

When Anti-VEGF Injections Lead to Cataract Complications

Over the last decade, ophthalmology has witnessed the remarkable success of anti-VEGF injections in preserving and even improving vision in patients with retinal diseases. Given the treatment's track record of effectiveness and overall safety, it's no wonder that tens of millions of Americans now receive the treatments.

However, despite the injections' positive safety profile, adverse events do occur. In fact, recent studies in the field of cataract surgery have found an association between intravitreal anti-VEGF injections and posterior capsular rupture (PCR)—although the mechanism of action remains unclear. As researchers look further into the risk factors for this complication, it's evident that cataract surgeons must take particular care with this growing population of patients.

A Look at the Data

Highlights from selected studies reveal the following outcomes:

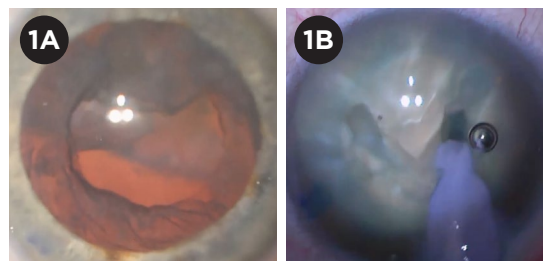
Surgical complications. A 2016 analysis of a 5% sample of Medicare claims data conducted by researchers at Duke University in Durham, North Carolina, found that prior intravitreal anti-VEGF injections were associated with a 126% increase in the risk of subsequent removal of retained lens fragments after cataract surgery.¹

In a second 2016 study conducted by members of the Duke team, including

Terry Kim, MD, 197 eyes of cataract surgery candidates with a history of intravitreal injections were compared with an equal number of matched control eyes without prior injection. Intraoperative complications, including PCR, were noted in 3% of the eyes that had received prior intravitreal injections. In contrast, 0% of the control eyes experienced complications during surgery.²

And in a 2017 study, Zaid Shalchi, FRCOphth, MRCP, MSc, and his colleagues at Moorfields Eye Hospital in London examined electronic health records on all cataract surgery procedures that took place between Jan. 1, 2012, and Aug. 31, 2015. The PCR rate for the entire cohort of 62,944 cataract surgeries was 1.04% of eyes (n = 650). However, for the subset of 906 eyes that had previously received intravitreal injections, the PCR rate was 1.88% (n = 17).³

Endophthalmitis. Intravitreal injections have also been associated with an increased risk of endophthalmitis after cataract surgery. In the Duke team's 2016 Medicare claims analysis, a history of prior anti-VEGF injections was the primary factor associated with increased risk of both acute



CASE REPORT. One of Dr. Oetting's patients had received several intravitreal injections for AMD. (1A) During cataract surgery, after an uneventful capsulorrhexis and hydrodissection of the lens, the nucleus became mobile and started to descend posteriorly through a posterior capsular defect. (1B) Dr. Oetting used the V-groove nucleofractis technique. He placed a posterior chamber IOL into the sulcus and positioned just the optic into the bag. Several days later, the patient underwent pars plana vitrectomy to remove the fallen nucleus.

endophthalmitis (diagnosed within 40 days of surgery) and delayed endophthalmitis (diagnosed from 40 to 365 days after surgery).¹

The researchers called for further analysis of Medicare claims data to determine if the increased risk of endophthalmitis is primarily an outcome of cataract surgery or can be associated with a history of intravitreal injections. Given the risk of the latter, the researchers urged cataract surgeons to increase "preoperative assessment, intraoperative caution, and postoperative vigilance" when treating patients with a history of intravitreal injections.¹

What's to Blame?

Dose response? Intuitively, it makes sense that the number of injections would play a role. And in one study, the

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risk of PCR increased with each intravitreal injection—and 10 or more previous injections were associated with a 2.59 times higher likelihood of PCR.⁴ But Dr. Shalchi and his colleagues did not find a dose response in their study, even in those who had received multiple intravitreal injections.³ Thus, he cautioned, the underlying association remains unclear.

Injection technique? Dr. Kim and his colleagues suggested that the physician learning curve with intravitreal injections may contribute to iatrogenic trauma. “Needle-induced lenticular trauma may be a result of variability in technique or skill of intravitreal injections associated with physicians of various levels of experience,” they wrote.²

Comorbidity? Dr. Shalchi also noted that patients who’ve received intravitreal injections may be at risk for PCR because of other factors, such as surgical challenges linked to difficulties in positioning AMD patients for surgery or the presence of brunescant cataracts.

Avoiding Trouble

As the research continues, some surgeons are taking steps to minimize the risk of complications.

Pre-op. As in all cataract surgery cases, it’s essential to evaluate the type and density of the cataract. “For example, if the patient has a posterior polar cataract, the surgeon needs to take precautions,” said Dr. Kim. “This would be the same for a patient with a capsular defect. The surgeon should also examine the nucleus to check the density of the lens as well as any other associated anomalies, like pseudoexfoliation.”

Thomas A. Oetting, MD, at the University of Iowa in Iowa City, suggested that surgeons consider using optical coherence tomography (OCT) or ultrasound imaging preoperatively to assess the posterior capsule and predict the likelihood of a tear. And Dr. Kim said that he often uses a red reflex test of the lens to help highlight any marks indicating injury from intravitreal injections.

When dealing with a patient with a potential injury to the posterior capsule, Dr. Oetting also cautioned that the

preoperative consent discussion should be modified to include the possibility of dropped lens material and subsequent vitrectomy.

Intraoperative strategies. “The surgeon needs a strategy for nucleofractis that does not involve hydrodissection,” Dr. Oetting said. Dr. Kim agreed, emphasizing the importance of avoiding hydrodissection and only using hydrodelineation techniques to avoid premature capsular rupture.

How dense is that lens? Overall, Dr. Oetting’s surgical approach depends on lens density:

- When the lens is fairly soft with a posterior capsule defect, he will “bowl out most of the nucleus and then try hydrodelineation and viscodissection to remove the remaining shell of lens material,” he said.
- When the lens is medium in density, he makes a 2 mm-wide groove and then cracks the lens in two. “After splitting the lens in half, I will try hydrodelineation. But with the lens split, fluid can get out from behind the lens, beneficially reducing the pressure on the capsule.”
- When the lens is dense, Dr. Oetting uses a V groove. “I make two grooves in the lens that join in the subincisional area, forming a V shape. Then without any hydro, I crack at the two grooves, breaking the lens into three pieces. I take the middle piece, which comes out easily. Then I use viscodissection, if needed, to move the two side pieces into the middle.”

Additional cautions. During lens removal, the surgeon needs to tread carefully while getting to the cortex—and during cortex removal, the surgeon should avoid grabbing the capsular bag, Dr. Kim said. He also avoids polishing the capsule in any case that involves a posterior polar cataract.

What’s Next?

Need for additional research. Clearly, further research is needed into the etiology of complications related to anti-VEGF injections and how to avoid or reduce their incidence.

Need for communication among clinicians. In the meantime, retina specialists can alert cataract surgeons if they suspect iatrogenic harm from an

intravitreal injection, Dr. Kim said. He stressed that communication between retina specialists and cataract surgeons is crucial to efforts to avoid or reduce the incidence of complications.

Need for alternative drug delivery. Alternative methods of delivering anti-VEGF medications might eventually offer a solution. For instance, intravitreal implants that provide a sustained drug delivery for months or years could result in fewer injections, thereby reducing the risk of complications during cataract surgery, Dr. Shalchi pointed out. He noted that this would be “in stark contrast” to current protocols, which require repeat injections. Alternatively, “finding anti-VEGF agents with a longer half-life may be a possible solution,” he said.

However, Dr. Shalchi concluded, “all of this presumes that the reason for increased risk of PCR [and other complications] is physical trauma from injection and not something else. The jury is still out on this one.”

1 Hahn P et al. *Eye (Lond)*. 2016;30(8):1101-1109.

2 Hahn P et al. *Ophthalmology*. 2016;123(2):309-315.

3 Shalchi Z et al. *Am J Ophthalmol*. 2017;177:77-80.

4 Lee AY et al. *Ophthalmology*. 2016;123(6):1252-1256.

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