Impact of Glaucoma Medications on Co-morbidities

In 2008 over 31,000 veterans were dispensed medicines for glaucoma. The systemic absorption of glaucoma eye drops can lead to adverse drug events and also impact on co-morbidities.

In particular topical beta blockers have well documented systemic effects due to the presence of beta adrenoreceptors in vascular smooth muscle, the heart and bronchial tree. DVA prescribing data indicates that the use of timolol eye drops is associated with an increase in bronchoconstriction as evidenced by increased use of beta agonists and inhaled steroids, and increased hospitalisation for respiratory conditions.

This therapeutic brief aims to: outline the different drugs used in the management of primary open angle glaucoma, highlight how drug selection may impact on coexisting cardiovascular and respiratory disease and suggest how to minimise systemic absorption by optimising eye drop instillation.

A key principle in glaucoma management is optimal communication between the ophthalmologist, who typically initiates and monitors the glaucoma treatment, and the GP to whom the patient may be more likely to present with systemic side effects.

Key points

- Eye drops have systemic effects which can impact on co-morbidities.
- Concurrent use of verapamil and topical beta blockers is contraindicated.
- Avoid topical beta blockers in veterans with bradycardia, decompensated heart failure and heart block.
- Topical beta blockers and pilocarpine can cause bronchoconstriction; enquire about respiratory symptoms and inhaler use.
- Ensure good communication between ophthalmologist, GP and patient.
Management of primary open angle glaucoma

The aim of glaucoma therapy is to reduce the IOP. This has been shown to reduce the risk of long term visual field loss in those with glaucoma and ocular hypertension. There is no threshold for the initiation of treatment and no standard guidelines for the optimal target IOP. Treatment is adjusted based on close follow up of visual fields and optic disc damage. Target pressures are lowered if there is disease progression despite treatment.

Intraocular pressure can be lowered by topical and systemic medical therapy (see table 1), laser therapy and surgery. Glaucoma medications lower IOP by reducing the production of aqueous humour or increasing its outflow.

Table 1: Classes of drugs currently used

<table>
<thead>
<tr>
<th>Class</th>
<th>Generic names</th>
<th>Brand names</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostaglandin analogues</td>
<td>Latanoprost</td>
<td>Xalatan 0.005%</td>
</tr>
<tr>
<td></td>
<td>Travoprost</td>
<td>Travatan 0.004%</td>
</tr>
<tr>
<td></td>
<td>Bimatoprost</td>
<td>Lumigan 0.03%</td>
</tr>
<tr>
<td>Beta blockers</td>
<td>Timolol (beta, and beta, receptor blocker)</td>
<td>Tenopt, Timoptol, Timoptol-XE 0.25% and 0.5% and Nyogel 0.1%</td>
</tr>
<tr>
<td></td>
<td>Betaxolol (beta, receptor blocker)</td>
<td>Betoptic S 0.25% and Betoptic 0.5%, BetoQuin 0.5%</td>
</tr>
<tr>
<td>Alpha, agonists</td>
<td>Apraclonidine</td>
<td>Iopidine 0.5%</td>
</tr>
<tr>
<td></td>
<td>Brimonidine</td>
<td>Alphagan and Enidin 0.2%</td>
</tr>
<tr>
<td>Carbonic anhydrase inhibitors</td>
<td>Brinzolamide</td>
<td>Azopt and BrinzQuin 1%</td>
</tr>
<tr>
<td></td>
<td>Dorzolamide</td>
<td>Trusopt 2%</td>
</tr>
<tr>
<td></td>
<td>Acetazolamide (oral)</td>
<td>Diamox 250mg</td>
</tr>
<tr>
<td>Cholinergics</td>
<td>Pilocarpine</td>
<td>Pilopect, PV Carpine, Isopto Carpine 1%/2%/4%; Pilopect, PV Carpine 6%</td>
</tr>
<tr>
<td>Combination Products</td>
<td>Timolol 0.5%/Brimonidine 0.2%</td>
<td>Combigan</td>
</tr>
<tr>
<td></td>
<td>Timolol 0.5%/Dorzolamide 2%</td>
<td>Cosopt</td>
</tr>
<tr>
<td></td>
<td>Timolol 0.5%/Latanoprost 0.005%</td>
<td>Xalacom</td>
</tr>
<tr>
<td></td>
<td>Timolol 0.5%/Travoprost 0.004%</td>
<td>Duotrat</td>
</tr>
<tr>
<td></td>
<td>Timolol 0.5%/Bimatoprost 0.03%</td>
<td>Ganfort</td>
</tr>
</tbody>
</table>

Glaucoma treatment and co-morbidities

Eye drops used in the treatment of glaucoma have significant systemic absorption. After instillation 80% drains through the nasolacrimal duct and enters the systemic circulation through the nasal mucosa avoiding first pass metabolism in the liver. Glaucoma medications may then impact on co-morbidities, particularly cardiovascular and respiratory disease. The incidence of adverse effects in clinical practice depends on the risk profile of the population being treated.

The systemic side effects of topical beta blockers – bradycardia, bronchospasm, hypotension, syncope – are especially relevant to the elderly veteran population (average age 80 yrs with 7 co-morbidities).

Local and systemic adverse effects of glaucoma medications can limit their use (see table 2). However, systemic adverse effects can be reduced by correct installation of eye drops (see page 3).
Cardiovascular disease and glaucoma

Topical beta blockers should be avoided in those with bradycardia, decompensated heart failure and heart block. The co-prescribing of a topical beta blocker and verapamil should be avoided because of the risk of profound bradycardia. Analysis of the DVA prescribing data for 2008 showed 830 veterans were dispensed verapamil and were also receiving treatment for glaucoma. Of these, 38% had been prescribed topical timolol to treat their glaucoma. Topical and systemic beta blockers are co-prescribed in about 20% of patients with glaucoma. It is important that ophthalmologists are made aware that a patient is taking systemic beta blockers as the IOP lowering efficacy of the topical beta blocker will be reduced and the risk of systemic side effects increased. This is particularly relevant in veterans with chronic heart failure where systemic beta blockers are frequently used. In 2008, 46% of veterans with chronic heart failure and glaucoma were treated with topical beta blockers.

Apraclonidine should be used with caution in those with cardiovascular disease, coronary insufficiency and recent MI as it can rarely cause hypotension and chest pain. Brimonidine can also cause hypotension and should similarly be used with caution in those with severe cardiovascular disease and postural hypotension. For both drugs there is a potential additive effect with antihypertensives.

Prostaglandin analogues do not appear to have significant cardiovascular adverse effects and are suitable for use in veterans with stable co-morbid cardiovascular disease.

Respiratory disease and glaucoma

Studies indicate that topical beta blockers used in the treatment of glaucoma and ocular hypertension can cause bronchospasm in those predisposed (including those with no previous diagnosis of asthma). They should be used with caution in veterans with asthma or COPD. Analyses performed on the DVA prescribing data indicate use of timolol is associated with increased bronchoconstriction as evidenced by increased use of beta agonists and inhaled corticosteroids and hospitalisation for respiratory conditions. Beta, selective beta blockers (such as betaxolol) have a higher affinity for beta, receptors in the heart with less effect on beta, receptors in bronchi and peripheral vasculature, however this effect is dose-dependent and diminishes at higher doses.

Pilocarpine can cause bronchoconstriction due to its cholinergic effects and should also be used with caution in veterans with asthma or COPD. Large doses of prostaglandins can cause bronchoconstriction and cases of asthma and dyspnoea have uncommonly been reported with prostaglandin analogue eye drops. Analysis of the DVA prescribing data indicates latanoprost was associated with increased use of inhaled beta agonists. In view of this, exercise caution when prescribing prostaglandin analogues for veteran patients with reactive airways disease and, at follow up appointments, enquire specifically about shortness of breath or increased use of inhaled beta agonists.

Corticosteroids and glaucoma

Corticosteroids may raise intraocular pressure when administered in any form, including inhaled steroids used in the management of asthma and COPD, and nasal sprays. However topical corticosteroid eye drops are the most potent cause of raised intraocular pressure. All corticosteroids should be used with caution in those with POAG.

The amount of systemic absorption can be reduced by up to two thirds by correct instillation of eye drops. The ‘double DOT’ technique – Don’t Open eyes Technique and Digital Occlusion of the Tear duct Administer the eye drop then close the eye and apply digital pressure over the lacrimal sac for 2 to 3 minutes If 2 or more drops are being administered wait at least 5 minutes between drops
Optimising glaucoma management

Optimal treatment of glaucoma requires a high level of adherence to therapy; for a condition which is frequently asymptomatic this can be difficult to achieve. Non adherence rates in glaucoma have been reported to vary from 24 to 59%. Patient adherence can be improved by:

- Educating the patient about glaucoma and the importance of ongoing effective treatment.
- Simplifying the treatment regimen as much as possible.
- Observing the patient or carer instilling eye drops.
- Providing written instructions to the patient or carer including technique for correct instillation of eye drops.
- Enquiring about changes to health, new medications and possible side effects.

Consider a medicines review by an accredited pharmacist which may reveal potential drug interactions, systemic side effects or difficulties with administration of eye drops.

References

1. Veteran’s Datamart, University of South Australia, QUMPRC. Accessed November 2009
2. Frishman WH et al. Cardiovascular considerations in using topical, oral and intravenous drugs for the treatment of glaucoma and ocular hypertension; focus on β-adrenergic blockade. Heart Disease 2001; 3: 386-397

Further reading

Australian Medicines Handbook 201012


We acknowledge the contribution of the Fellows of The Royal Australian and New Zealand College of Ophthalmologists (RANZCO) in developing this material.

It is essential to optimise communication between all healthcare providers:

1. In particular that the ophthalmologist is made aware of the patient’s current medication regime and co-morbidities and the GP is aware of all treatments prescribed by the ophthalmologist.

This is especially relevant when the initial referral was made by an optometrist not the GP.

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