Fixed-Combination Medical Therapy for Glaucoma

Three surgeons discuss the clinical scenarios in which they prescribe these drugs.

BY L. JAY KATZ, MD; ROBERT J. NOECKER, MD, MBA; AND JAMES C. TSAI, MD, MBA

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Fixed-combination drug therapy offers ophthalmologists an attractive option for certain glaucoma patients. More than 50% of patients who fill prescriptions for glaucoma medications take more than one drug,1,2 and there is a direct correlation between the number of glaucoma bottles and decreased adherence.3 For a disease such as glaucoma—a chronic condition with few or no symptoms until it progresses to an advanced stage—patients’ compliance with a daily medical drug regimen is frequently compromised. Furthermore, because there is no immediate negative consequence of nonadherence, patients are less motivated to be overly concerned with compliance. The hope is that, by simplifying patients’ drug schedules and limiting the number of glaucoma drug bottles, their adherence will improve, and their glaucoma will be adequately treated and stabilized.

Fixed combinations of glaucoma drugs approved for use in the United States include timolol-dorzolamide (Cosopt; Merck & Co., Inc.), timolol-brimonidine (Combigan; Allergan, Inc.), and the most recent addition, brinzolamide-brimonidine (Simbrinza; Alcon Laboratories, Inc.). Frequently, ophthalmologists prescribe a fixed-combination drug in addition to a prostaglandin analogue, which may signal maximal medical therapy for most patients prior to laser or surgical options. Adding further complexity to prescribing fixed-combination therapy is the favored status of generic versions of glaucoma drugs. Formulary plans may require the initial use of generics, even though multiple bottles are required, rather than cover a brand-name fixed-combination product.

Patients are instructed to wait 5 minutes between multiple applications of glaucoma drugs. If the intervals are shorter due to impatience, the concern is that the newly instilled drug will wash out the previously administered agent. Additionally, there is growing evidence of preservative toxicity associated with benzalkonium chloride that is correlated with duration of use and multiple doses.4,5 The commercial release of fixed-combination glaucoma drug therapy has been a welcome development and has helped to control glaucoma in many of my patients.

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I prescribe fixed-combination glaucoma medications in multiple clinical scenarios. When a patient is already taking two drugs from two different bottles, a combination of eye drops in one bottle makes sense. Compared with using multiple individual components, combination eye drops can help to minimize the chance of tolerability issues, washout effects, costs in terms of associated copayments, and improper dosing.

In many cases, a single agent such as a prostaglandin analogue will lower IOP effectively and safely in patients with glaucoma or ocular hypertension. There may be cases, however, in which patients are intolerant of a prostaglandin analogue or its use is contraindicated. If I do not think that monotherapy will adequately lower IOP, I will prescribe a combination eye drop to improve the patient’s chance of lowering IOP to the desired level.

As a general rule, the more severe an individual
patient’s glaucoma is, the more likely I am to use a fixed-combination formulation rather than a single-agent preparation. As a tool to further lower IOP in patients who already take a prostaglandin analogue, the addition of a fixed-combination therapy is attractive, because the best single-agent therapy for glaucoma has failed. For patients in whom a more a modest reduction in IOP is required, I may first add a single eye drop before switching to a combination product. When advancing therapy after a first agent is partially effective, I prefer to switch to a fixed-combination therapy versus multiple agents in individual bottles.

With experience, I have come to realize that the real world can interfere with successful glaucoma therapy, and I am always motivated to minimize the number of eye drops that a patient must use on a daily basis. Combination eye drops help to simplify glaucoma therapy, which is always a good thing.

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Many patients require more than one class of medication to reach their targeted IOP level (based on data from multiple studies, including the Ocular Hypertension Treatment Study [OHTS] and Collaborative Initial Glaucoma Treatment Study [CIGTS]). Although multiple topical drug regimens are commonly used, the inherent complexity of their use (ie, multiple bottles) makes it difficult for patients to adhere to prescribed therapy. Fixed-combination drugs, defined as two or more drugs combined into a single formulation, are available and may offer distinct advantages when compared with concomitant drug therapy. Given the simplicity of monotherapy, fixed-combination drugs theoretically improve patients’ adherence and eliminate the washout effect observed when the time between the application of drops is inadequate. Fixed-combination therapy, however, has the disadvantages of limiting the clinician’s flexibility in individualizing and customizing therapeutic dosing regimens and of potentially delivering more medication than is needed to lower IOP.

In patients with significant risk factors for glaucomaous progression, I often prescribe fixed-combination therapy in concert with evening dosing of a prostaglandin analogue (because no fixed-combination drugs currently approved in the United States contain a prostaglandin analogue and all reduce aqueous production). I strongly believe that IOP control can best be achieved via the additive effects of enhanced aqueous outflow and reduced inflow. Fixed-combination agents allow me to achieve this synergistic effect by adding only one bottle to a prostaglandin analogue. If the adjunctive fixed-combination drug contains timolol in its formulation (with the potential 24-hour action of a β-blocker), I will often consider prescribing the medication for morning dosing only (in combination with the evening dosing of a prostaglandin analogue).

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