Benzalkonium Chloride and Glaucoma Management Today

Many patients' tolerability to medications can improve with aggressive treatment of ocular surface disease.

BY STEVEN T. SIMMONS, MD

Benzalkonium chloride (BAK) is the most common preservative used in commercially available topical glaucoma therapy. BAK is a quaternary ammonium compound with cationic surfactant properties that act on microorganisms by altering the permeability of cell membranes.[1] As a preservative, BAK prevents bacterial, fungal, and amoebic growth, and inhibits bottle contamination and colonization with active pathogens associated with ocular infection.

BAK has become a source of controversy in the treatment of glaucoma, because BAK has been reported to accumulate in ocular tissues, causing different types of cell injury with frequent dosing.[2] The agent is a recognized cause of corneal and conjunctival toxicity. This toxicity has been implicated to cause changes to the corneal and conjunctival surfaces, ocular discomfort, tear film instability, conjunctival inflammation, subconjunctival fibrosis, and epithelial apoptosis.[3] It has been inferred that BAK damages the trabecular meshwork as well.[4]

CLINICAL RELEVANCE

Although several preclinical studies using both in vitro and in vivo models have suggested that BAK may damage the ocular surface, the clinical relevance of these findings remains unclear, because the BAK exposure in these reports is typically much greater than that experienced clinically.[3] Champeau and Edelhauser found that, in rabbits, for example, BAK may remain in the conjunctiva for 14 days, yet there is no evidence of accumulation of BAK in human conjunctiva.[5] According to Berdy at al, BAK does not appear to have significant adverse effects at concentrations and dosing used clinically unless it is dosed more than four to six times daily.[6] Furthermore, a study that compared the ocular surface tolerability of BAK versus SofZia (Alcon Laboratories, Inc.) in patients previously treated with latanoprost (Xalatan; Pfizer, Inc.) did not find significant differences between the two preservatives with respect to objective measures of conjunctival hyperemia, corneal staining, and tear breakup time.[7]

THE PRESERVATIVE VERSUS THE MEDICATION

How should clinicians treating glaucoma respond to this information? For one, we must remember that the tolerability of glaucoma medications and preservatives, namely BAK, are not synonymous. There are many components to topical medications in addition to preservatives that affect tolerability such as pH, viscosity agents, and the therapeutic agent itself.

When reformulating medications, changing the preservative can dramatically affect the tolerability of an agent such as Alphagan P 0.1% (Allergan, Inc.). In the case of this medication, the preservative was not the only modification in this reformulation. The pH was raised to 7.8 to improve drug penetration, allowing the concentration of brimonidine to be reduced by 50%. The result was much improved safety and tolerability.[8] Removing BAK from Travatan to create Travatan Z (both by Alcon Laboratories, Inc.) but leaving the pH and drug concentration the same, however, resulted in equivalent tolerability between the two medications.[9,10] Unfortunately, only changing the preservative from BAK to SofZia had no effect on the drug's overall tolerability.

IMPROVE TOLERABILITY

In treating glaucoma, it is critical to identify patients who have the greatest problem using topical medications. In my practice, patients with ocular surface disease (OSD) top this list. In addition to treating glaucoma, it is also important to focus on aggressively treating the underlying OSD (dry eye syndrome, blepharitis, and rosacea) as well. Oral doxycycline (50-100 mg daily) for rosacea, short-term treatment consisting of an antibiotic and steroid ointments for blepharitis, and Restasis (Allergan, Inc.) for dry eye are effective strategies for improving OSD and the underlying tolerability of patients'

glaucoma therapy. Particularly when treating dry eye, it is important that physicians monitor the "drop burden" that our patients deal with. It is hard for our glaucoma patients to use two to three medications to treat their glaucoma plus artificial tears four to six times a day. This exceeds the number of drops a normal person can take and thus exceeds the "drop burden." Restasis reduces this burden and can be helpful in improving our patients' tolerability when used early.

AN ARMAMENTARIUM OF OPTIONS

One out of seven patients will become visually handicapped because of glaucoma,[11] and so it is vital that all treating physicians never use tolerability to topical medications as an excuse not to achieve the necessary target IOP. Our armamentarium of topical glaucoma medications has never been better and has never been tolerated so well by patients. Recent reformulations of Lumigan 0.01% (Allergan, Inc.) and Alphagan P 0.1% and the introduction of preservative-free Zioptan and Cosopt (both by Merck & Co., Inc.) have further expanded glaucoma specialists' options for effective, well-tolerated medical therapy. The ability to maximize glaucoma medical therapy today, without using medications with BAK, further demonstrates how our armamentarium has improved in the past few years. But, when medications fail to stabilize a disease, it is critical that every doctor not stop there.

As surgical options continue to expand, we all can turn to these modalities early in our patients' care, when it is clear medications are not working. ■

Steven T. Simmons, MD, is codirector of the Glaucoma Consultants of the Capital Region in Albany, New York. He is a consultant to Allergan, Inc., on the speakers' bureau for Merck & Co., Inc., and has received research support from Alcon Laboratories, Inc., Allergan, Inc., and Glaukos Corporation. Dr. Simmons may be reached at glaucomaconsult@aol.com.

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