

How to Give Intravitreal Injections

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Intravitreal injection enables highly targeted drug therapy, maximizing therapeutic drug delivery to the posterior pole while minimizing systemic toxicity. With the increasing use of intravitreal anti-VEGF agents in the treatment of neovascular age-related macular degeneration (AMD), diabetic macular edema, retinal vein occlusion, and various other retinal vascular disorders, intravitreal injection has become the most common ophthalmic procedure performed in the United States.

This review offers practical guidance for the delivery of intravitreal injections based on published, peer-reviewed literature, and expert consensus where evidence is lacking.

Overview

Background and indications. Intravitreal injection was first described in 1911 with the use of an air bubble to tamponade a retinal detachment. Triamcinolone acetonide (Kenalog) became the first intravitreal agent with widespread application, used as a treatment for macular edema associated with a variety of etiologies, such as diabetic retinopathy and retinal vein occlusion. It also was used as an adjunct to photodynamic therapy in the treatment of choroidal neovascularization (CNV) related to AMD.

Potential complications. These include intraocular inflammation, retinal detachment or perforation, traumatic lens damage, intraocular

hemorrhage, sustained ocular hypertension, and hypotony.¹

Of all postinjection complications, endophthalmitis has greatest potential to be visually devastating. According to studies assessing the safety profile of intravitreal injection, the rate of endophthalmitis has been found to be as low as 0.05 percent per injection.²

Contraindications. Active external eye infection (including conjunctivitis, meibomianitis, and significant blepharitis) is a contraindication to intravitreal injection and should be treated prior to injection.³ Glaucoma is common among patients requiring intravitreal injection and is not a contraindication to therapy despite the transient rise in intraocular pressure (IOP) that may occur following injection. Despite the theoretical increased risk of intraocular hemorrhage in patients on long-term anticoagulation who receive intravitreal injection, that risk has not been substantiated in studies.

Preinjection Risk Management

We recommend the following steps: 1) Apply a topical anesthetic; 2) apply 5 percent or 10 percent povidone-iodine drops and/or periocular povidone-iodine eyelid preparation; 3) insert a sterile speculum to separate the lids; and 4) reapply povidone-iodine immediately over the injection site prior to injection.

Local anesthetic. Nearly all injections are performed with local anesthesia, with topical anesthetic drops employed most commonly. Studies



PATIENT PREP. The patient should be instructed to direct his gaze away from the site of needle entry.

show no significant difference in injection-related pain with the use of topical drops, subconjunctival anesthesia, or topical anesthetic gel. There is some concern that viscous anesthetic gel may prevent adequate sterilization of the ocular surface.

Povidone-iodine. Povidone-iodine is the only agent shown to decrease bacterial colonization as well as the risk of endophthalmitis. Application of povidone-iodine to the conjunctival surface, eyelids, and lashes is recommended prior to introducing the sterile speculum. (The speculum prevents the needle tip from touching the lids or lashes prior to needle insertion.) Studies have found that a 5 percent povidone-iodine solution is as effective as 10 percent and is less irritating to the eye. There is controversy as to

whether using drops or a flush is more effective. We recommend reapplication of povidone-iodine immediately over the injection site prior to injection.

Antibiotics. The use of preinjection antibiotics is controversial. There is evidence showing decreased colonization of the ocular surface with the use of preinjection antibiotics, particularly in conjunction with povidone-iodine; however, there is no evidence to suggest that the use of preinjection antibiotics actually decreases the risk of endophthalmitis. Moreover, repeat injections are associated with more resistant flora.

Using a face mask. The use of a face mask for the injecting physician, injection assistants, and the patient is not currently considered standard of care.⁴ However, recovery of common respiratory flora from vitreous culture aspirates in patients diagnosed with endophthalmitis after intravitreal injection strongly supports efforts to minimize talking, coughing, or sneezing during the injection procedure.⁵

Bilateral injections. For bilateral injections, we recommend separate preparation of each eye. Separate instruments and medication vials should be used for each eye to decrease the risk of potential bilateral contamination.

IOP rise. A transient, volume-related rise in IOP is common following injection. There is no evidence to suggest that prophylactic IOP-lowering agents are effective in preventing the postinjection volume-mediated IOP spike, and their use is not recommended.

Peri-injection Risk Management

Injection volume. An injection volume of 0.05 mL is most commonly used. The maximum safe volume to inject without preinjection paracentesis is believed to be 0.1 mL to 0.2 mL. Larger injection volumes are uncommon, with two exceptions: the injection of gas for pneumatic retinopathy and the injection of multiple intravitreal agents in one session.

Needle selection. Needle size varies according to the substance injected, with 27-gauge needles often used for crystalline substances such as triam-

cinolone acetate and 30-gauge needles commonly used for the anti-VEGF agents ranibizumab, bevacizumab, and aflibercept. Studies suggest that smaller, sharper needles require less force for penetration and result in less drug reflux. Some physicians have begun using 31-gauge needles (the size commonly used by diabetic patients to test blood sugar and inject insulin), as smaller needle size may decrease patient discomfort.

Needle length between 0.5 and 0.62 inches (12.7 to 15.75 mm) is recommended, as longer needles may increase risk of retinal injury if the patient accidentally moves forward during the procedure.

Injection site. The patient should be instructed to direct his or her gaze away from the site of needle entry (Fig. 1). The injection is placed 3 to 3.5 mm posterior to the limbus for an aphakic or pseudophakic eye, and 3.5 to 4 mm posterior to the limbus for a phakic eye. Injection in the inferotemporal quadrant is common, although any quadrant may be used.

Sterile ophthalmic calipers or the hub of a sterile tuberculin syringe may be used to mark the injection site and to verify that adequate anesthesia has been achieved.

Injection technique. Some guidelines suggest pulling the conjunctiva over the injection site with forceps or a sterile cotton swab to create a steplike entry path. While this approach may, in theory, decrease reflux and risk of infection, a straight injection path is most commonly employed.⁶

After the sclera is penetrated, the needle is advanced toward the center of the globe and the solution is gently injected into the midvitreous cavity. The needle is removed, and a sterile cotton swab is immediately placed over the injection site to prevent reflux.

Postinjection Risk Management

Antibiotics. These are used by many physicians postinjection and often consist of a fourth-generation fluoroquinolone. However, as with preinjection antibiotics, there is no evidence showing clinical benefit of use. Ex-

perimental evidence suggests insufficient penetration into the vitreous to prevent infection. There is also an increase in resistant bacterial strains with repeated use.

IOP measurement. Postinjection IOP may be measured, especially for patients who have glaucoma, who are receiving large injection volumes, or who complain of pain or reduced vision. Some guidelines recommend a funduscopy examination after each injection to assess central retinal artery perfusion and identify injection-related hemorrhage or retinal detachment. Instead, many physicians employ functional tests such as a determination of at least counting fingers vision or assessment of absence of light perception.

Central retinal artery occlusion is indicated by the absence of light perception. In this case, paracentesis is indicated in an attempt to restore central retinal artery perfusion immediately. Vision is typically recovered quickly after decreasing IOP with rapid paracentesis. Routine pre- or postinjection paracentesis is not recommended for standard 0.05 mL intravitreal injections.

Complications. Transient, mild elevations of IOP are common, although IOP usually drops below 30 mmHg 15 to 20 minutes postinjection and returns to within 4 to 5 mmHg of baseline after 30 minutes. IOP normalization may take slightly longer in patients with glaucoma.

As noted above, endophthalmitis is the most feared complication of intravitreal injection, because of the potential for severe vision loss.

If postinjection endophthalmitis is suspected, recommended management includes immediate vitreous tap (for culture) and injection of intravitreal antibiotics (vancomycin 1 mg/0.1 mL and ceftazidime 2.25 mg/0.1 mL). Urgent vitrectomy may be considered.

Pseudoendophthalmitis is a sterile inflammatory reaction that does not involve true microbial infection. This has been reported most commonly following injection of triamcinolone acetate and bevacizumab. Unlike

true endophthalmitis, pseudoendophthalmitis occurs earlier, typically within one day of injection, and often subsides without specific treatment.

Follow-up. After the injection, all patients should be provided with information regarding the signs and symptoms of complications, such as eye pain or discomfort, redness, photophobia, and diminished vision. Patients should be instructed to contact the physician's office immediately if symptoms develop.

NOTE: For a slideshow of images illustrating the steps outlined in this article, go to www.eyenet.org. It will be available in mid-April.

- 1 Jager RD et al. *Retina*. 2004;24(5):676-698.
- 2 Bhavsar AR et al. *Am J Ophthalmol*. 2007; 144(3):454-456.
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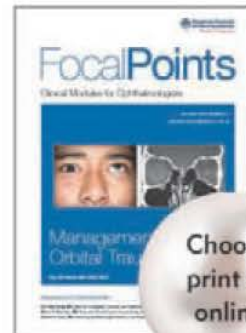
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