

The role of intravitreal anti-vascular endothelial growth factor (VEGF) in diabetic retinopathy

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What is vascular endothelial growth factor (VEGF)?

VEGF is a protein that occurs naturally in the body. When our tissue is not getting enough oxygen, it releases VEGF that signals the need for additional oxygen.

Our blood vessels will sense the presence of VEGF and grow new vessels in response, a process known as angiogenesis. This brings a new pathway of blood supply into the oxygen needed tissues.

Angiogenesis is essential for normal development, wound healing, and reproductive functions in adults. Abnormal regulation of angiogenesis has been implicated in the pathogenesis of several disorders, including cancer, diabetes, and macular degeneration.

What is the association between VEGF and diabetic retinopathy?

VEGF plays an essential role in the development of both proliferative diabetic retinopathy (PDR) and diabetic macular oedema (DMO), both of which are leading causes of visual impairment in adults in the developed world.

Poor blood glucose control in diabetes causes damage to the blood vessels in the retina. As the disease progresses, the retina becomes deprived of oxygen and increases the secretion of VEGF. VEGF stimulates the formation of fragile abnormal vessels in the retina and the anterior chamber of the eye.

Without timely treatment, these new vessels can bleed, cause fibrovascular proliferation and tractional retinal detachment (retinal detachment due to contraction of fibrous tissue), as well as neovascular glaucoma (increased pressure in the eye), ultimately leading to blindness.

VEGF contributes to DMO by causing increased permeability in the capillary walls, allowing leakage of fluid into the macula (the part of the retina that is responsible for central vision and seeing fine details), resulting in significant visual impairment.

What are anti-VEGF agents?

Anti-VEGF agents are drugs that block the activity of VEGF, and hence cause the regression of these abnormal new vessels and reduction of vascular leakage. Anti-VEGF therapy has been used with success in the treatment of wet age-related macular degeneration (ARMD).

Current treatment options for PDR and DMO are limited, consisting primarily of laser photocoagulation and vitrectomy.

Although these treatments generally reduce loss of visual acuity, they are destructive, associated with undesirable side effects, and treat only the later stages of the disease.

Early studies have shown that anti-VEGF therapy is a promising treatment option for PDR and DMO.



What are the types of anti-VEGF drugs available?

The anti-VEGF drugs currently available include:

- Macugen (Pegaptanib)
- Lucentis (Ranibizumab)
- Avastin (Bevacizumab)

How is anti-VEGF therapy administered?

Anti-VEGF therapy is administered via an intra-vitreous injection, that is, an injection through the sclera (the white of the eye) into the vitreous cavity (the inner cavity of the eye). It is done under sterile conditions to minimise the chance of an infection, and is carried out under topical (eyedrop) anaesthesia.



A small amount of the drug (Lucentis 0.05 mls, 0.5 mg, Avastin 0.05 mls, 1.25 mg) is injected via a very fine needle, and the entire procedure takes a few minutes. The patient may notice some floaters in the eye after the injection. Repeated injections may need to be administered a month apart.

What are the risks involved?

Intra-vitreous anti-VEGF injections have been safe with little reported complications. The rate of adverse effects in the eye is less than 1.5% per patient per year. Potential ocular adverse effects include:

- Endophthalmitis (serious inflammation of the eye)
- Cataract

- Vitreous haemorrhage (bleeding into the inner cavity of the eye)
- Retinal detachment

Although generally not reported, anti-VEGF drugs may potentially enter the systemic circulation and cause the following systemic adverse effects:

- Hypertension
- Delayed wound healing
- Increased cardiovascular events such as heart attack and stroke

We await clinical trials to evaluate the long-term safety of anti-VEGF therapy.

References:

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