ONLINE CE NEWSLETTER SERIES FOR OPTOMETRISTS
WITH ONLINE TESTING AND INSTANT CE CERTIFICATE

EYE ON GLAUCOMA™
CASE CHRONICLES IN GLAUCOMA AND OCULAR SURFACE DISEASE

CASE 4 IN A SERIES OF 4

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LEARNING METHOD AND MEDIUM
This educational activity consists of a case report and ten (10) study questions. The participant should, in order, read the Learning Objectives contained at the beginning of this activity, read the material, answer all questions in the post test, and complete the Activity Evaluation/Credit Request form. To receive credit for this activity, please follow the instructions provided below in the section titled To Obtain CE Credit. This educational activity should take a maximum of 1.0 hour to complete.

CONTENT SOURCE
This continuing education (CE) activity captures content from a roundtable discussion.

ACTIVITY DESCRIPTION
There is a growing awareness of the impact of ocular surface disorders on the successful management of patients with ocular hypertension and glaucoma. Recent studies provide new insights into patient problems and concerns, and an increasing awareness of the significance of preservatives on ocular health. Improved versions of current therapies, and the availability of new therapies, provide opportunities for improved outcomes toward the prevention of glaucoma progression. Recently, a group of experts convened to discuss their insights and approaches for managing these patients. This CE activity brings you highlights from these case discussions in a 4-part series.

TARGET AUDIENCE
This educational activity is intended for optometrists.

LEARNING OBJECTIVES
Upon completion of this 4-Part CE Case Series, participants will be better able to:

- Assess ocular surface health in patients on ocular antihypertensives
- Review the evidence on the effects of preservatives on the ocular surface as they relate to ocular hypertension treatment regimens
- Employ appropriate ocular antihypertensive strategies in patients with glaucoma or ocular hypertension to manage OSD

ACCREDITATION DESIGNATION STATEMENT
This course is COPE approved for 1.0 hour of CE credit for optometrists.
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3. that all reasonable clinical alternatives will be discussed when making practice recommendations.

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CASE PRESENTATION
Dr Sowka:

Chief Complaint
A 70-year-old man is referred for glaucoma management because of poor intraocular pressure (IOP) control following selective laser trabeculoplasty (SLT) in both eyes. The patient’s medical history is significant for hypoparathyroidism as well as spinal fusion surgery. At present, he is not using any ophthalmic medications.

History
Diagnosed with glaucoma 4 years earlier, this patient has been prone to sensitivity and adverse reactions to many therapeutic classes of ocular antihypertensives, including prostaglandin analogs, carbonic anhydrase inhibitors, alpha-2 agonists, and beta-blockers. Specifically, he was initially treated with 0.005% latanoprost (Xalatan), but this was discontinued for an unspecified adverse reaction. He was switched to dorzolamide, 2% (Trusopt), but this also was discontinued because a rash that developed on
his neck was attributed to the medication. He then was placed on brimonidine, 0.2% (Alphagan), which was discontinued because of ocular allergies and poor IOP response. The patient had also used generic timolol, 0.5%, which was stopped because he reported that it altered his heart rate and made him feel "jittery".

Three years ago, the patient underwent SLT in each eye. In the immediate postoperative period, he developed profound keratitis with significant corneal edema as well as folds in the Descemet membrane. Following an unsuccessful attempt to treat the keratitis by his ophthalmologist, the patient self-referred to another ophthalmology group. There, the patient was treated successfully with topical steroids, nonsteroidal anti-inflammatory medications, and hyperosmotic solution. The ophthalmologist speculated that the patient had developed an allergic reaction to benzalkonium chloride (BAK) in either the gonioscopic contact solution used during the SLT procedure or in the anti-inflammatory (prednisolone acetate, 1%) prescribed immediately after the surgery. It was noted at that time that the patient did not tolerate the prednisolone acetate very well and was thought to have had a BAK toxic reaction. Ever since his SLT 3 years earlier, however, the patient has not used any ocular antihypertensive medications.

**EXAMINATION**

**Allergy History:** Adverse reactions to the following ocular antihypertensives: latanoprost, dorzolamide, brimonidine, and timolol; possible reaction to BAK and/or gonioscopic solution

**Visual Acuity (Best-Corrected):**

20/20 OD    20/20 OS

**Anterior Segment Examination:**

Conjunctiva:

Clear and quiet

Cornea:

Arcus OU – otherwise clear and unremarkable

Anterior chamber (including angle assessment):

Deep and quiet; anterior chamber angles open to ciliary body band completely in each eye

Lens:

Mild nuclear sclerosis OU

**IOP:**

26 mm Hg OD    27 mm Hg OS

**Pachymetry:**

565 OU

**Optic Nerve/ Retinal Nerve Fiber Layer (RNFL)/ Retina:** ([Figures 1A and 1B](#))

Optic nerve head OD: 0.85/0.8; marked notching of the neuroretinal rim superior and inferior

Optic nerve head OS: 0.9/0.8; marked notching of the neuroretinal rim superior and inferior
Figures 1A and 1B: Marked neuroretinal rim compromise in OU. Small optic disc with ISNT rule not obeyed OU. Inferior notch developing OD while notch is noted in the superior portion of the optic disc. Extensive parapapillary atrophy noted OU.

*Photos Courtesy of Joseph Sowka, OD*

Marked absence of RNFL OU; retina otherwise unremarkable OU

Imaging: Not performed

**Visual Fields (SITA Standard):** *(Figures 2A and 2B)*

Marked superior and inferior arcuate defects in each eye; more severe OS. Comparison with fields taken 3 years earlier in another office demonstrated progression OU.

*Figures 2A and 2B: Significant superior and inferior arcuate defects OD, OS.*

*Figures Courtesy of Joseph Sowka, OD*

**ASSESSMENT AND INITIAL TREATMENT**

With IOPs of 26 mm Hg OD and 27 mm Hg OS, the patient came to me with uncontrolled primary open-angle glaucoma with progression demonstrated. He was informed that ocular antihypertensive therapy was needed to further reduce the IOP. The patient was prescribed travoprost preserved with a non-BAK preservative (0.004% travoprost, Travatan-Z), but he complained of an unacceptable degree of hyperemia and ocular discomfort with the travoprost; therefore, the ocular antihypertensive was switched to bimatoprost, 0.03%, preserved with BAK (Lumigan). At that time, preservative-free prostaglandins were
not available. With bimatoprost, the patient experienced less hyperemia; he reported experiencing a foreign body sensation (FBS), however, which he felt was tolerable at the time. He wore contact lenses occasionally socially, but found them poorly tolerable after starting glaucoma medical therapy. He rarely wore contact lenses at this point. His IOP was reduced to 17 mm Hg OD and 18 mm Hg OS on bimatoprost.

The patient was maintained on bimatoprost for 4 years. His anterior segment evaluation remained unchanged except for mild cataract progression and a slightly reduced tear break-up time. He developed hypertrichosis and trichiasis periodically while using bimatoprost. During each visit, he mentioned FBS, and the offending lashes were epilated because it was thought that the trichiasis explained his FBS. He acknowledged slight improvement immediately following each epilation. Eventually, I referred him to an oculoplastic surgeon for permanent treatment of trichiasis. The patient underwent successful electrolysis with permanent resolution of the trichiasis. Disappointingly, this failed to relieve his FBS in any way. The patient now felt that the FBS was a significant quality-of-life issue: he could no longer wear contact lenses at all, and wished to do so again.

**DISCUSSION**

**Dr Fingeret:** How would you test patients to determine if they have a true BAK allergy, are intolerant to BAK, or are experiencing BAK toxicity?

**Dr Sowka:** There is no clinical test easily available to optometrists, though an allergist could perhaps test for BAK allergy. We are making an educated guess based on the patient's history. The fact that the case patient used bimatoprost preserved with BAK relatively successfully argues against his having a true allergic response to BAK.

**Dr Fingeret:** If the patient did not have an allergic reaction to BAK, then was it BAK intolerance or BAK toxicity? Do these 2 reactions present differently? ([Table])

<table>
<thead>
<tr>
<th>Type of Reaction</th>
<th>Definition</th>
<th>Possibility of Continuing Agent</th>
<th>Symptoms</th>
<th>Local or Systemic Reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>Greater than commonly experienced adverse effects to an agent</td>
<td>Yes, but with discomfort</td>
<td>Discomfort, irritation</td>
<td>Local</td>
</tr>
<tr>
<td>Intolerance</td>
<td>High degree of sensitivity that precludes continued use of the agent</td>
<td>No</td>
<td>Burning, stinging, irritation</td>
<td>Local</td>
</tr>
<tr>
<td>Toxicity</td>
<td>Damage to tissues that is dependent on dose, route of administration, and time of exposure</td>
<td>No</td>
<td>Redness, damage to inferior third of the eye and/or corneal epithelium</td>
<td>Local</td>
</tr>
<tr>
<td>Allergy</td>
<td>Immune system hypersensitivity reaction</td>
<td>No</td>
<td>Itching, rash, welts, skin peeling, hyperemia, chemosis (swelling of conjunctival tissue around the cornea)</td>
<td>Local and/or Systemic</td>
</tr>
</tbody>
</table>
Dr Sowka: In the immediate post-SLT period, this patient's ophthalmologists considered the possibility that he had reacted to BAK and/or medications used around the time of the procedure. We should consider the possibility that the patient could have had deleterious effects from overload of BAK insults to his eyes: BAK from the gonioscopic solution, BAK from the multiple topical steroids or from other medications used after the procedure.\(^3\)

However, in my opinion, the patient probably experienced BAK toxicity following the SLT. I think sensitivity to BAK means that patients experience irritation with the medication, but can still use it.\(^2\) Intolerance would represent a higher degree of sensitivity such that the patient would not be able to tolerate the medication.\(^1\) It appears that this patient had toxicity due to BAK, as demonstrated by the keratitis in the post-SLT period and the intolerable FBS that he felt after he had been on the BAK-preserved bimatoprost for some time. His acuity had always been excellent at 20/20 OD, OS, save for the time that he had keratitis immediately after the SLT when it was reduced to 20/50.

Dr Hom: In my experience, if there is a dense keratitis, it could be a toxic reaction to BAK. If it is irritation or sensitivity to BAK, I may see conjunctival staining and redness. That is how I distinguish BAK sensitivity from BAK toxicity.

Dr Gaddie: The gonioscopic solution used during SLT, depending on brand and formulation, can be very toxic to the eye short term. We have tried several formulations in our practice and have found the one best tolerated by most of our patients, which we now use. However, I think something other than the BAK could conceivably have been responsible for the keratitis and discomfort in this patient's immediate postoperative period. Perhaps the toxicity from the gonioscopic solution itself was enough to push the patient into BAK intolerance. The history of triachiasis with resultant keratitis probably compounded this situation as well.

Dr Fingeret: I believe that the patient was experiencing concurrent problems: eyelash irritation along with toxicity to BAK. When a patient is having problems tolerating a particular therapeutic class of ocular antihypertensives, switching to a different class makes sense, as Dr Sowka did. Additionally, clinicians have the option to switch to either a preservative-free agent or one that uses a different preservative. Dr Sowka, how did you manage his suspected BAK toxicity and glaucoma?

Dr Sowka: Interestingly, the patient did not tolerate travoprost with the non-BAK preservative very well; he had experienced hyperemia and ocular discomfort. He had less hyperemia when he was switched to bimatoprost with BAK. However, on bimatoprost he experienced FBS and his symptoms worsened to the extent that he was chronically uncomfortable and electrolysis of the offending lashes gave him no relief whatsoever.

Some of the available preservative-free ocular antihypertensives, such as preservative-free dorzolamide-timolol, 2%/0.5%, and preservative-free timolol, were eliminated from consideration as possible therapies for this patient based on his previously reported adverse events. Specifically, his primary care physician objected to the use of topical beta-blockers because the patient previously reported an altered heart rate and jitteriness associated with ocular timolol therapy. Also, he had reported the development of a neck rash with the use of dorzolamide. He and I discussed the option of trabeculectomy, but I explained to him that his eyes may never look or feel the same again after that procedure because the procedure might result in a permanent bleb, with the possibility of persistent FBS. I suggested that there was likely to be less harm in trying what at the time was a new prostaglandin analog that did not have any preservatives, specifically preservative-free tafluprost.

According to Janulevičienė and colleagues, switching patients from a BAK-preserved prostaglandin to the new preservative-free tafluprost can result in improvements in associated ocular discomfort. Twelve weeks after patients were switched from BAK-preserved latanoprost to preservative-free tafluprost, they experienced significantly normalized tear osmolarity, improved tear break-up time, decreased corneal staining, and decreased ocular discomfort with effectively controlled IOP.\(^4\)

This patient discontinued bimatoprost and began preservative-free tafluprost. When he came back for a 1-month follow-up after using preservative-free tafluprost, he said his FBS pain was gone. Remarkably,
he was now pain-free and able to wear contact lenses again. His IOP readings, 17 mm Hg in each eye, are now roughly the same with preservative-free tafluprost as they were with bimatoprost. Admittedly, these IOPs are at the high range of target pressures, but the patient's ocular antihypertensive options are limited, and his fields will be closely monitored. Review of visual fields done in other offices showed a significant degree of progression with a threat to fixation occurring at IOP levels in the mid-20s. Given his good health, his age, and threat of visual disability, 17 mm Hg represents the highest target that this patient should have. If his pressure rises above that level, or if there are further visual field or optic nerve changes, then additional treatment or modified therapy will need to be considered.

**Dr Hom:** I have seen that a prostaglandin analog alone, without preservatives, can cause symptoms of ocular surface disease (OSD) in some individuals.\(^5,6,7\) Therefore, if I am treating a patient with an ocular antihypertensive and he or she subsequently develops OSD, I have to ask myself if it is the preservative or if it is the prostaglandin analog component causing the problems. In this patient's case, it is clear to me that it was the preservative that was causing the main problem, because removing the preservative in his ocular antihypertensive agent appeared to have eliminated his OSD.

**REFERENCES**