

Topical Glaucoma Treatment and the Cornea

Alternative strategies may benefit patients with a compromised ocular surface.

BY ADAM C. REYNOLDS, MD

During the past decade, clinicians' attention to the effect of topical medical glaucoma treatments on corneal and ocular surface health has grown. Practitioners have generally moved away from using pilocarpine and epinephrine derivatives due to their well-known association with ocular surface complications. Current categories of topical agents, namely prostaglandin analogues, β -blockers, α -agonists, and topical carbonic anhydrase inhibitors (CAIs), are better tolerated, but prolonged exposure to these drugs produces long-term side effects and a compromised quality of life. Additionally, the preservatives used in these topical agents, especially benzalkonium chloride (BAK), affect the health of the ocular surface.

ENDOTHELIAL CELL FUNCTION AND CAIs

Endothelial cell function depends on carbonic anhydrase enzymatic action to maintain corneal clarity. Many studies of eyes with a normal corneal endothelium have discredited concerns that topical CAIs compromise endothelial function.^{1,2} In patients with endothelial cell dysfunction due to Fuchs corneal dystrophy, surgically induced endothelial failure, or post penetrating keratoplasty, however, the use of topical CAIs can permanently compromise endothelial function.^{3,4} For patients with the potential for further compromise of previous underlying corneal endothelial disease, I would recommend considering alternatives to topical CAIs. If CAIs must be used for glaucoma management in these individuals, then it is important to monitor corneal thickness, specular endothelial cell studies, and other parameters closely.

SPECIFIC CORNEAL TOXICITY AND OCULAR SURFACE DISEASE

The deleterious effects of topical glaucoma treatment on the cornea, ocular surface, and tear film and the resultant ocular discomfort and visual compromise have been well documented. In vitro research has demonstrated the toxic effects of BAK used in many preparations,⁵ yet clinicians tend to underestimate the harmful effects of topical glaucoma medications.⁶ Fechtner and colleagues reported that Ocular Surface Disease Index scores are significantly decreased in 50% of patients using topical glaucoma medications, and the scores are affected by the number of medications used.⁷ Particularly troubling is how significant, and probably underestimated, the effect of ocular surface disease (OSD) symptoms is on patients' adherence to glaucoma management.⁸ Patients with glaucoma tend to be older and have OSD that is almost always worsened to some degree by topical glaucoma therapy.^{9,10}

ALTERNATIVE STRATEGIES

The easiest way to decrease the negative effect of glaucoma therapy on the ocular surface is to minimize the number of medications used. I recommend stopping medications while keeping safety of IOP levels in mind to be sure of the drugs' IOP-lowering effect. This should be done especially when the IOP-lowering ability of an agent is in doubt historically in a specific patient. Many of the different classes of topical medications are now available in fixed combinations, which may reduce preservative loads on the cornea and decrease toxicity. The benefits of fixed-combination drugs must be weighed against the usual increased out-of-pocket cost to the

CORNEAL HYSTERESIS

By Felipe A. Medeiros, MD, PhD

Corneal hysteresis has attracted considerable interest in recent years. Corneal hysteresis is a measure of the viscoelastic dampening of the cornea, and it can be estimated by analyzing corneal responses to deformation induced by an air pulse using a commercially available instrument (Ocular Response Analyzer; Reichert).



The measurement of corneal hysteresis has been shown to be associated with the risk of glaucomatous progression.¹⁻³ In a prospective, longitudinal study, my colleagues and I found that patients with lower hysteresis had significantly faster rates of progressive visual field loss compared to those with higher hysteresis.³ Importantly, the hysteresis measurements had a stronger ability to predict visual field progression than measurements of corneal thickness. It is hypothesized that these results may be explained by a relationship between corneal hysteresis and the structures in the back of the eye, the lamina cribrosa, and peripapillary sclera.

The ability of the cornea to resist deformation may reflect the constitution of its extracellular matrix, which could, in turn, be related to the extracellular matrix composition of these posterior ocular tissues linked to glaucomatous damage. An eye with a more deformable cornea or with a lower hysteresis could have an optic disc that is more susceptible to IOP-related damage. Although this is an attractive hypothesis to explain the significance of hysteresis as a risk factor of glaucoma, it still remains to be proven.

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patient for these preparations compared to generic single agents.

Another strategy is to switch to alternatively preserved or preservative-free formulations of the various classes of topical medications. Again, these medications may come at a higher cost. They may also be more difficult to administer—small vials for patients with compromised hand coordination and decreased vision. Switching to preservative-free options, however, can significantly decrease corneal toxicity in patients whose ocular surface is compromised for reasons other than glaucoma treatment.¹¹

A third option is to decrease topical treatment with laser trabeculoplasty (LTP). Argon laser trabeculoplasty and selective laser trabeculoplasty are both effective options for primary and adjunctive treatment of most forms of open-angle glaucoma. In my opinion, LTP is underutilized, particularly in glaucoma patients with underlying OSD. I encourage clinicians to consider LTP as a primary or early adjunctive treatment when appropriate.

CONCLUSION

Specific issues of corneal toxicity in glaucoma treatment include limiting the use of topical CAIs in patients at risk of endothelial dysfunction. For patients who have or who are at risk for surface toxicity and exacerbation of OSD, if possible, I recommend limiting their

exposure to BAK and the number of medications they use by selecting alternatively preserved or preservative-free preparations or prescribing a fixed combination. In many cases, LTP is another viable option. ■

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