Adverse events and complications associated with intravitreal injection

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- Endophthalmitis
- Rhegmatogenous retinal detachment
- Intraocular pressure elevation
- Ocular hemorrhage
- Floaters
- Cataract and glaucoma
- Injury of the lens
- Systemic complications

Endophthalmitis

Infectious endophthalmitis remains one of the most devastating complications of intravitreal injections. 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%

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

Recent studies reported that endophthalmitis caused by Streptococcus species was significantly more frequent after intravitreal injection than after intraocular surgery

The most important factor in reducing the risk of endophthalmitis following intravitreal injection is attention to issues before, during, and after the injection. Following the recent outbreaks of post-intravitreal bevacizumab injection endophthalmitis, special attention has been 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 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

- It may be difficult to differentiate sterile intraocular inflammation from infectious endophthalmitis. In one study the 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

Rhegmatogenous Retinal Detachment

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

- 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% 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.

Floaters

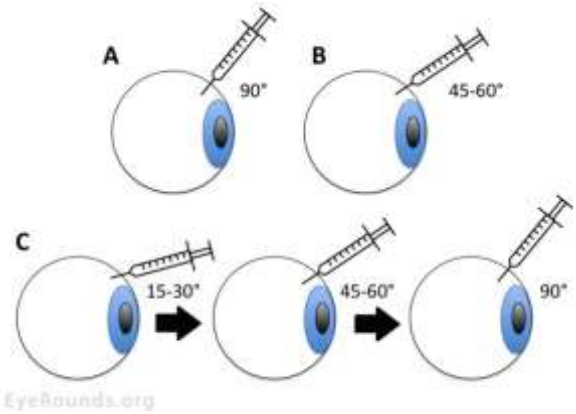
- Patients receiving intravitral injection medications often report seeing floaters particularly in association with triamcinolone acetonide.

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.

Injury of the lens

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



Systemic effects

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

Adverse events following intravitreal anti-VEGF injections: 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

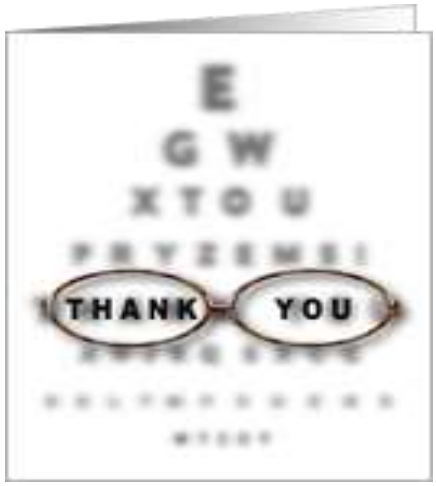
Age-related macular degeneration

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

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