TEAR OSMOLARITY IN A GLAUCOMA PRACTICE

The role of point-of-care testing in dry eye disease and glaucoma management.

BY LESLIE E. O'DELL, OD

Topical IOP-lowering medication is a first-line treatment for glaucoma, but many of these agents contain preservatives such as benzalkonium chloride (BAK) that harm the ocular surface with prolonged use.[1] Studies have shown that 60% of patients treated for open-angle glaucoma or ocular hypertension experience symptoms of dry eye disease (DED), including burning or stinging sensations, foreign body sensation, and tearing.[2] A chronic multifactorial ocular disease, DED can complicate the treatment of glaucoma by reducing patients' adherence to prescribed medical treatment and further decreasing their quality of life[3,4] and quality of vision. A key clinical strategy, then, is to identify patients at risk of or currently suffering from DED. Point-of-care testing can help.

UNDER ATTACK

The tear film is a dynamic structure consisting of lipid, aqueous, and mucin layers that are continuously being turned over and replenished. Because the tear film is the first refractive surface of the eye, any disruption of it can degrade vision.[5] In 2007, the Tear Film and Ocular Surface Society released the International Dry Eye Workshop, which redefined DED as a disease of the tear film and ocular surface accompanied by increased tear osmolarity and inflammation.[6]

Multidose topical glaucoma medications contain preservatives—mainly BAK, Purite (Allergan), and sofZia (Alcon)—to prevent contamination inside the bottle and biodegradation of the medication. BAK ranges in concentration from 0.004% to 0.02%; examples include bimatoprost, dorzolamide, timolol, and latanoprost solutions containing BAK in concentrations of 0.005%, 0.008%, 0.001%, and 0.02%, respectively (Table). Although early research showed preservatives were needed to improve drug availability,[7] recent work by Irkec and colleagues demonstrated that preservatives were not needed to improve the efficacy of glaucoma medications.[8]

A quaternary ammonium compound, BAK acts as a detergent: it disrupts cell membranes, leading to cell death and increased permeability. This detergent also disrupts the homeostasis of the ocular surface by stripping the outermost lipid layer, increasing evaporation, and initiating a vicious circle of tear film instability, hyperosmolarity, inflammation, loss of goblet cells, and corneal cellular abnormalities. The risk of disrupting homeostasis rises with increasingly frequent dosing of medications containing BAK and the use of a larger number of medications containing BAK.[9]

THE ROLE OF TEAR OSMOLARITY

Osmolarity is a noninvasive test providing a measure of the tear status. The TearLab Osmolarity System (TearLab)[10] collects and analyzes a 50-nL sample of tears obtained from the inferior lateral meniscus and lid margin. The TearLab Osmolarity System is the first objective and quantitative measure of osmolarity. This point-of-care test is CLIA (Clinical Laboratory Improvement Amendments) waived but requires a CLIA license. Hyperosmolar tears are found in both types of DED, aqueous and evaporative; it is not diagnostic of the cause of DED but is a helpful diagnostic tool nonetheless. Normal osmolarity ranges from 290 to 300 mOsm/L, with three severity levels as follows: less than 308 mOsm/L is considered normal, 309 to 328 mOsm/L is categorized as mild to moderate, and higher than 328 mOsm/L is considered severe.[10] Lemp described osmolarity as the single best metric for diagnosing DED.[11]

In a busy glaucoma practice, tear film osmolarity is a superior predictor of DED compared with other measures such as Schirmer testing, tear breakup time, and even corneal staining for several reasons. First, patients undergo extensive pretesting and receive diagnostic eye drops that degrade the ocular surface and tear film before these individuals are seen by the eye care provider. Second, the level of technicians' involvement in a patient's visit is high. Adding osmolarity testing to routine glaucoma management will improve the diagnosis and management of both coexisting and iatrogenic DED.

GLAUCOMA AND DED: PROTECTING THE OCULAR SURFACE

As Terrence O'Brien, MD, has stated, the "chronic use of topical preserved ophthalmic solutions can exacerbate DED in glaucoma patients."[12] Herreras and colleagues demonstrated elevated tear film osmolarity in patients using topical IOP-lowering medications long term. This finding was in the absence of other ocular surface abnormalities, namely decreased tear

TABLE. CONCENTRATION OF BAK IN IOP-LOWERING MEDICATIONS

Brand-Name Drug (Generic Name)[a]	BAK Concentration, %
Xalatan (latanoprost)	0.02
Travatan (travoprost)	0.015
Betoptic S (betaxolol hydrochloride)	0.01
Azopt (brinzolamide)	0.01
Timoptic (timolol)	0.01
Simbrinza (brinzolamide-brimonidine tartrate)	0.003
Alphagan (brimonidine)	0.005
Lumigan (bimatoprost)	0.005
Betagan (levobunolol)	0.005
Combigan (brimonidine tartrate-timolol maleate)	0.005
Cosopt (dorzolamide hydrochloride-timolol maleate)	0.0075
Trusopt (dorzolamide hydrochloride)	0.0075

Abbreviation: BAK, benzalkonium chloride.
Author's note: when selecting adjunctive therapy, it is worth considering overall BAK load on the ocular surface as well as efficacy.
[a]Xalatan (Pfizer); Travatan, Betoptic S, Azopt, Simbrinza (Alcon); Timoptic (Valeant Pharmaceuticals); Alphagan, Lumigan, Betagan, Combigan (Allergan); Cosopt, Trusopt (Mundipharma Ophthalmology Products).

breakup time and an abnormal Schirmer test result.[13] The long-term administration of topical drops preserved with BAK also heightens the potential of failed filtration surgery.[14]

A change in treatment patterns is in order. Rather than wait for symptoms to present, the providers of glaucoma care can strive to diagnose DED early. By evaluating the ocular surface and tear status with osmolarity before initiating glaucoma therapy and repeating this testing regularly thereafter, practitioners can identify patients at increased risk of or already experiencing DED.

All classes of glaucoma medication have an effective nonpreserved agent available in single-use vials.[15,16] One step that an eye care provider can take is to prescribe nonpreserved or alternatively preserved medications from the outset. Another option is to perform laser trabeculoplasty early in the course of disease. In addition, many studies have shown that switching patients to nonpreserved solutions or solutions with alternate preservatives improves the health of the ocular surface and patients' symptoms.[2,15,17-19] Prostaglandin analogues have become a first-line therapy, because the simplicity of their dosing is thought to lessen their side effects and the barriers to adherence.[20] In a recent study, switching patients from a BAK-containing prostaglandin to tafluprost dosed once daily significantly decreased mean tear osmolarity over a 12-week period from a baseline of 315.7 mOsm/L to 302.0 mOsm/L. Osmolarity improved for 81.7% of the patients.[16] ■

AT A GLANCE

- Studies have shown that 60% of patients treated for open-angle glaucoma or ocular hypertension experience symptoms of dry eye disease (DED), which can reduce adherence to prescribed medical treatment and further decrease quality of life and quality of vision.
- The long-term use of topical glaucoma medication preserved with benzalkonium chloride can exacerbate DED.
- Elevated tear film osmolarity is diagnostic of DED. By evaluating osmolarity prior to initiating medical glaucoma therapy and regularly repeating this testing thereafter, eye care providers can identify patients experiencing DED and take action.

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Leslie E. O'Dell, OD
- director, Dry Eye Center of PA at Wheatlyn Eye Care, Manchester, Pennsylvania
- lesliod@hotmail.com; www.wheatlyneyecare.com; Twitter @HelpMyDryEyes
- financial disclosure: speaker for Allergan and RPS; consultant to Bruder and Paragon BioTech