Eye on Glaucoma™
Case Chronicles in Glaucoma and Ocular Surface Disease
CASE 2 IN A SERIES OF 4

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LEARNING METHOD AND MEDIUM
This educational activity consists of a case report and four (4) 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 on the post test and Activity Evaluation/Credit Request form. This educational activity should take a maximum of 0.75 hour to complete.

CONTENT SOURCE
This continuing medical education (CME) activity captures content from a roundtable discussion held July 2013.

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 CME activity brings you highlights from these case discussions in a 4-part series.

TARGET AUDIENCE
This activity is intended for comprehensive ophthalmologists and glaucoma specialists.

LEARNING OBJECTIVES
Upon completion of Part 2 of this 4-Part CME 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 STATEMENT
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- Operating System: Windows or Macintosh
- Media Viewing Requirements: Flash Player or Adobe Reader
- Supported Browsers: Microsoft Internet Explorer, Firefox, Google Chrome, Safari, and Opera
- A good Internet connection
CASE 2

Dr Hutnik: A 77-year-old woman, distraught, presented to me for a second opinion, stating that she was very concerned about her eyes. She was anxious and tearful, and before I could even collect a history, I had to spend some time calming her down. Widowed 2 years ago, she lives alone, is fiercely independent and very active, and very concerned about remaining independent. When she was calmer, she related that she had been diagnosed with glaucoma 10 years ago with very high intraocular pressure (IOP) in the 30- to 40-mm Hg range. She has no family history of glaucoma, has no significant systemic medical issues, and is using no nonocular systemic medications. Her history and examination on the day she presented to me are summarized below.

HISTORY AND EXAMINATION

Presentation

Patient's Chief Complaint: 77-year-old woman with a 10-year history of well-controlled glaucoma who recently has experienced consistent IOP elevations requiring multiple additional medications as well as visual field progression over the past 2 years. She states that her eyes are chronically red and sore.
Ocular History

- Onset of glaucoma: 10 years ago
- Medical therapy history: bimatoprost, 0.01%; brimonidine, 0.15%; dorzolamide, 2%/timolol, 0.5% fixed combination; oral methazolamide
- Surgical or laser history: 360º selective laser trabeculoplasty

Past Medical History: none
Nonocular Systemic Medications: methazolamide
Nonocular Surgical History: none
Family History of Glaucoma: none

Examination:

Visual Acuity (best corrected visual acuity at distance)
OD: 20/25 OS: 20/25

IOP (method of measurement - applanation in mm Hg)
OD: 14 OS: 13

Central Corneal Thickness Microns
OD: 540 OS: 545

Visual Fields (Figure 1):
OD: inferior nasal step and arcuate defect OS: paracentral changes (perhaps lens)
Figure 1. Visual fields, Case 2.

Courtesy of Cindy M.L. Hutnik, MD, PhD

SLIT-LAMP BIOMICROSCOPY

Lids and Lashes: As shown in Figure 2, striking periorbital erythema, lid margin telangiectasia and thickening

Conjunctiva: As shown in Figure 2, diffuse, moderate conjunctival hyperemia

Cornea: Few superficial punctate erosions

Anterior Chamber: Deep and quiet

Lens: Early nuclear sclerotic cataracts
Anterior Vitreous: Unremarkable

Gonioscopy: Open to a grade III, all quadrants, both eyes

Dilated Fundus Examination (see Figure 3)

Figure 2. External examination of patient in Case 2.
Photo Courtesy of Cindy M.L. Hutnik, MD, PhD, with permission

Figure 3. Optic nerve photographs, Case 2.
Photos Courtesy of Cindy M.L. Hutnik, MD, PhD
Dr Hutnik: A review of this patient's visual fields (Figure 1), optic nerve photographs (Figure 3), and optic nerve imaging studies (Figure 4) suggests that her glaucoma was generally stable until approximately 2 years ago, roughly the time when her husband died. In response to this progression, her referring physician had added several adjunctive medications to further lower her IOP. When she presented to me, she was using a multi-drug regimen consisting of bimatoprost, brimonidine, the dorzolamide/timolol fixed combination, and even an oral carbonic anhydrase inhibitor (CAI), methazolamide; she has also already undergone 360° selective laser trabeculoplasty.

Dr Parrish: What is the panel's approach to this patient?

Dr Lewis: Does she have cataracts?

Dr Hutnik: Yes, but they are mild. Her best corrected visual acuity is 20/25 in both eyes.
**Dr Lewis:** If there was an indication for cataract surgery, you would have the opportunity to consider a minimally invasive glaucoma procedure.

**Dr Hutnik:** Surgery was among my considerations as well. But to further complicate the situation, her sister-in-law recently cautioned her that glaucoma surgery could blind her. Then she tearfully admitted to nonadherence with her IOP-lowering therapy. As each additional topical medication was added, her eyes began to get irritated—which she referred to as “toxicity.” One reason she was so distraught was that she thought the irritation was indicative of worsening glaucoma. She also was not taking her methazolamide faithfully because it made her feel unwell.

**Dr Lewis:** Several interconnected factors are at play in this case. The patient is depressed over the loss of her husband and has stopped taking care of herself. She stopped using her drops faithfully and had some disease progression, which prompted further escalation of therapy. The added medications are now causing ocular irritation, thus contributing further to nonadherence. Aggravating the situation even more, long-term use of oral carbonic anhydrase inhibitors can cause depression insidiously and so may be perpetuating a vicious cycle.

**Dr Parrish:** On the basis of the examination and her history, what was your next step in this patient's management?

**Dr Hutnik:** Clearly, her glaucoma therapy was adversely affecting her quality of life. I wasn't convinced that she needed to be on so many drops. Her history suggested that they were not added because of limited efficacy, but rather as a result of previously undetected nonadherence. My goal was to reduce her medication burden. I began by discontinuing her oral CAI and washing out the brimonidine. I coupled this strategy with some conservative interventions for her ocular surface disease, including warm water compresses, nonpreserved artificial tears, and lid hygiene. At her next visit, she reported feeling less malaise upon stopping the methazolamide. She also felt that her eyes were a little less irritated. But now her IOP had risen to 21 mm Hg in the right eye and to 19 mm Hg in the left eye. She assured me she was taking all her IOP-lowering medications as prescribed. We were making progress, but we still were not at our target. My next step was to lessen her exposure to benzalkonium chloride (BAC). Studies support that transitioning from a BAC-preserved drug to a non-BAC-preserved\textsuperscript{1,2} or to a preservative-free drug\textsuperscript{3,4} can improve ocular surface health. I told her that she needed to be on medications for her glaucoma, but that to improve her ocular surface disease, she required minimal chemical exposure.

**Dr Parrish:** What are our BAC-free options?
**Dr Lewis:** There are some formulations of glaucoma medications that contain preservatives other than BAC, and there are others that are entirely preservative-free. Travoprost is preserved with a proprietary non-BAC preservative,\(^5\) and brimonidine is also preserved with a non-BAC preservative.\(^6\) Tafluprost,\(^7\) timolol,\(^7\) and the dorzolamide/timolol fixed combination\(^8\) are available in preservative-free formulations. The truly preservative-free formulations are packaged in single-dose vials, which can be expensive; not all insurance carriers cover these agents.

**Dr Parrish:** What did you choose for this patient?

**Dr Hutnik:** I switched her to the travoprost, 0.004%, BAC-free prostaglandin analogue and the preservative-free formulation of the dorzolamide/timolol fixed combination.

**Dr Parrish:** Did her eye irritation improve at all, and if so, how long did that take after eliminating exposure to BAC from her ocular surface?

**Dr Hutnik:** It took a full 2 to 3 months before she started to feel and look better. Her raccoon eyes improved, but it did not happen overnight.

**Dr Pflugfelder:** In my experience, it can take months to see improvements in ocular surface inflammation after discontinuing exposure to BAC.

**Dr Parrish:** What changes can we expect to see?

**Dr Pflugfelder:** The corneal epithelial disease will certainly improve, which in turn improves the symptoms because of reduced stimulation of the corneal nerves, but these improvements can take several months. Sometimes, a brief course of topical steroids will hasten the process.

**Dr Hutnik:** Interestingly, once her eyes cleared up, her pressures were lower on fewer medications—they were 16 and 15 mm Hg in the right and left eye, respectively, on several visits after the medication transition.

**Dr Parrish:** I have seen this effect in patients as well. When the eyes are cleared up and the drops no longer burn and cause pain, adherence improves and IOP decreases.

**Dr Pflugfelder:** I see this all the time. Many times, if the eyes are very inflamed, I often can achieve better IOP control in a patient by replacing 3 BAC-preserved drugs with a single preservative-free agent. I often have wondered if the inflammation itself is contributing to the elevated pressure.
Dr Parrish: Dr. Hutnik, you conducted and published a study evaluating the tolerability and effectiveness of the preservative-free dorzolamide/timolol fixed combination in patients with open-angle glaucoma. Please summarize the study and your findings.

Dr Hutnik: We conducted a multicenter, open-label trial in which newly diagnosed and treatment-naïve glaucoma patients completed a glaucoma symptom score questionnaire before and after (at 4 weeks and at 8 weeks) starting therapy with preservative-free dorzolamide/timolol fixed combination. Mean IOP reductions were on the order of 38%, which is what we expect from the preserved formulation; hence, the lack of BAC did not reduce efficacy. Symptom scores remained statistically unchanged from before therapy to 8 weeks after beginning therapy, demonstrating excellent tolerability of the preservative-free product.

Dr Parrish: A similar study evaluated the preservative-free prostaglandin tafluprost and gleaned similar results. This is an important finding, given that as many as 50% to 60% of glaucoma patients have symptoms consistent with ocular surface disease. [Readers: Please see Dr Pflugfelder's Top 5 Ocular Surface Assessments approach at the end of this case discussion.]

Dr Lewis: This case is of interest because it represents a very typical glaucoma patient who has ocular surface disease, adherence issues, a reluctance to have surgery, and depression—a constellation of problems that we all face in clinical practice. The management of the case as documented herein demonstrates a few clinical pearls: Listen to your patient—he or she will tell you what the problem is; Pay attention to complaints about ocular discomfort, because they may underlie adherence issues that are compromising glaucoma management; Take advantage of BAC-free or preservative-free formulations in the patients for whom they are appropriate. You did all of these things. This lady was fortunate to have come to you for a second opinion.

DR PFLUGFELDER’S TOP 5 OCULAR SURFACE ASSESSMENTS FOR THE COMPREHENSIVE OPHTHALMOLOGIST

1. Lacrimal Puncta

*Are there signs of ectropion or stenosis of the puncta?* Many older patients have either a subtle ectropion or some stenosis of their puncta, which will interfere with tear drainage and thereby delay drug clearance.

2. Posterior Lids (Meibomian Glands)

Express the lids! *Has gland dropout occurred? What is the quality of the meibum? Is vascularization present (Figure A)?* Many older patients also have lid margin changes due to posterior
blepharitis/meibomian gland dysfunction. Decreases in the quantity and/or quality of meibum lead to lipid deficiency that can destabilize the tears and potentiate the deleterious effects of ocular antihypertensives.

3. Tear Film Layer

What are the results of a fluorescein tear break-up time test? Fluorescein tear break-up time may be the easiest test that an eye care clinician performs. When I conduct the test, I first moisten the fluorescein strip with preservative-free saline, then touch the patient's inferior tarsal conjunctiva, and ask the patient to blink to disperse the fluorescein. Viewing under cobalt blue illumination, I ask the patient to blink and keep his or her eye open until I begin to observe discontinuities in the tear film, which usually occur in the center or the inferior cornea. I count in seconds to determine the amount of time it takes for the tears to break up. There is some debate about what the normal tear break-up time is. I consider 7 seconds or less to be abnormal. In many older patients, tear break-up is instantaneous.

4. Cornea

Is erosion present? Once fluorescein is instilled, I examine the cornea to determine the presence of punctate fluorescein staining. Staining in the center of the cornea indicates greater severity of erosion, which has the potential to reduce vision.

5. Conjunctiva

Is redness present? Is there staining with lissamine green dye (Figure B)? Is conjunctival chalasis present? Redness and fluorescein staining in the conjunctiva indicate epithelial disease. Conjunctival chalasis, or loosening of the conjunctiva, can interfere with the spread of tears. This condition manifests as lid parallel folds in the conjunctiva (Figure C). Conjunctival chalasis tends to compartmentalize the tears, typically in the center of the lower lid, because the condition blocks the flow of the tear meniscus both temporally and sometimes nasally. Conjunctival chalasis also interferes with tear clearance and increases the concentration of ocular medications over the cornea. Typically with ocular antihypertensive toxicity, most of the redness occurs in the lower third of the eye, on the inferior bulbar conjunctiva and the inferior tarsus, particularly medially, where the tears are swept toward the lacrimal drainage system. When I observe redness on the inferior tarsus in a patient who is using 1 or more ocular antihypertensives, I suspect toxicity.
**Figure A.** Meibomian gland disease with obstructed ductal orifices, prominent telangiectatic lid margin vessels.

*Figure B.* Nasal lissamine green staining of the conjunctiva in a patient with meibomian gland disease who also has severe staining of the lower lid.
Figure C. Conjunctivochalasis with lid parallel conjunctival folds nasally and tear pooling centrally with elevated inferior tear meniscus.

Photos Courtesy of Stephen C. Pflugfelder, MD

REFERENCES


