area (Figure 1). The incidence of IOP spikes has been reduced to nearly zero and postoperative incidence of macular edema is similar to previous years; however, persistent inflammation following surgery remains in a small percentage of patients (unpublished data). We surmise that the more localized nidus of depot was associated with more IOP spikes. From the conclusions of Xu et al., the reduction in IOP spikes from the more dilute injection is presumably from lower anterior chamber concentrations, either at its peak or cumulatively. The potential efficacy of triamcinolone acetonide injection has been reinforced recently by the results of the Prevention of Macular Edema randomized trial in Europe. In the diabetic arm of the study, 85% of patients had diabetes without retinopathy and the incidence of visually significant, optical coherence tomography-proven macular edema following cataract surgery was about 8%. This incidence was reduced to 0% with the addition of triamcinolone acetonide 40 mg injection subconjunctivally (P = .007), but with an attendant IOP rise equal to or higher than 25 mm Hg in 6 patients. The exact location of the injections was not reported. The reduction in macular edema incidence with triamcinolone acetonide injection was impressive.

The advantages of injection versus daily drops include not only patient convenience but assured delivery of the drug over a sustained period of time. The challenge with triamcinolone is determining the optimal dose and location to suppress inflammation and prevent macular edema without risking significant IOP rise. Xu et al.’s study brings us one step closer.

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**REFERENCES**


**OTHER CITED MATERIAL**


**Reply:** Shorstein et al. made interesting observations and comments on the location of the sub-Tenon triamcinolone injection. The assumed mechanism for steroid-induced elevation of IOP is that steroids increase aqueous outflow resistance by formation of reversible actin networks as well as by increased deposition of extracellular matrix within the outflow pathway. It is very likely that the magnitude of such steroid-induced effects would be in relationship to steroid levels in the aqueous humor. It is well documented that intravitreal triamcinolone causes more frequent IOP elevation than sub-Tenon triamcinolone. Investigators have shown that peak triamcinolone in the aqueous humor was 10 times higher after an intravitreal (4 mg) than after sub-Tenon (40 mg) triamcinolone.2,3 For prophylaxis of macular edema after the cataract procedure in patients with diabetes, posterior sub-Tenon should be the location of choice because the macula is the pharmacological target. Furthermore, to avoid triamcinolone suspension from spilling into the anterior segment, a concentrated smaller volume than the commonly used 1 mL or 500 μL may be preferable and beneficial in reducing the risk of IOP elevation. There is more vessel distribution in the conjunctiva and episclera at the anterior segment than that at the posterior segment. These vessels contribute to not only higher triamcinolone distribution into aqueous but also more triamcinolone absorption into the systemic circulation. With a small volume of a concentrated formulation of triamcinolone (40 or 20 mg in 0.4 mL), peak triamcinolone in systemic circulation is around 1 ng/mL, while it is over 30 ng/mL after a commonly used formulation (40 mg in 1 mL).4

In Shorstein et al.’s letter, a 2 mg dose of subconjunctival triamcinolone demonstrated equivalent prophylactic effect against macular edema as well as persistence of postoperative inflammation as compared to the steroid eyedrops, except for a small number of patients who had IOP spikes greater than 30 mm Hg. They observed a smaller or no IOP spike after changing the subconjunctival injection from a small volume (2 mg in 50 μL) to a large volume (3 mg in 300 μL), although the percentage of IOP elevation or statistical significance was not available. One possible explanation for their observation is that a concentrated or small volume injection helps to build up a concentration gradient for the drug to penetrate the eyewall into the aqueous humor or diffuse into arteries supplying the iris and ciliary body. In contrast, a large volume injection with low concentration leads to...
less intraocular penetration and more drug may diffuse into lower pressured veins at the conjunctiva and episclera with resultant higher systemic drug concentration, although they did not provide triamcinolone levels in the aqueous humor or plasma.

In summary, it seems that a concentrated small volume of triamcinolone suspension at the sub-Tenon of the posterior segment may be a better choice for prophylaxis of macular edema after a cataract procedure in diabetic patients. For alleviation of pain and procedure-related inflammation, anterior sub-Tenon or subconjunctival triamcinolone is of advantage over steroid eyedrops; however, further study is needed regarding the optimal formulation and location of the injection.—Lingyun Cheng, MD

REFERENCES

Primary descemetorhexis without endothelial keratoplasty to promote awareness and caution

We read with great interest the article by Kaufman et al., that describes a simple descemetorhexis to resolve corneal edema while at the same time not limiting future cataract extractions. Of most interest to us is this revolutionary technique to treat Fuchs endothelial dystrophy. These unanticipated cases of corneal clearing led us to publish a review concerning in vivo corneal endothelial regeneration, gathering all case reports of unexpected corneal clearing. Not only did we collect 47 patients who had such a descemetorhexis (65% clearing) but also 41 cases (80.5% clearing) with complicated endothelial keratoplasty and 12 cases of corneal clearing after troublesome cataract extraction (100% success).

We observed 2 findings recurring in this case report. First, we are convinced that removal of guttae is imperative for proper migration, which has also been shown by in vitro studies. The descemetorhexis was more successful in cases when the size was approximately 4.0 to 6.0 mm, suggesting this treatment is applicable for early-stage Fuchs endothelial dystrophy patients. Such a diameter removes all (central) guttae and leaves behind plenty of healthy cells.

The authors observed that “guttae surrounding the descemetorhexis…gradually increased and became confluent,” suggesting that the descemetorhexis might have been slightly too small, although we cannot argue with the result. We are curious as to their progression and whether they will accumulate over time, resulting in recurrent Fuchs endothelial dystrophy.

Second, we noted that corneal edema should resolve within a critical time period of approximately 3 months. Here, the patient’s cornea cleared within 6 weeks, which indeed classifies this patient a (fast-)responder. If no initial clearing is detected within the first 2 months, we believe a salvage endothelial keratoplasty should be performed. All salvage surgeries reported were successful and performed within 4.0 to 8.5 months after descemetorhexis.

Removal of the guttae, a limiting factor of migration, is not the only hurdle to overcome. In the cohort we studied, all cases with normal endothelium cleared, whereas only 65% of Fuchs endothelial dystrophy patients improved. We suspect that the migratory/proliferative capacity of the peripheral Fuchs endothelial dystrophy endothelium is further affected to different degrees, rendering outcomes unpredictable at present.

Regardless of migration, the authors mention that this phenomenon is mediated by an “unidentified intraocular chemical messenger.” Indeed, the mechanism in humans in vivo is not identified yet; however, we would like to mention that when looking to in vitro and neonatal animal studies, there are reasons to believe that an immature differentiation status of the peripheral endothelium and a process called contact inhibition in relation to upregulation of cyclin-dependent kinases are most likely involved.

To conclude, we are excited about studies in this specific domain and hope to elucidate the intrinsic mechanism together with clinicians and scientists in the coming years. Once we succeed to fine-tune this therapy, corneal donor lists would be shortened significantly as the largest patient population now are Fuchs endothelial dystrophy patients, as Kaufman et al. indicated.

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