Complications And Adverse Events Associated With Intravitreal Injection

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- Intravitreal injection (IVI) is usually a safe procedure, however some rare complications, which may be sometimes catastrophic, can still occur.
- These complications may be related to :

1- The technique and settings of the injection

2- The injected substances

3-The patient's systematic condition.

1- complications related to the technique:

- Endophthalmitis
- Rhegmatogenous retinal detachment
- Intraocular pressure elevation
- Ocular hemorrhage
- Injury of the lens

2- complications related to the substance:

A- steroids:

- Floaters
- Cataract and glaucoma

B-Anti VEGF:

- Intraocular inflammation

C- Antibiotics :

- corneal or retinal toxicity

D- Systemic complications

1- complications related to the technique:

- Endophthalmitis
- Rhegmatogenous retinal detachment
- Intraocular pressure elevation
- Ocular hemorrhage
- Injury of the lens

Endophthalmitis

Infectious endophthalmitis remains one of the most devastating complications of intravitreal injections (worst nightmare).

In multicenter clinical trials with anti-VEGF therapy the incidence of endophthalmitis per patient has been reported to range from 0.019 to 1.6% (1/540 - 1/60)

The rate of endophthalmitis seems to be the same among different anti-VEGF agents, different injection settings, and different geographical locations.

Endophthalmitis caused by Streptococcus species was significantly more frequent after intravitreal injection than after intraocular surgery.

Noncompliance with recognized standards, poor aseptic technique, active external infection(blepharitis) and eyelid abnormalities such as ectropion should be considered

The most important factor in reducing the risk of endophthalmitis following intravitreal injection is attention to issues before, during, and after the injection. special attention should be focused on aseptic preparation of the bevacizumab syringes.

- The use of 5% povidone– iodine in the conjunctival fornices is an accepted universal practice and is a strong recommendation for preventing endophthalmitis.

Topical antibiotics (pre /post injection) have been demonstrated to significantly reduce ocular surface bacteria, but have not been proven to have a significant impact on reducing the risk of endophthalmitis.

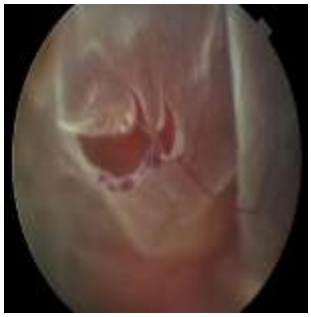
- During the injection procedure, the use of a sterile lid speculum is recommended to avoid needle contact with lids and lashes.
- The use of a sterile drape is optional but gloves, part of universal precautions, are appropriate.
- Recent studies emphasize the use of face mask and avoidance of talking on the reduction of bacterial contamination.

- Those performing intraocular injections should consider taking precautions against droplet contamination, such as not talking, talking with the mouth turned away from the field, or wearing a mask, especially if experiencing an upper respiratory infection, during intravitreal injection

Rhegmatogenous Retinal Detachment

The overall incidence of rhegmatogenous retinal detachment (RRD) after intravitreal injection of anti-VEGF agents is low (0 to 0.67%) (0 – 1/149).

The etiology of RRD after intravitreal injection have been proposed to be an induction of posterior vitreous detachment or an incorrect technique of injection the precise site of injection (3.5–4mm posterior to the limbus), using smaller gauge needles, and tunnelled insertion of the needle for avoiding vitreous wick and reflux.



Intraocular pressure elevation

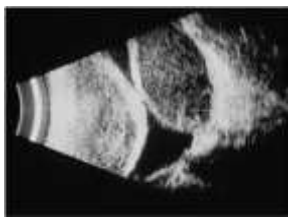
- Acute rise of intraocular pressure (IOP) after intravitreal injection is injection procedure-related and lasts a few hours at most.

- Corticosteroids induce physical and mechanical change in the trabecular meshwork architecture, resulting in an increase in resistance to outflow of aqueous humor.

- Patients with pre-existing glaucoma have higher rates of IOP elevation compared with those without pre-existing glaucoma.
- Several theories, including a pharmacologic effect of VEGF blockade, an inflammatory mechanism/ trabeculitis, impaired outflow owing to protein aggregates/silicone droplet debris, and damage to outflow pathways due to the repeated trauma and/or IOP spikes associated with the injection procedure.

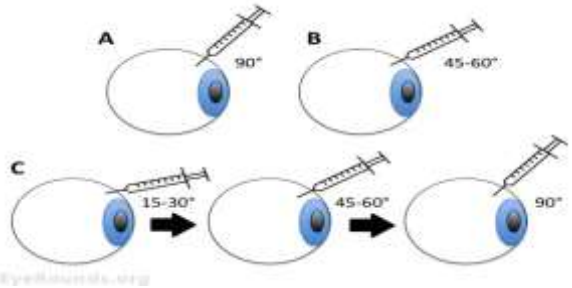
Ocular hemorrhage

- Subconjunctival hemorrhage has been reported to occur in nearly 10% (1/10) of injections, with higher frequency in patients who were receiving aspirin.
- There has been a report of a massive choroidal detachment/ hemorrhage following intravitreal bevacizumab injection. Massive subretinal hemorrhage has been reported after ranibizumab and bevacizumab injections.



Injury of the lens

- An injury to the lens occurred because the needle hit the posterior capsule of the lens during the intravitreal injection.



2- complications related to the substance:

A- steroids:

- Floaters
- Cataract and glaucoma

Floaters

- Patients receiving intravitral injection medications often report seeing floaters particularly in association with triamcinolone acetonide.

Cataract

- local corticosteroids inducing cataracts is due to release of growth factors, such as fibroblast growth factor-2, insulin, insulin-like growth factor-1, epidermal growth factor, transforming growth factor-b, lens epithelium-derived growth factor, platelet-derived growth factor and bone morphogenic proteins, as well as a local activation of glucocorticoid receptors in the lens, which, through their effect on the lens epithelial cells, cause a down regulation in apoptosis and increased proliferation and migration, resulting in aberrant cells and the formation of a posterior subcapsular cataract.

B-Anti VEGF:

- Intraocular inflammation
- Rare complications

Intraocular inflammation

- is one of the main ocular adverse events associated with intraocular anti-VEGF pharmacologic agents. In the large clinical trials of intravitreal injection of ranibizumab for AMD, the rates of significant ocular inflammation were 1.4–2.9% (1/70- 1/35). The reported rate after bevacizumab injection is lower (0.09–0.4) (1/1100 -1/250); however, several lot-specific severe ocular inflammatory events were reported.

- It may be difficult to differentiate sterile intraocular inflammation from infectious endophthalmitis. Time of presentation, presence of pain, and the severity of clinical findings were helpful. The symptoms began at an average of 2.55 days (range, 1–6 days) after injection in the endophthalmitis group and less than 1 day in the acute intraocular inflammation group.

- Rare ocular adverse events include anterior ischemic optic neuropathy after bevacizumab injection, retinal venous occlusions after bevacizumab injection, retinal artery occlusions, hemorrhagic macular infarction, development or exacerbation of ocular ischemic syndrome, and sixth nerve palsy following bevacizumab injection.
- Rare systemic events include formed visual hallucinations, erectile dysfunction, and acute decrease in kidney function

C- Antibiotics :

- corneal or retinal toxicity

- Corneal opacification and retinal toxicity
- Retinal toxicity with aminoglycosides, most notably gentamicin (even as low as 0.1mg)
- ***Macular infarct***

3- Systemic complications

Systematic complications

- Thromboembolic events
- Myocardial infarction
- Stroke
- Hypertension
- Kidney disease

Considerations in specific diseases

Diabetic retinopathy and retinal vascular occlusions

progression of tractional retinal detachment (TRD), Ghost cell glaucoma has been reported following the use of bevacizumab as an adjunct to vitrectomy for PDR

Age-related macular degeneration

Retinal pigment epithelium (RPE) tears may occur spontaneously or after therapeutic intervention in patients with Pre-existing RPE detachment (PED) or fibrovascular PED is considered the major risk factor for RPE tear AMD

ROP

The fibrotic component of neovascularization may accelerate after inhibition of angiogenesis and the retinal detachment might worsen

Eales' disease

Intravitreal bevacizumab injections may be associated with the development of secondary RRD in patients of Eales' disease within 7 days of injection