The effect of corticosteroids on IOP is well known to all clinicians. Whether the agents are dosed systemically, topically, or intraocularly, even the short-term use of steroids can significantly raise the IOP to levels that threaten the health of the optic nerve. The occurrence of steroid-related ocular hypertension (OHT) is unpredictable and can be unnerving, because the problem is entirely iatrogenic and often requires additional intervention for IOP management. For patients who need an immediate decrease in pressure, selective laser trabeculoplasty (SLT) may be an effective alternative to more invasive intervention.

THE NEW REALITY OF STEROID-RELATED OHT

Changes in practice patterns over the past decade or so have increased the frequency—and the severity—of steroid-related OHT. The intravitreal injection of triamcinolone acetonide has become commonplace in the management of a variety of ocular conditions, ranging from macular degeneration to diabetic macular edema to posterior uveitis. In recent clinical trials, up to one in three eyes receiving intravitreal triamcinolone therapy required IOP-lowering treatment, depending on the steroid dose received.\textsuperscript{1,2} The popularity of steroid-eluting implants has also grown during the past several years. Retisert (Bausch + Lomb, Rochester, NY) is a posterior segment intraocular implant that slowly releases fluocinolone acetonide into the vitreous cavity over a 2- to 3-year period. It is labeled for the treatment of noninfectious posterior uveitis. Three-quarters of eyes implanted with the Retisert will require IOP-lowering medications, and one in three will require trabeculectomy.\textsuperscript{3}

The management of steroid-related OHT remains problematic. The effect of steroids on IOP is temporary upon discontinuation, so physicians’ first choice is to consider stopping the steroids. This is easy to do with systemic or topical steroid therapy. There will be a lag, however, before the IOP returns to normal. The clinical conundrum occurs when a patient has an unacceptably high IOP on maximal medical therapy and does not have the luxury of waiting for the steroid’s effect to wear off. A filtering procedure seems like overkill in this situation—a potentially permanent solution to a temporary problem.

Removing a steroid depot from the sub-Tenon’s space or the vitreous cavity or explanting a device requires a surgical intervention. It is worth remembering that the steroids were administered for a reason and removing them might have worse consequences than would an IOP-lowering procedure. For example, posterior uveitis has a horrible prognosis, and most eyes require constant steroid therapy to maintain vision. In this case, a trabeculectomy might be preferable to explantation of the Retisert device.

Is There a Role for SLT in Managing Steroid-Related OHT?

This procedure may offer a temporary solution to what is often a temporary problem.

BY TONY REALINI, MD

“The clinical conundrum occurs when a patient has an unacceptably high IOP on maximal medical therapy and does not have the luxury of waiting for the steroid’s effect to wear off.”
Clearly, safe and effective IOP-lowering intervention is needed for eyes with medically uncontrolled steroid-related OHT, whether the elevation in IOP lingers after the discontinuation of steroid therapy or ceasing steroid treatment is impractical or imprudent.

THE EVIDENCE FOR SLT

The literature on the use of SLT in eyes with steroid-related OHT is limited but growing. In the first case report, published in 2006, a 63-year-old white man presented with an IOP of 45 mm Hg in one eye 3 months after receiving an intravitreal injection of triamcinolone in that eye. On maximal tolerated medical therapy, his IOP remained 38 mm Hg. After SLT, the IOP dropped substantially. His IOP was 16 mm Hg on no medications 2 months after SLT, and it was 15 mm Hg with no medications 6 months after the procedure. Unfortunately, this report provides no information on the patient’s IOP immediately after SLT.

According to a similar report published in 2009, a 44-year-old man with medically uncontrolled IOP (36 mm Hg) 4 months after an intravitreal injection of triamcinolone underwent two 180º SLT sessions 1 month apart. His IOP had dropped to 20 mm Hg by 1 month and to 12 mm Hg by 2 months after the second 180º treatment. All medications were discontinued, and the eye maintained an IOP of 12 mm Hg.

Case reports are an effective means of announcing novel therapeutic options, but they lack evidentiary gravitas. The summarized reports do not exclude the possibility that the steroid response ran its course during the 1 to 2 months after treatment and that SLT had little or no real effect on IOP.

Rubin and colleagues reported a retrospective series of seven eyes undergoing SLT for medically uncontrolled IOP after intravitreal injections of triamcinolone. The mean baseline IOP of all seven eyes was 38.4 mm Hg. All were re-examined within 3 weeks of SLT, at a mean of 9 days after the procedure. At this first post-SLT visit, the IOP was 25.6 mm Hg, a reduction of nearly 14 mm Hg. One, 3, and 6 months after SLT, the mean IOP was approximately 26, 24, and 16 mm Hg, respectively. Five of these eyes had preexisting open-angle glaucoma or OHT, four of the seven eyes required a second SLT procedure, and five of the seven were deemed therapeutic successes (the other two underwent surgery). The rapid decrease in IOP in these eyes provides compelling evidence that SLT was directly related to the observed reduction in pressure.

It is worth mentioning that the IOP benefit in steroid-related OHT may not be unique to the selective laser system. Two groups have reported similarly significant reductions in IOP among eyes with steroid-related OHT that were treated with argon laser trabeculoplasty (ALT). Decreases of 10 to 20 mm Hg were measured in as few as 3 days after treatment.

MECHANISM OF ACTION

Why would trabeculoplasty be so effective in eyes with steroid-induced OHT? The mechanism by which trabeculoplasty lowers IOP in eyes with primary open-angle glaucoma remains poorly understood. Mechanical, cellular, and biochemical mechanisms have been proposed for ALT, and it has been suggested—based on their similar efficacy and safety profiles—that ALT and SLT likely work by the same mechanism.

One intriguing biological theory involves the recruitment of macrophages into the trabecular meshwork after trabeculoplasty. There, they mediate remodeling of the extracellular matrix and clearing of the debris responsible for obstructing aqueous outflow, resulting in improved outflow facility and thus a reduction in IOP. If the material clogging the meshwork in steroid-related OHT is particularly amendable to macrophage-mediated removal, this might explain the magnitude of trabeculoplasty’s observed effect. Indirectly supporting this theory is that unilateral SLT significantly reduces the IOP in untreated fellow eyes. These findings could be due to patients’ improved compliance with medical therapy. It might also occur, however, if macrophages recruited to the treated eye gain access to the systemic circulation and find their way to the trabecular meshwork in the fellow eye.

The author and colleagues recently probed this theory in a trial in which subjects undergoing bilateral SLT received topical steroids for 1 week in one randomly selected eye. The hypothesis was that, if macrophages mediated the IOP-lowering effect of SLT, then steroid therapy to suppress macrophage activity might reduce the effectiveness of the procedure. The study found no significant difference in IOP reduction among eyes that did and did not receive steroids after SLT. The mechanism by which SLT lowers IOP in steroid-related OHT remains unclear.

CLINICAL APPLICATION

For some eyes with steroid-related OHT, SLT (and probably ALT) appears to provide a rapid and dramatic reduction in IOP. When faced with a patient who has medically uncontrolled IOP after steroid therapy, it is reasonable for physicians to consider SLT before proceeding with incisional surgery. More than one SLT

(Continued on page 48)
More than a third of all patients on long-term corticosteroid therapy will develop a steroid response in addition to systemic side effects. Overall, immunomodulatory agents have been safely used on an off-label basis for the treatment of severe, sight-threatening, corticosteroid-resistant noninfectious uveitis and of uveitic patients who cannot tolerate corticosteroid therapy. The efficacy of immunomodulatory agents for noninfectious uveitis has been demonstrated in numerous case series.\(^6\)\(^-\)\(^10\) The dosing as well as the frequency and duration of treatment, however, have yet to be determined by large clinical studies. Despite these limitations, immunomodulatory agents play a crucial role in the treatment of ocular inflammatory diseases. ❏

John J. Huang, MD, is an associate professor and the director of the Ocular Immunology and Uveitis Service, and he is on the faculty of the Vitreo-Retina Service, Yale University Department of Ophthalmology and Visual Science, New Haven, Connecticut. Dr. Huang may be reached at (203) 785-5037, john.huang@yale.edu.