Intravitreal Injections: Guidelines for Injections in Noninfective Retinal Conditions

Pradeep Susvar
Department of Vitreoretina, Medical Research Foundation, Sankara Nethralaya, Chennai, Tamil Nadu, India

Correspondence: Pradeep Susvar, Department of Vitreoretina, Medical Research Foundation, Sankara Nethralaya, College Road, Chennai-600006, Tamil Nadu, India, e-mail: drpds@snmail.org

ABSTRACT

Intravitreal injection is fast becoming the most ‘sought after’ treatment modality for many medical retina conditions. Also, many guidelines have evolved for dispensing these injections. These guidelines may differ from region to region as far as environmental factors and sterility is concerned especially in developing countries. There are few grey zones in the periprocedural aspects of these injections which need to be cleared. Our guidelines help in these situations for a simplified and safe administration of the intravitreal injections.

Keywords: Intravitreal injections.

INTRODUCTION

With the advent of anti-VEGF injections and steroids as treatments for various retinal disorders, a significant time of the vitreoretinal surgeon is being spent on administering these injections in one’s practice. There is need for clarity regarding all aspects of ‘periprocedural care’ to be inculcated during the procedure. Though there is no standard of care for this invasive procedure, what follows is probably an acceptable approach. Appropriate application of these guidelines should reduce the risk of these procedures. These guidelines can be divided into preinjection, peri-injection and postinjection management.

Important indications for anti-VEGF therapy are:
- Choroidal neovascular membrane
- Macular edema secondary to diabetes, vein occlusions, etc.
- In proliferative vascular retinopathy, especially before surgery
- Retinopathy of prematurity
- Idiopathic polypoidal choroidal vasculopathy.

Indication for triamcinolone acetonide:
- Macular edema secondary to diabetes, vein occlusion, etc.
- CME in chronic uveitis.

Preinjection antibiotics: Where possible it is a general practice to instill antibiotics topically for a period of 2 days before injection. However, there are many practitioners who dispense away with this step. It is impossible to prove the benefit, or otherwise, of preinjection antibiotics. However, we feel that given the fact that this is an invasive step, when possible, it may be preferable to use topical antibiotics a day or two before injection.

Antiplatelet agents or oral anticoagulants do not require to be stopped. Active external ocular surface infection, such as blepharitis, conjunctivitis, active herpetic keratitis, etc. need to be controlled and treated before the use of the intravitreal therapy. Pre-existing glaucoma needs to be ruled out for intravitreal steroid. Allergy to povidone iodine should be enquired into.

PREPROCEDURAL ISSUES

1. Informed consent: Informed consent should mention the drug being administered and the complications specific to the drug as well as the injection process. Specifically, the risk of endophthalmitis must be mentioned. The possibility of nonresponsiveness of the disease to the injection and the frequent need for repeat injections should be mentioned.

2. Confirmation of the patient identity, eye and the medication to be injected (Beware: In a large unit wherein all intravitreal injections are given in one dedicated facility by one person, there can be scope for mix-up between identity of patients and the eye to be injected).

3. Pupillary dilatation

4. Where to perform the injection: Outpatient set-up, dedicated semi-sterile area or operation theatre?

Most of the prospective clinical trials involving the anti-VEGF agents did not insist on an operating theatre set-up for administering the injections. In the developed countries, the injections are routinely administered in the consultation suite. In some hospitals, a separate semi-sterile area has been created for the purpose of intravitreal injections.

Considering the environmental factors (dust and pollution) and sometimes less than acceptable personal hygiene, in the developing countries, we recommend a sterile/semi-sterile area for the injections—at least a segregated dedicated facility, if not a full blown operation theater set-up.
INJECTION PROCEDURE

Standard Eye Preparation

1. Topical anesthetic applied to the eye twice at 5 minutes interval. Additionally, one usually placed a cotton tipped applicator soaked in anesthetic solution at the site of proposed injection for a minute
2. 5% povidone iodine drops applied in the conjunctival cul-de-sac
3. Lid speculum must be used to isolate the eye lashes from the site of injection.

Issues

1. Need to prep the eyelids and skin in the vicinity with 10% povidone iodine. We recommend this step although a few surgeons believe that this is superfluous.
2. Need to use sterile drape to isolate the eye. Considering that there is no flow of fluid, use of sterile drape around the eye is optional.

Preparation of the Injection

1. Drugs dispensed in single dose vials or used for one injection, e.g. ranibizumab (Lucentis), triamcinolone acetonide. The central aluminium disk on the seal of the vial is removed. The surface of the rubber cork is cleaned with alcohol swab and a drop of povidone iodine is placed on it for a period of 2 to 3 minutes. The povidone iodine is removed with a sterile cotton tipped applicator by soaking the fluid but avoiding back and forth brushing. A sterile 1 cc syringe connected to a 26G needle is used to aspirate the drug. Lucentis comes with a syringe and special long needle that reaches the bottom of the vial. The 26G needle is exchanged with a 30G needle and the excess of the drug is discarded.
2. Drugs dispensed in preloaded syringe, e.g. pegaptanib sodium (Macugen): No special preparation is required.
3. Drugs dispensed in multidose vial, e.g. bevacizumab (Avastin):
   a. Single dose sterile injections dispensed by pharmacy—no special preparation needed
   b. One vial distributed among many patients by the ophthalmologist: The accepted practice would be to divide the vial among as many syringes as required under sterile conditions (in the operating room, after surgical scrub and keeping the syringes with capped needles) in a sterile tray with lid. The vial is prepared similar to Lucentis or triamcinolone acetonide before drawing the drug (sterilizing the rubber cork with povidone iodine). All the patients are injected in one lot within 20 to 30 minutes to minimize the amount of time the loaded syringes are kept in the tray. There is no scientific justification to preserve the loaded syringes in the tray for use next day or beyond, since there is no preservative.

SURGEON’S PREPARATION

The least that the ophthalmologist can do is to don a pair of sterile gloves. Handling of the speculum and syringe becomes easy with no risk of accidental contamination. Hands can be disinfected with a surgical scrub or antiseptic hand rubs or both before donning the gloves.

ADMINISTRATION OF THE INTRAVITREAL INJECTION

Site of Injection

There is no preferred quadrant for injection. Any accessible quadrant can be used. While injecting triamcinolone acetonide, inferior quadrants are preferred to minimize the spread of the opaque drug throughout the vitreous cavity. Anteroposteriorly, a site 3 to 3.5 mm from limbus is chosen.

The eye wall is stabbed with the needle directly and once the needle has penetrated to about 5 to 6 mm, the hub of the needle is stabilized with one hand while the piston is pushed with the other. This two-hand technique will avoid accidental injury to lens, especially if the patient suddenly rolls the eye upwards.

Once the needle is withdrawn, any of the following may happen:
1. A bleb may form at the site of injection due to the liquid vitreous coming out
2. A spot of subconjunctival hemorrhage may form at the site of injection
3. More fluid than usual may leak in an already vitrectomized eye.

However, the leak is never significant and no special measures are required except perhaps a transient application of cotton tipped applicator at the site of injection.

POST-INJECTION PROCEDURE

It is a good practice to do indirect ophthalmoscopy after any intravitreal injection. If not, at least the vision should be grossly tested by show of fingers. This ensures that the disk is perfused. In a few cases (especially after injection of triamcinolone acetonide which requires 0.1 ml to be injected vs others that need only 0.05 ml), there can be transient central retinal artery occlusion. The patient will complain of total blackout immediately after injection. One need not panic and unnecessarily perform a paracentesis. Waiting for a few seconds will invariably enable the central retinal artery to open up as evidenced by return of vision.

A drop of povidone iodine can be placed in the conjunctival cul-de-sac and the eye patched for 1 hour. The patient can be instructed to use antibiotic drops for 2 to 3 days after the injection (this step is also considered unnecessary by many surgeons and is optional).

ISSUES

Should the surgeon see the patient on the day after injection?
Many surgeons instruct the patient to come back only, if there is vision disturbance or on the next scheduled visit after 1 month or so.

We recommend a routine examination a day after injection for the following reasons:
1. The level of vision can be variable at the time of injection depending upon the condition of the eye, and hence the ability of the patient to detect moderate levels of drop in vision will also vary.
2. The level of understanding of individual patients can vary, especially, if one is dealing with illiterate or semiliterate population.
3. An abnormal reaction without significant drop in vision can alert the clinician to keep a close follow-up while the patient may be blissfully unaware of the trouble that is brewing. The first post-injection day examination need not be thorough. A slit-lamp examination is all that is needed to make sure that no signs of abnormal inflammation are missed. Intraocular pressure need not be recorded at this stage since steroid induced raise in intraocular pressure usually takes time to build up.

Further Follow-up
This would depend on the disease, the type of drug injected and the long-term plan for the individual patient. All patients who had steroid injection should have IOP and lens status monitored periodically. In general the follow-up will be after one month. At this visit, the examination will include optical coherence tomography in addition to the clinical evaluation. The efficacy of the drug is best judged at this stage and any need for further treatment or change of strategy is decided.

REFERENCES