will be able to prescribe topical medicines for glaucoma. Rarely, in a crisis situation, e.g. the patient has IOP > 30 mmHg, where there is an immediate risk of nerve damage and venous or arterial occlusion and access to an Ophthalmologist is problematic, then initiation of treatment in primary care may be appropriate.

Treatment targets

When glaucoma treatment is initiated, an Ophthalmologist will set an IOP target that is predicted to halt nerve damage and vision loss. This target will take into account the extent of damage to the optic nerve, baseline IOP, the speed of disease progression and other risk factors. An initial drop in IOP may occur within minutes to hours of medicine administration.[3] The patient's response is assessed by an Ophthalmologist after two to six weeks.[6]

Topical intraocular pressure-lowering medicines

Topical medicines for glaucoma are introduced in a step-wise method; a single medicine is given before another is added.[1] Patients who are on maximum treatment will therefore be using multiple medicines. Treatment of slowly-progressive glaucoma is sometimes trialled in one eye first to determine if the patient is responding, with the other eye acting as a control.[6] Alternative medicines will be introduced if there is not a clinically significant reduction in IOP or the patient is experiencing adverse effects.

There are five classes of medicines used to reduce IOP and their efficacy for achieving IOP targets may vary from up to 30% for prostaglandin analogues to 15% for carbonic anhydrase inhibitors.[3] Almost exclusively these are available as topical medicines which act by one or a combination of mechanisms, including decreasing production of aqueous humour in the ciliary body, increasing outflow through the trabecular meshwork, or increasing uveoscleral outflow:[1, 6]

- Prostaglandin analogues increase uveoscleral outflow
- Beta-blockers decrease production of aqueous humour
- Sympathomimetics (alpha2-adrenoceptor agonists) decrease aqueous humour production and increase uveoscleral outflow
- Carbonic anhydrase inhibitors decrease production of aqueous humour – an oral form of this medicine is available for the treatment of glaucoma in patients unable to tolerate topical IOP-lowering medicines
- Miotics (cholinergics) increase trabecular outflow through papillary constriction – this class of medicine is now restricted to the management of acute angle-closure crisis due to its significant adverse effects, e.g. headache and iris cysts, and the availability of more effective medicines

A topical prostaglandin analogue is usually the first choice for the treatment of glaucoma due to a higher treatment efficacy and the once daily dosing of this class of medicine.[3] Evening dosing is generally recommended for topical prostaglandins as the first studies conducted on latanoprost (Table 1) reportedly showed a beneficial effect when the medicine was administered in the evening compared with the morning.[17] This may be due to diurnal variations in IOP.[17]

Topical beta-blockers are recommended as an alternative treatment in the initial management of glaucoma, unless they are contraindicated.[3] When patients cannot tolerate topical prostaglandin analogues or beta-blockers, or they are ineffective at reaching the target IOP, other topical medicines will be considered before systemic administration is considered.[3]

Confirm that the patient's administration technique is optimal

The Double DOT (Digital Occlusion of Tear duct and Don't Open Technique) is the preferred method for eye drop administration because it maximises the efficacy of topical medicines and reportedly reduces systemic absorption by up to 70%.[6] The drop should be placed in the eye with the head horizontal. Immediately after it is placed the eye should be closed and forefinger placed in the corner of the eye, gently against the nose (punctual occlusion) for at least two minutes. Older patients should be advised to sit or lie in the supine position as this may make administration easier. If two or more drops are being administered to the same eye leave an interval of five minutes between applications.[6]

Soft contact lenses should be removed before administering topical treatments as they can absorb components of the solution resulting in prolonged ocular exposure. Contact lenses can be replaced 15 minutes after the eye drops have been administered. Gel-forming solutions and combination eye drop formulations reduce the need for patients to administer multiple medicines or multiple doses (Table 1).

The adverse effects and interactions of glaucoma medicines

Medicines that are administered topically to the eye move quickly through the nasolacrimal duct and into the nose. The nasal mucosa is highly vascular and rapid absorption into systemic circulation occurs without first-pass metabolism. Therefore medicines that are delivered via this route circulate directly to the heart and then to the lungs. IOP-lowering medicines may have clinically significant systemic effects for some patients. In particular, it is widely accepted that topical beta-blockers will produce some degree of systemic blockade and can also cause significant central nervous system adverse effects (Table 1).[3]

Table 1: Intraocular pressure-lowering medicines available in New Zealand for the treatment of intraocular hypertension and glaucoma[6, 18]

Medicine class	Indication	Dosage	Topical adverse effects	Systemic adverse effects
First-line treatments				
Prostaglandin analogues, i.e. bimatoprost (Lumigan 0.03%), latanoprost (Hysite 0.005%) and travoprost (Travatan 0.004%)	Ocular hypertension and open-angle glaucoma	One drop in the eye(s), daily, preferably in the evening	Blurred vision, stinging, conjunctival hyperaemia, foreign-body sensation, itching, reversible macular oedema, increased iris or skin pigmentation, longer, darker and thicker lashes, reactivation of herpetic infection, iritis/uveitis	Rare
Beta-blockers, i.e. betaxolol (Betoptic 0.25%, 0.5%), levobunolol (Betagan 0.25%, 0.5%) and timolol (Arrow-Timolol and Timoptol XE gel forming solution 0.25%, 0.5%)	Primary open-angle glaucoma	One drop in the eye(s), twice daily or once daily for gel-forming solution	Burning, stinging, photophobia, itching, tearing, decreased corneal sensitivity, hyperaemia, punctuate keratitis, diplopia	Bronchospasm, hypotension, bradycardia, heart block, can mask hypoglycaemia, adverse lipid effects, impotence, fatigue, depression, syncope, confusion and alopeica
Second-line treatments				
Sympathomimetic (alpha2-adrenoceptor agonists), i.e. brimonidine (Alphagan, Arrow-Brimonidine, Brimonidine 0.15%, 0.2%)	Ocular hypertension and open-angle glaucoma, or as an adjuvant treatment for inadequately controlled IOP	One drop in the eye(s), twice daily	Allergic reaction, burning, stinging, blurring, foreign-body sensation, itching, hyperaremia (increased blood flow), lid retraction, conjunctival blanching, photophobia, mydriasis (pupil dilation)	Central nervous system depression, oral dryness, headache, fatigue, drowsiness
Combination medicines, i.e. brimonidine+ timolol (Combigan 0.2% + 0.5%), dorzolamide + timolol (Cosopt or Dorzolatim 2% + 0.5%), timolol + travoprost (Duotrav 0.004% + 0.5% not subsidised)	Ocular hypertension and open-angle glaucoma not responding to monotherapy	Brimonidine+ timolol, Dorzolamide + timolol: one drop in the eye(s), twice daily. Timolol + travoprost, Latanoprost + timolol: one drop in the affected eye, once daily.	Similar to individual components	Similar to individual components
Topical carbonic anhydrase inhibitors, i.e. brinzolamide (Azopt 1%) and dorzolamide (Trusopt 2% – partly subsidised)	Brinzolamide and dorzolamide drops to reduce IOP, treat ocular hypertension and open-angle glaucoma. Dorzolamide can be used as adjunctive treatment with a ophthalmic beta-blocker.	Brinzolamide, one drop in the eye(s), twice daily. Dorzolamide, 1 drop in the eye(s), three times daily.	Drops may cause: burning, stinging, itching, keratopathy	Drops may cause: bitter taste, headache, nausea, fatigue

Third-line treatments				
Oral carbonic anhydrase inhibitor, i.e.acetazolamide (Diamox 250 mg tablet)	Oral acetazolame to reduce IOP in open-angle and secondary glaucoma, also peri-operatively following angle-closure glaucoma	Acetazolamide tablets for open-angle glaucoma, 250 mg – 1 g, daily, in divided doses	Acetazolamide tablets can cause transient myopia	Up to 50% of patients do not tolerate oral acetazolamide. Treatment may cause: fatigue, anorexia/weight loss, gastrointestinal symptoms, paraesthesia, depression, loss of libido.
Miotics (cholinergics), i.e. pilocarpine (Pilopt and Isopto Carbine 0.5%, 1%, 2%, 3%, 4%, 6%) and pilocarpine nitrate. N.B. 0.5% and 3% solutions are not subsidised. (Minims Pilocarpine Nitrate 2%, preservative free, subsidised under Special Authority)	Pilocarpine hydrochloride for open-angle glaucoma. Pilocarpine nitrate for emergency treatment of glaucoma.	One to two drops in the eye(s), up to four times, daily	Eye pain, decrease in night vision, blurred vision, miosis	Headache, salivation, urinary frequency, diarrhoea, abdominal cramps

Periocular allergic dermatitis can be caused by brimonidine drops or by preservatives in multi-use eye drop solutions. The erythema, oedema and excoriation will often form a distinctive pattern from the conjunctival sac to the lower nasal punctum and extend towards the cheek.[6] If allergic dermatitis is suspected then refer the patient to an Ophthalmologist for consideration of another medicine.[6]

The cardiovascular effects of IOP-lowering medicines

Topical beta-blockers can cause systemic effects and may exacerbate underlying cardiovascular conditions or combine with oral cardiovascular medicines causing an additive effect. Topical beta-blockers are contraindicated in patients with bradycardia, sick sinus syndrome, second or third degree atrioventricular block, severe hypotension or uncontrolled heart failure.[3] Topical beta-blockers should not be used with verapamil, diltiazem or digoxin unless under the supervision of a Cardiologist.[3] Topical beta-blockers and oral beta-blockers should not be prescribed concurrently.[3]

Topical beta-blockers can also interact with other medicines and result in an excessive drop in blood pressure.[3] This interaction can be significant for older patients who are at an increased risk of falls. If hypotension is not a concern topical beta-blockers can be safely used with dihydropyridine calcium channel blockers that have no effect on cardiac conduction, e.g. amlodipine.[3] Topical beta-blockers can impair peripheral circulation and worsen symptoms of peripheral vascular disease and Raynaud's syndrome.[3]

Sympathomimetics should be used with caution in patients with severe cardiovascular disease as these medicines can cause hypertension and may worsen the patient's symptoms.[3]

Other medicines used for the management of glaucoma can be taken safely by patients with cardiovascular disease.[3]

Topical beta-blockers can exacerbate asthma

Worsening of asthma following the use of beta-blockers is not uncommon.[3] Non-selective topical beta-blockers, e.g. timolol, are contraindicated in patients with asthma, although selective topical beta-blockers, e.g. betaxolol, may be used with caution.[3] Prostaglandin analogues and miotics rarely cause exacerbation of asthmatic conditions and are a safer treatment option for patients with asthma.[3]

Patients with COPD are less likely to experience adverse effects with the use of topical beta-blockers compared with patients with asthma.[3] However, there is a possibility that COPD may be exacerbated.[3]

Prescribe topical beta-blockers with caution to patients with diabetes

Topical beta-blockers can be safely prescribed to patients with diabetes, however, this should be done cautiously.[3] Patients with diabetes who are at risk of hypoglycaemia should be aware that topical beta-blockers may mask their symptoms of hypoglycaemia, e.g. increased heart rate and tremor.[3]

Topical beta-blockers may mask signs of hyperthyroidism
When considering prescribing topical beta-blockers for patients with a history of hyperthyroidism be aware that this treatment can mask the clinical signs of the condition, e.g. tachycardia.[3]

Medicines for depression and glaucoma may interact
Depression is a possible adverse effect of topical beta-blockers and sympathomimetics.[3] Tricyclic antidepressants (TCAs) and selective serotonin re-uptake inhibitors can cause acute angle-closure crisis in susceptible patients due to their anticholinergic effect which can cause pupil dilation.[3]

Carbonic anhydrase inhibitors and hepatic and renal impairment
Acetazolamide is contraindicated in patients with severe hepatic impairment due to an increased risk of hepatic encephalopathy.[3] The safety of topical carbonic anhydrase inhibitors, i.e. dorzolamide and brinzolamide, in patients with hepatic impairment is unknown.[3]

Acetazolamide given orally or intravenously is contraindicated in patients with severe renal impairment due to the risk of severe acidosis.[3] In patients with creatinine clearance 10 – 30 mL/min, the dose of acetazolamide should be reduced.[3] Acetazolamide also increases the risk of urolithiasis. There is a lack of information about the use of topical carbonic anhydrase inhibitors in patients with reduced renal function, therefore it is recommended that the same caution be applied as for oral acetazolamide.[3]

Monitoring long-term treatment

After glaucoma treatment has started patients are generally reassessed by an Ophthalmologist at three to 12 month intervals depending on the patient's risk profile, degree of glaucoma progression and ability to self-manage their treatment regimen.[3] Patients who are not achieving their IOP target will be seen more frequently.[3] Regular glaucoma medicine reviews in primary care are likely to assist with treatment adherence and emphasise the need for regular eye examination of other family members.

The glaucoma medicine review check-list:

1. Ensure the patient is persisting with treatment, has sufficient medicine until their next prescription renewal or repeat and that they understand the potential consequences if treatment is stopped
2. Confirm the patient is using the Double DOT method of medicine administration
3. Review any new diagnoses or treatments that may interact with glaucoma treatment
4. Confirm the patient is attending follow-up consultations with an Ophthalmologist
5. Ensure the patient has discussed the diagnosis of glaucoma with their family and that first-degree relatives understand the need to have their eyes examined at least five years earlier than the age when the patient developed the condition

Many patients do not persist with treatment

Because glaucoma is asymptomatic in its early stages some patients may not appreciate the importance of treatment. It has been estimated that after one year following treatment initiation only 10% of patients will be taking their medicines as prescribed and less than 50% of patients can be expected to be persisting with treatment at all.[7, 19] Patients who understand that glaucoma is progressive and if untreated will eventually lead to blindness are more likely to see the value of treatment.

Assessing treatment adherence in primary care
If a patient is not responding to IOP-lowering treatment it is important to confirm they are using the Double DOT technique for medicine administration. For patients who sometimes forget to administer eye drops, linking administration to daily routines, e.g. brushing of teeth, may improve adherence. A small study has suggested that patients may prefer morning administration of once daily eye drops.[17] This may be appropriate for patients taking travoprost as there is no strong evidence that evening dosing for this medicine is more effective compared to morning dosing.[17] Other prostaglandins analogues are recommended to be dosed in the evening, but if adherence issues mean that the medicine is not being taken at all, the possibility of morning dosing can be discussed with an Ophthalmologist.

Co-morbidities, e.g. arthritis, may be a barrier to self-administration of eye drops. Suggest to patients that administration may be easier while they are lying down in bed before sleeping, and/or before getting up.

Changes to the patient's management plan

If the visual field or optic nerve continues to deteriorate then an Ophthalmologist will recommend a change in the patient's medicine regimen. An eye examination will then be conducted two to eight weeks after making this change to assess the patient's response as well as to monitor for adverse

effects during the washout period of up to six weeks when the previous medicine will still have pharmacological effects.[3] Occasionally the patient's visual field loss or optic nerve deterioration will proceed atypically, raising the suspicion of other causes of nerve damage including: brain (especially pituitary) tumours, stroke and inflammation. Appropriate neuro-imaging is arranged for patients with atypical or suspicious features.

Additional treatment options

Laser techniques, incision or implant surgery are the only other routine treatment options currently available to reduce the risk of vision loss in patients with glaucoma who are unresponsive to topical medicines or unable to tolerate them. Topical medicine may still be required after surgery, but for patients prescribed multiple treatments the number of medicines may be able to be reduced.

Laser iridotomy involves creating a hole in the iris to disrupt the pupillary block which usually halts the progression of synechial closure and "opens up" the angle of the anterior chamber.[3] Prophylactic iridotomy of the unaffected eye is generally recommended.[3]

Laser trabeculoplasty is often used to treat open-angle glaucoma that cannot be controlled by medicines and tends to be more successful in patients with PFX syndrome.[3] This technique increases aqueous outflow through the trabecular meshwork and is reported to successfully control glaucoma in 80% of patients.[3]

Surgical techniques which lower IOP include trabeculectomy and glaucoma drainage device implantation, e.g. Molento Implant. These operations create a new pathway for aqueous drainage from the eye with reduced resistance to outflow. It is reported that there are no detectable differences between the change in visual field defects between patients with glaucoma who are treated by topical medicines or surgery.[7] However, surgery is associated with increased eye discomfort, increased cataract risk and a slight reduction in distance vision at five years.[7]

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