HOW EASY IT WOULD BE IF EVERY PATIENT’S IOP COULD BE LOWERED TO ITS TARGET LEVEL WITH A SINGLE AGENT! The results of major clinical trials such as the Ocular Hypertension Treatment Study (OHTS)—as well as physicians’ collective experience in the clinic—demonstrate that many patients need more than one medication. In the OHTS, 40% of patients required two or more medications to achieve the modest decrease in IOP required of at least 20%. Using more than one IOP-lowering agent is therefore a fact of life for many patients.

HOW WELL DOES ADJUVANT THERAPY WORK?
Due to spatial constraints, I am limiting my discussion to topical IOP-lowering agents that have been approved by the FDA. For this article, I am defining adjuvant as something added to something else. I have taken the liberty of including fixed-combination therapy (one bottle, two drugs) under the umbrella of adjuvant therapy as well as concomitant therapy (more than one bottle, one drug per bottle).

The law of diminishing marginal utility is at work in topical glaucoma therapy just as it is in other areas of people’s lives. In other words, the IOP-lowering effect of introducing a second agent will rarely be as great as was that of the first agent. For instance, in a meta-analysis of studies in which α-2 adrenergic agonists, β-adrenergic antagonists, or topical carbonic anhydrase inhibitors were added to a prostaglandin analogue, Tanna et al found that the mean additional decrease in IOP was between 2 and 3 mm Hg, with a maximum of 3.2 mm Hg for the α-2 agonist at its peak. This finding can be compared to the mean IOP lowering of 7 to 8 mm Hg that is typical for monotherapy with a prostaglandin. Data on the additional effect of third and fourth agents are sparse, but one can assume that it is miniscule.

PREREQUISITES FOR CONSIDERING ADJUVANT THERAPY
One prerequisite for the use of adjuvant therapy, either concomitant or in a fixed combination, is evidence of the first agent’s efficacy. For example, if the difference between the untreated IOP and the desired (target) IOP is 8 mm Hg, and the first agent has convincingly lowered the IOP by 5 mm Hg, then the addition of a second agent is reasonable (although cessation of the first agent and its replacement with a second agent is also reasonable). If the effect of the first agent is marginal or nonexistent (1-2 mm Hg), however, then cessation and replacement, rather than addition, are the proper course of action. I suspect that, too often (even in my practice), one ineffective agent is added to another ineffective agent, with no consequence other than decreased adherence or a red, irritated eye.

FIXED-COMBINATION VERSUS CONCOMITANT ADJUVANT THERAPY
Providing two IOP-lowering agents in the same bottle has distinct advantages over administering the same agents from separate bottles. It is logical to assume that the convenience of one bottle over two will lead to better adherence. One study by Robin et al that supports this supposition demonstrated that the addition of a second agent in a second bottle decreased the refill rate for the first agent. In addition, the patient’s total exposure to preservatives will be less with the fixed combination than with drugs from two separate bottles.

On the other hand, compromises are made with fixed combinations such as frequency of administration and timing of doses. For instance, when considering a fixed combination of a prostaglandin and a β-adrenergic blocker (not available in the United States), the clin...
cian must make a compromise regarding the timing of administration, because morning is generally preferred for a β-adrenergic blocker and evening for a prostaglandin. On balance, however, once I have convinced myself that a single agent is effective but insufficiently so alone, I will generally switch to a fixed combination containing the single agent rather than add another bottle. I believe that the switch from one bottle to another is psychologically easier on the patient than the obvious escalation of therapy suggested by the addition of a second bottle.

WHY NOT SKIP ADJUVANT THERAPY ALTOGETHER?

The Preferred Practice Pattern Guidelines: Primary Open-Angle Glaucoma state that laser trabeculoplasty (LTP) is a reasonable first-line treatment to lower IOP in glaucoma patients, so clearly, the procedure is a reasonable option after an initial eye drop’s performance is inadequate. LTP, however, does not work in all patients, does not last forever, and occasionally has side effects. Adjuvant therapy, therefore, has an important role. I always offer patients the option of LTP when initiating therapy and push for it a little harder after a single topical agent has failed. If LTP proves ineffective, I can always prescribe adjuvant therapy at that time.

KEY POINTS

First, physicians must try to verify that the agent to which they are adding a second drug is actually having an effect. Second, I recommend using fixed-combination therapy as opposed to concomitant therapy when possible. Finally, practitioners should not hesitate to offer LTP, while reassuring the patient that laser treatment does not preclude the later use of additional eye drops.

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