What Is Maximal Medical Therapy in 2012?

The answer is highly variable and influenced by commercial considerations, the patient, and the physician.

BY NICHOLAS P. BELL, MD

The definition of *maximal medical therapy* for the treatment of glaucoma may seem to evolve with time but, in the strictest interpretation, does not change at all. What constitutes maximal medical therapy, however, is highly variable and affected by commercial considerations as well as by the patient and the physician.

COMMERCIAL CONSIDERATIONS

A limited number of practitioners can recall medically treating glaucoma when the only available options were pilocarpine, epinephrine, and oral acetazolamide. In the late 1970s, timolol maleate was added to the topical armamentarium. Epinephrine was improved upon by its prodrug, dipivefrin, and later replaced by more specific α-2 agonists. Topical carbonic anhydrase inhibitors (CAIs) became available in the 1990s; although the oral CAIs are more effective at lowering IOP, a desire to avoid their systemic side effects drove the market toward topical use. In 1996, the first prostaglandin F2α-receptor agonist became available commercially. Within the past 10 years, the prostaglandin analogues (PGAs) received approval for first-line use in the treatment of glaucoma.

Truly maximal medical therapy uses one choice from each available class of antiglaucoma medication. Many clinicians who treat glaucoma consider current maximal medical therapy to be the use of four classes of medication, including a PGA, β-blocker, CAI, and α-2 agonist. Various fixed combinations of topical glaucoma medications have provided more aggressive treatment without increasing the number of bottles with which the patient must contend. Because timolol maleate 0.5% is available in the United States in a fixed combination with dorzolamide HCl 2% (Cosopt; Merck & Co., Inc.) and also with brimonidine tartrate 0.2% (Combigan; Allergan, Inc.), three medications can be administered using two bottles. Although fixed-combination agents simplify the dosing schedule, the component drugs' potential side effects still exist, and the cost to patients may not improve much, depending on their insurance coverage.

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Geography also plays an important role in what represents maximal medical therapy. Outside the United States, numerous other fixed combinations are com-

mercially available, including PGAs mixed with timolol. A triple combination of dorzolamide HCl 2%-timolol maleate 0.5%-brimonidine tartrate 0.2% (Krytantek Ofteno; Laboratorios Sophia) is marketed in Latin America.

THE PATIENT

Patient-related factors can affect practitioners' choices regarding the treatment of elevated IOP. With additional medications comes a higher risk of local or systemic side effects, allergic reactions, or toxicity from the active or inactive ingredients. Preservatives such as benzalkonium chloride may be administered to each of a patient's eyes in five to 10 doses per day, depending on his or her medication schedule. The cumulative toxicity can cause discomfort and render the patient unwilling to comply with the prescribed regimen. The selection of preservative-free or alternatively preserved eye drops can be helpful.

Another patient-related consideration that affects treatment options is price. The cost of adding a medication may be prohibitive, especially for patients on fixed incomes. The one-time cost of a successful surgery can be significantly less expensive over time than years of purchasing eye drops every month.

Furthermore, the number of doses per day of prescribed medication is inversely related to patients' adherence to the regimen.[1] If the treatment plan becomes too complicated, he or she may feel overwhelmed. Fixed combinations can help improve compliance.

THE PHYSICIAN

Just because an additional medication is available does not mean it is necessary to add it when escalating therapy. The concept of optimal medical therapy has evolved to replace maximal medical therapy.[2] Prescribing fewer medications to lower IOP limits the potential side effects, contains costs, and makes patients' dosing schedules less complex. The "return on investment" for additional medications begins to decline after the second-line therapy.[2] The value of an additional 1 to 2 mm Hg of IOP lowering may not justify the use of a fourth-line medication, especially as safer surgical alternatives to traditional filtering surgery mature.

Within the past decade, glaucoma surgeons have increasingly begun to use options other than medication at earlier stages of disease. Although the treatment effect does not last forever, laser trabeculoplasty can assist in maintaining IOP control prior to the initiation of any medications or serve as a second- or third-line intervention. The goal of various ab interno and ab externo procedures is to lower IOP with less risk of intraoperative and postoperative complications than traditional filtering surgery.

> "As surgical options pose less risk ..., the risk-benefit ratio moves away from employing four (or five) classes of medication prior to considering incisional surgery."

As surgical options pose less risk of catastrophic complications, the risk-benefit ratio moves away from employing four (or five) classes of medication prior to considering incisional surgery. Although it is difficult to reliably achieve an IOP in the low teens without filtering surgery or an aqueous shunt, laser trabeculoplasty and microinvasive glaucoma surgery may serve as first-line surgical therapy in conjunction with one or two medications. Moreover, the role of lens extraction (with or without other surgical procedures) cannot be ignored for the management of IOP.

CONCLUSION

Maximal medical therapy today is not as easy to define as it was 10 years ago. With many new and exciting procedures, physicians are not limited to exhausting all classes of medication before considering surgical intervention. Glaucoma treatment must be individualized to optimally manage each patient. ■

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