INTRAVITREAL INJECTIONS

Adapted from the
Consensus Statement of the Vitreo-Retina Society of the Philippines
on Intravitreal Injection Technique 2013[1]
and the
Preferred Practice Guidelines
of American Academy of Ophthalmology 2014[2]

BACKGROUND/DEFINITION

Intravitreal injections are the infusion of a pharmacologic agent into the vitreous cavity with the use of a syringe and needle, penetrating the sclera through the pars plana.

They are used to treat a variety of conditions. These include endophthalmitis, intraocular lymphoma, cytomegalovirus (CMV) retinitis, submacular hemorrhage, vitreous hemorrhage, macular edema due to retinal vascular occlusive disease, diabetic retinopathy and neovascular age-related macular degeneration (AMD)

The introduction of Anti-VEGF agents which include pegatanib (Macugen®), ranibizumab (Lucentis®), Aflibercept (Eylea®), . dexamethasone (Ozurdex®), an intravitreal implant and Bevacizumab (Avastin®) in an off-label use; has increased the frequency of intravitreal injections both locally and overseas.

The above mentioned intravitreal anti-VEGF agents provide a more effective treatment for center-involved Clinically Significant Macular Edema (CSME) from Diabetic Retinopathy and for macular edema associated with retinal vein occlusion and for Neovascular AMD.[2-18]

RECOMMENDATIONS FOR PATIENT CARE

The Eye MD performing the procedure should have received training in the technique from a training institution accredited by the Philippine Board of Ophthalmology .

The specific guidelines for intravitreal injections have been developed by the VRSP in its Consensus statement .[19,20]

PROCEDURE

Pre- injection:

1) Establish an accurate diagnosis
2) Develop a treatment plan
3) Obtain informed consent.[21] The consent form should include the name of the drug to be injected, the indication for injection, the potential risks and benefits of the use of anti-VEGF agents and of the procedure itself. These must be fully explained and understood by the patient. A consent form specific for an individual drug is likewise recommended.
4) Assess the patient for any condition that could increase complications from the intravitreal injection (e.g. pre-existing glaucoma, active infection, allergies to povidone-iodine)[22] Currently, there is no data that indicates anticoagulant use will affect visual outcomes after intravitreal injection. However, there is an increased likelihood of subconjunctival hemorrhage at the site of injection.
5) Medical Clearance.

a. The benefits, risks and indications of anti-VEGF injections should be carefully reconsidered in the following situations:
    i. Patients with a history of myocardial infarction, any cardiac event requiring hospitalization, stroke, transient ischemic attack, or treatment for acute congestive heart failure within the past 4 months.
    ii. Major surgery within 28 days
    iii. Uncontrolled hypertension
    iv. Pregnancy
b. Necessity for medical clearance is at the discretion of the attending ophthalmologist. While arteriothromboembolic events have been reported, the direct causative relation between stroke and intravitreal anti-VEGF injection use has not been established.

Injection

1) Clinical setting of care. It is recommended that the procedure be performed in an operating theater or in a room/facility specifically dedicated for intravitreal injections.
2) Surgical Site Preparation
    a. Intravitreal injections are intraocular procedures that merit equal attention to adherence to principles of asepsis and sterile technique as for conventional intraocular surgeries.
    b. As part of the World Health Organization Surgical Safety Checklist, “time-out” or surgical site marking is recommended.
    c. There is no evidence to support that the instillation of a topical antibiotic solution prior to injection reduces the risk of subsequent intraocular infection
    d. Pre-operative disinfection of the peri-ocular skin with 10% povidoe iodine and a minimum exposure time of 3 minutes is suggested. 10% aqueous chlorhexidine may be used as an alternative in patients with hypersensitivity to povidone iodine.
    e. The use of newly opened bottle of topical anesthetic is recommended.
    f. 5% povidone iodine should be applied onto the conjunctival cul-de-sac or lower fornix with a minimum contact time of 30 seconds.
    g. The use of a sterile solid-blade lid speculum or any type of occlusive dressing is recommended to isolate the lashes from the site of injection.
3) Injection of a Single Eye
    a. As part of good surgical practice, the use of a sterile eye sheet or equivalent drapes, the donning of sterile surgical gloves and the wearing of a surgical mask are advised.
    b. The injection site should be 3 to 3.5 mm from the corneoscleral limbus for aphakic and pseudophakic eyes, and 3.5 to 4 mm for phakic eyes.
    c. The use of a sterile 30-gauge needle is recommended for intravitreal injection of anti-VEGF drugs
    d. The needle should be inserted transconjunctivally through the sclera at the pars plana with the tip aimed toward the center of the globe to avoid the posterior lens.[2]
    e. Once the needle is withdrawn, the ophthalmologist may apply a sterile cotton applicator to prevent reflux of liquid vitreous.
    f. The ophthalmologist should assess central retinal artery perfusion by checking for gross vision or venous pulsation via indirect ophthaloscopy.
    g. Anterior chamber paracentesis may be performed in cases with evidence of a sustained rise in intraocular pressure.
    h. There is no evidence that the instillation of post-injection antibiotics confers additional benefit in reducing the risk of endophthalmitis following intravitreal injections.
4) Bilateral same day injection.
    a. Each eye should be prepared with povidone iodine separately.

b. A completely new and different surgical set of sterile eye sheet, lid speculum, instruments, 30-gauge needle and syringe should be utilized.
c. Whenever feasible, separate vials of medication with different log numbers should be used for each eye.

Post-injection Management

1) Post injection follow-up is recommended within 7 days.
2) Patient should be instructed to return sooner if with symptoms of inflammation or infection.
3) Examine for retinal tears/detachment/ Central Retinal Artery Occlusion (CRAO), lens trauma, vitreous hemorrhage, etc
4) Inform the patient of post-operative complications
5) Determine the need for additional procedures. This includes assessment of visual function, response to initial therapy, status of the fellow eye and results of ocular imaging studies.

RISKS

Risks or post-operative complications of intravitreal injections can be vision threatening and will require prompt diagnosis and treatment, possibly additional major surgery. These include: endopthalmitis,[23] severe inflammatory reactions, cataracts, retinal tears, retinal detachment and vitreous hemorrhge,[24] Increased Intraocular Pressure (IOP), CRAO, vein occlusions. Rarely Retinal Pigment Epithelial tears, uveitis, optic atrophy, corneal epitheliopathy, maculopathy, and anaphylactic reaction to the injected agent. [24-26]

Possible iatrogenic injuries include lens injury, corneal abrasion, intraocular hemorrhage and retinal tears. [22,23] These injuries may eventually need additional surgery such as cataract removal, repair of retinal tear and/or retinal detachment.[18,24,27,28]

During and immediately after the injection, intra-ocular pressure (IOP) can increase temporarily. The ophthalmologist may need to reduce the IOP. [29]

Occlusion of the central retinal artery may occur . An anterior chamber tap[30] may be needed which in itself carries the same risks as the intravitreal injection ie. Cataract, endophthalmitis,

COMPLICATONS/OUTCOME

Intravitreal injections of various agents have been reported in numerous studies. The overall risk of complications is low in the hands of experienced ophthalmologists. [24,30]

Potentially life threatening complications from intravitreal injections have also been reported. The Anti-VEGF's have been reported to be associated with thromboembolic events, eg. stroke, myocardial infarcts angina[31] hypertesive crisis. [32]

The ophthalmologist needs to monitor the possibility of these systemic side effects as well.

The optimal outcome for a patient after intravitreal injections depends on an accurate diagnosis, screening patients for possible systemic adverse events and intraocular events as well as considering alternative methods. Outcome is likewise dependent on the technical skill of the ophthalmologist. Moreover, the knowledge and skill of the ophthalmologist to determine post-operative ocular and systemic side effects will reduce vision threatening complications.

A meta-analysis of the literature between January 2005 and May 2012 found that the rate of endophthalmitis was (0.056%) based on 197 of 350,535 intravitreal anti-VEGF injections. The

most common organisms isolated were coagulase-negative Staphylococcus (38.24%) and Streptococcus species (29.41%).[33] Another meta-analysis of the literature from 2005 to March 2010 found a rate of 0.049% (52/105,536 injections). The organisms identified in culture positive cases were Staphylococcus in 65.4% and Streptococcus species in 30.8% of the time.[34] Unless treated effectively in a timely fashion, endophthalmitis can result in severe vision loss or blindness. Treatment includes appropriate antibiotic therapy and possible surgical procedures, such as a pars plana vitrectomy. In a case series and case control study of 27,736 injections performed between 2009–2010, no modifiable risk factors to prevent endophthalmitis were identified.[35]

A multicenter case series found the incidence rate of rhegmatogenous retinal detachment to be 0.013% (5/35,942) per injection.[36] Other studies have identified sustained intraocular pressure as a complication to be monitored after injections. [37-39] Hemorrhages, including subconjunctival, choroidal and subretinal hemorrhages, have been reported in a systematic review of the literature from 2005 to 2012.[40]

POLICY

Patients who will need trans-pars plana intravitreal injections deserve the care of an ophthalmologist who is knowledgeable, skilled and comfortable in the diagnosis and comprehensive management of retinal diseases for which anti-VEGF treatment is indicated. The ophthalmologist should be adept at minimizing risks and recognizing the potential complications that may eventually need major surgical intervention.

As the sole physician organization of vitreoretinal specialists in the country, the Vitreo-Retina Society of the Philippines (VRSP) in coordination with the Philippine Academy of the Ophthalmology (PAO) recommends that all intravitreal injections should be performed by ophthalmologists certified by the Philippine Board of Ophthalmology (PBO) and who have access to a retinal specialist.

DISCLAIMER

This statement is subject to re-evaluation and revision as new evidence-based studies on intravitreal anti-VEGF become published and new practice patterns evolve.

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