Topical Medical Therapy's Impact on Visual Quality

In addition to lowering IOP, physicians have a responsibility to maximize their glaucoma patients' visual quality of life.

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Medical therapy continues to be the mainstay of the treatment of glaucoma in the United States. Most patients with glaucoma use topical therapy to reduce their IOP over an extended period of time—sometimes for decades. Although topical therapy can slow or minimize the progression of the disease, all of the currently available therapies have side effects that may affect a given patient's visual quality of life.

Because glaucoma is a chronic disease and individuals need medication to control their IOP long term, choosing the best therapy for a given patient must be an educated decision. All eye care providers are aware that medications differ in terms of efficacy and duration of action as well as their effects on the ocular surface and the internal structures of the eye.

EFFICACY

The most important issue in preventing irreversible vision loss in the glaucoma patient is the reduction of IOP. In accordance with the Ocular Hypertension Treatment Study (OHTS), IOP needs to be reduced by at least 20% in patients with ocular hypertension or mild glaucoma.[1] The prostaglandin analogues (PGAs) have become the gold standard in terms of IOP reduction and systemic safety. These drugs tend to have a long half-life and seem to be effective at reducing IOP at night, when some other classes of medication appear to have little-to-no effect on IOP.[2,3] PGAs are dosed once a day, which, in terms of adherence to medical regimens, probably provides the patient with the best chance of success with therapy. The branded agents available in the United States are Xalatan (latanoprost ophthalmic solution; Pfizer, Inc.), Travatan (travoprost ophthalmic solution; Alcon Laboratories, Inc.), and Lumigan (bimatoprost ophthalmic solution; Allergan, Inc.). Despite significant long-term experience with these PGAs, there is limited information on the IOP-lowering ability of a generic formulation recently introduced on the market. One study from India suggested that a generic preparation of latanoprost did not lower IOP as well as Xalatan.[4]

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Other classes of medication reduce IOP as well as but probably for shorter durations than the PGAs. ß-blockers lower IOP well during the day but have little effect on IOP at night.[3] Dosing is once or twice daily, and the data suggest that up to half of patients on ß-blockers frequently need additional therapy after starting ß-blocker monotherapy.[5] $\alpha 2$ agonists and carbonic anhydrase inhibitors (CAIs) typically need to be dosed two or three times a day in order to maintain relatively flat diurnal IOP curves and reduce IOP significantly. Miotic agents such as pilocarpine need to be dosed three to four times a day to reduce the IOP to ranges that would prevent glaucomatous progression in most patients.

SIDE EFFECTS

Just as efficacy varies among the available medications, so do ocular side effects and tolerability. Pilocarpine

probably has the most profound effect on visual acuity and the ocular surface. Miotic agents constrict the pupil and alter accommodation, which can cause a fluctuation in refractive error and a darkening of vision that vary with the time of dosing. In addition, miotic agents tend to inflame the conjunctival surface, and frequent administration exposes the eye to relatively high loads of benzalkonium chloride (BAK) over the long term. As a result, physicians tend to prescribe miotic agents only for select patients, usually after other therapies have failed.

The most common ocular side effect of $\alpha 2$ agonists is ocular allergy. If patients experience this side effect, their tear film dynamics can become disrupted. They may develop blurred vision and ocular discomfort, including itching, swelling, and other symptoms associated with allergy. The allergy with this class of medication appears to relate to the oxidation of the active ingredient. The more active ingredient is present, therefore, the more likely allergy is to occur. Currently, three concentrations of brimonidine tartrate ophthalmic solution are available from Allergan, Inc.: 0.1% and 0.15% (Alphagan P) and 0.2% (Alphagan). Although allergy is fairly uncommon with the 0.1% formulation, the allergy rate with the 0.2% formulation has been reported to be higher than 25% over time in some populations.[6] The other factor with brimonidine is that the preservative differs for each of the commercially available products. The 0.1% formulation uses a fairly benign oxidizing agent, Purite (Allergan, Inc.); the 0.15% formulation uses polyquad; and the 0.2% formulation uses BAK. This difference in preservative may have different effects on the ocular surface in certain patients, with BAK's being the most toxic of the commonly used ophthalmic preservatives.[7]

The commercially available topical CAIs differ in their formulation as well. The pK_a of this class of drugs tends to be relatively acidic. For them to stay in solution, the formulation must have an acidic pH. Dorzolamide is formulated in an acidic, buffered solution, and brinzolamide is delivered as a suspension at a higher pH. The clinical implications are twofold. The more acidic solutions may cause greater discomfort and have a directly toxic effect on the corneal epithelium. The suspension tends to be more comfortable, but it could blur vision or accumulate on the surface if dosed excessively. The other issue with topical CAIs is the drug itself. A portion of the endothelial pump mechanism is CAI dependent, so in a cornea with deficient or compromised endothelial cells, corneal edema or thickening can occur after dosing, which may in turn decrease visual acuity.[8]

ß-blockers such as timolol can decrease tear production and destabilize the tear film. The first effect appears to be due to the active drug, whereas the second effect probably has more to do with the BAK and the formulation of the eye drop. These side effects can exacerbate the signs and symptoms of dry eye disease, especially in patients at risk.

Although dosed once daily, the PGAs appear to cause changes in the ocular surface with long-term use. The preservative concentration of some of the PGAs is higher than in most eye drop preparations, and susceptible patients can experience a decrease in tear breakup time, which can cause more ocular surface symptoms.[9] Travatan Z (Alcon Laboratories, Inc.) does not contain BAK. PGAs have also been shown to increase vascular leakage after cataract surgery, and they may place a patient at higher risk of cystoid macular edema or prolonged inflammation postoperatively. The aforementioned availability of generic latanoprost has introduced another variable into the clinical setting. Although this medication's active ingredients are the same as those of its branded counterpart, it is unclear whether the former will differ in terms of tolerability.

CONCLUSION

The primary goal in treating glaucoma is to lower the IOP to a level that stabilizes the disease. Because all of the available drugs can affect vision in some way, clinicians should consider these effects when choosing the optimal topical therapy for a patient with glaucoma. ❑

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