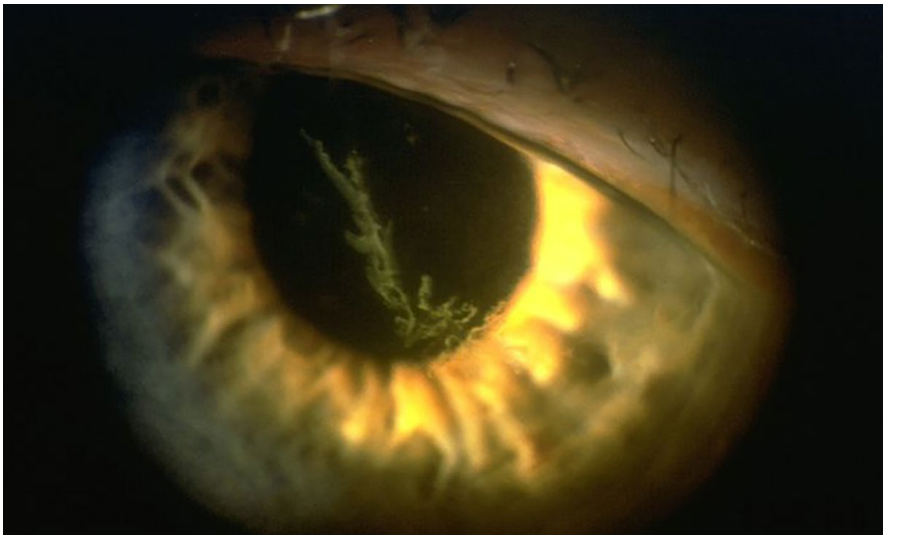

CORNEAL COMPLICATIONS. *Herpes zoster ophthalmicus can include corneal keratitis, in which the pseudodendrites differ in appearance from the dendrites that characterize herpes simplex keratitis.*

CORNEA

Vaccine Linked to Higher Risk of HZO Recurrence

THE RECOMBINANT ZOSTER VACCINE (RZV) Shingrix is linked to a higher risk of recurrence of herpes zoster ophthalmicus (HZO) in patients who have a prior history of the condition, according to recent research.[1]

The CDC recommends Shingrix for the prevention of herpes zoster (shingles) and related complications. The CDC recommends two doses of Shingrix separated by two to six months for immunocompetent adults aged 50 years and older: There is no specific amount of time a physician needs to wait before administering Shingrix to patients who have had herpes zoster. However, Shingrix should not be given to patients who are experiencing an acute episode of herpes zoster.[2] The authors wrote that patients who have had HZO should receive ophthalmic monitoring in the weeks and months following RZV vaccination in case the condition recurs.

Methodology. The retrospective cohort study published in *JAMA Ophthalmology* used outpatient pharmacy claims and medical data for people of all ages enrolled in commercial and Medicare Advantage plans through Optum Labs Data Warehouse. The researchers analyzed data from 16,408 patients—12,762 were unvaccinated and 3,646 received RZV. The investigators reported a 64% increased risk of recurrent HZO in people who received RZV compared with those who were unvaccinated.

"Since our study used insurance claims data, we don't have access to clinical information about these patients and what the recurrences looked like. We were very rigorous in our definition of a recurrence, though, as we required medication [information], including dose escalation of previous medications or new prescriptions, as well as an HZO diagnosis code with an optometrist or ophthalmologist within seven days," said lead author Nisha Acharya, MD, MS, the Elizabeth C. Proctor Distinguished Professor at the F.I. Proctor Foundation and Departments of Ophthalmology, Epidemiology, and Biostatistics at the University of California, San Francisco (UCSF).

She noted that medications used to treat HZO included systemic antivirals, ophthalmic corticosteroids, and systemic corticosteroids.

Why the findings matter. Dr. Acharya, who is also the Director of the Uveitis and Ocular Inflammatory Disease Service at UCSF, said that her team's findings raise important questions about the risk of recurrence of HZO following RZV vaccination—that their research is valuable because "the clinical trials that led to FDA approval of RZV with Shingrix excluded patients with prior herpes zoster and herpes zoster ophthalmicus."

Other epidemiological studies have shown that approximately 20% of patients with HZO can have recurrent chronic disease, she said, noting that "this might be due to virus reactivation with viral replication or result from immune activation directed toward viral antigens—remnants from the prior infection."

Bennie H. Jeng, MD, Director at Scheie Eye Institute at the University of Pennsylvania Perelman School of Medicine, said that the mechanism behind why HZO might recur in vaccinated individuals is that the immune system is most likely "ramping up" due to the presence of RZV.

"Although there is no active virus in

the vaccine, the immune response to the vaccine components could be driving upregulation of transcription of viral DNA that is already present in the cornea. This would result in reactivation of HZO," said Dr. Jeng, who is also Chair of the Department of Ophthalmology at the University of Pennsylvania Perelman School of Medicine. He was not affiliated with the UCSF research.

Addressing patient concerns. "HZO is a unique condition in that there can be recurrences of inflammation, and ophthalmologists have had questions about whether RZV is beneficial in patients with HZO. Our study helps to provide information on potential risks versus benefits of RZV for this

CATARACT

An Alternative Post-Cataract Therapy

A POST-CATARACT SURGERY REGIMEN OF INTRAVITREAL antibiotic corticosteroid (IVAS) injections plus topical nonsteroidal anti-inflammatory (NSAID) drops may be a viable alternative to traditional triple drop therapy, report researchers at the Dean McGee Eye Institute in Oklahoma City.[1]

A non-randomized, retrospective study—with no predefined primary measures and multiple comparisons—published in the *American Journal of Ophthalmology* compared two strategies, the IVAS-NSAID combination and a triple drop therapy—a combination of a topical antibiotic, corticosteroids, and NSAIDs—after cataract procedures. IVAS-NSAID therapy had postoperative outcomes and safety profiles comparable to the triple drop regimen.

Methodology. Study author Kamran M. Riaz, MD, Clinical Associate Professor and Director of Medical Student Research at Dean McGee Eye Institute, said to evaluate the efficacy of the IVAS-NSAID versus triple drop postoperative regimens, the researchers reviewed the charts of 2,143 eyes that had undergone uncomplicated cataract surgery between 2017 and 2022. Eyes were treated with either IVAS-NSAID (1,079) or triple drop (1,064) therapies.

The scientists looked at both preoperative and postoperative information. Preoperative details included patient age, medical and ocular histories, and iris color. Postoperative outcomes included best-corrected visual acuity (BCVA), IOP, and the need for IOP-lowering medications at one week, one month, and six months after surgery.

Postoperative complications—defined as persistent anterior chamber inflammation, persistent corneal edema (PCE), rebound inflammation, and cystoid macular edema (CME)—were compared between the two groups.

Outcomes. At all three time points, BCVA and IOP were similar between the IVAS-NSAID and triple drop therapy eyes. Postoperative complications occurred in 6.5% of the IVAS-NSAID treated eyes compared to 11.6% of triple drop treated eyes.

Questions answered. Although the study was not randomized, it suggests that IVAS injections may not cause elevated IOP postoperatively, particularly given surgeons' concerns for triamcinolone's well-known propensity to cause elevated IOP, said Dr. Riaz. In the two groups in the study, postoperative IOPs were comparable at all time points.

Dr. Riaz said that reducing the postoperative eye drop burden has numerous advantages over triple drop therapy, including better compliance, more convenience, lower cost for the patient, and a reduced risk of ocular surface damage from the drop preservative benzalkonium chloride.

In other findings, postoperative BCVA was similar at all time points. Also, risk factors of concern for postoperative inflammation, such as uveitis history, diabetic status, and epiretinal membrane, were not associated with increased inflammatory events in IVAS-NSAID eyes. There were no significant differences between the two groups when comparing persistent anterior chamber inflammation, rebound inflammation, CME, PCE, ocular discomfort, and new onset glaucoma.

"We were most pleased to see that CME rates were similar between the two groups," Dr. Riaz said.

Not for everybody. Patients in the IVAS-NSAID group who underwent femtosecond laser-assisted cataract surgery (FLACS) had increased rates of postoperative inflammation compared with triple drop patients who had FLACS. Also, IVAS-NSAID patients with darker irises had a higher incidence of CME, PCE, and rebound inflammation, according to the study.

Still, the researchers believe that these patients can receive an IVAS injection, although they may benefit from additional topical steroids postoperatively, the authors said.

Dr. Riaz, who has been using IVAS since 2014, said that nearly all of his patients receive an IVAS-NSAID injection, with the exception of glaucoma patients undergoing concurrent MIGS, young patients with severe myopia, and those with a history of retinal detachment.

Takeaway. IVAS-NSAID may be considered a safe alternative to topical drop regimens in non-FLACS patients and those with light irises, he said, adding that surgeons should exercise clinical judgment for glaucomatous eyes.

—Miriam Karmel

1 Mian OT et al. *Am J Ophthalmol.* 2024;260:37.

Relevant financial disclosures—Dr. Riaz: Ambrx: C; AudioDigest: L; Bausch and Lomb: C,L; CorneaGen: L; Exelixis: C; ImmunoGen: C; Medscape: L; PrecisionLens: L; Neumora Therapeutics: C.

group of patients," Dr. Acharya said.

Dr. Jeng said this study fills some knowledge gaps in understanding HZO recurrence in vaccinated people. "The purpose of giving RZV to a person who has had HZO is to prevent future episodes of herpes zoster in another location on the body," said Dr. Jeng.

"It is important for those patients who have had HZO and who have had RZV to be seen by an ophthalmologist within two months after vaccination, or sooner if symptoms occur," he said.

Even when a patient has a history of HZO, the vaccine is recommended, said Dr. Acharya. "It would be prudent to monitor them in the first couple of months post RZV in the event of recurrence," she added.

Questions for future study. Dr. Jeng said the study demonstrates an increased risk of reactivation immediately following vaccination, but it does not discuss the risk of reactivation over the long term.

"The vaccine is supposed to protect for 10 years, so it would be interesting to know if vaccinated individuals have a lower overall rate of reactivation over this longer period of time," he said.

Dr. Acharya said that while the study offered insights into RZV and HZO, it "does not provide a definitive answer," and it raises additional questions about the vaccine's risks and benefits in patients with a history of HZO.

She said it will be important to examine, from a clinical standpoint, "what these recurrences actually look like in the eye and what the consequence is in terms of vision. It would also be helpful to look deeper into whether particular subgroups of patients with HZO are more at risk for recurrences post RZV."

—Brian Mastroianni

1 Walia A et al. *JAMA Ophthalmol.* Published online Feb. 15, 2024.

2 https://www.cdc.gov/vaccines/vpd/shingles/hcp/shingrix/recommendations.html. Accessed Mar. 28, 2024.

Relevant financial disclosures—Dr. Acharya: AbbVie: S; Roche: A. Dr. Jeng: NEI: C.

RETINA

Investigating Retinal Capillary Stiffening in DR

RESEARCHERS HAVE IDENTIFIED A new mechanism underlying diabetic retinopathy (DR) pathogenesis, and they hope their finding may eventually help lead to the development of oral medications for early DR management—treatments that will stem the condition before it progresses.[1] The team includes researchers from Doheny Eye Institute, an independent, nonprofit research organization affiliated with UCLA Stein Eye Institute, in collaboration with vision researchers at UC Irvine.

Current treatments for late-stage DR may require laser surgery or repeated eye injections and "they are not effective in many patients," said Kaustabh Ghosh, PhD, Principal Investigator and Associate Professor of Ophthalmology at David Geffen School of Medicine, UCLA, and Doheny Eye Institute. "Tackling DR at the early stage is being recognized as the preferred approach," said Dr. Ghosh.

Looking at LOX. Inspired by cardiovascular research showing that diabetes induces stiffening in large blood vessels, Dr. Ghosh and colleagues wanted to investigate how retinal vascular inflammation and degeneration in diabetes might be mechanically regulated.

For their study, published in the journal *Diabetes*, the researchers aimed to identify the role of a collagen-cross-linking enzyme called lysyl oxidase (LOX) in diabetes-induced retinal capillary stiffening. To do this, they performed atomic force microscopy on retinal capillaries that they had isolated from eyes of both diabetic and nondiabetic mice.

"Using atomic force microscopy, a technique originally developed for physics and materials science research, we first showed that retinal capillaries in diabetic mice become stiffer in the early stages due to increased production of LOX," Dr. Ghosh said.

Diabetic mice displayed a two- to threefold increase in stiffness over nondiabetic mice, the researchers reported. And retinal capillary stiffening was found to persist in mice with longer-term diabetes (20-30 weeks in this study).

Exploring prevention of retinal stiffening. Next, the investigators evaluated LOX inhibition as a potential strategy for preventing retinal stiffening. They administered oral β-aminopropionitrile, a LOX inhibitor, to diabetic mice and assessed its effect on retinal capillary health and contrast sensitivity.

"Importantly, blocking this enzyme using an orally administered drug prevented the increase in retinal capillary stiffness in diabetic mice that, in turn, protected these capillaries from degeneration caused by toxic immune cells," said Dr. Ghosh.

Blocking this stiffness not only halted retinal capillary degeneration but also prevented the loss of contrast sensitivity, a common early hallmark of DR.

"We were pleasantly surprised to see that diabetic mice treated with the oral drug showed significant protection from this visual defect," Dr. Ghosh said.

Future research. These findings offer novel insights into DR pathogenesis by pinpointing retinal capillary stiffening as a key target for early management, said Dr. Ghosh.

These new findings provide rationale to develop new, sensitive imaging techniques to noninvasively detect subtle changes in retinal capillary stiffness, even before detectable capillary loss, he said.

"Success in this effort could have a huge impact on clinical DR management in the future," he said.

—Patricia Weiser, PharmD

1 Chandrakumar S et al. *Diabetes*. 2024;73:280-291.

Relevant financial disclosures—Dr. Ghosh: National Eye Institute/NIH: S; Research to Prevent Blindness: S; Stephen Ryan Initiative for Macular Research: S; W.M. Keck Foundation: S.

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