Class Room Article

What is Anti - VEGF

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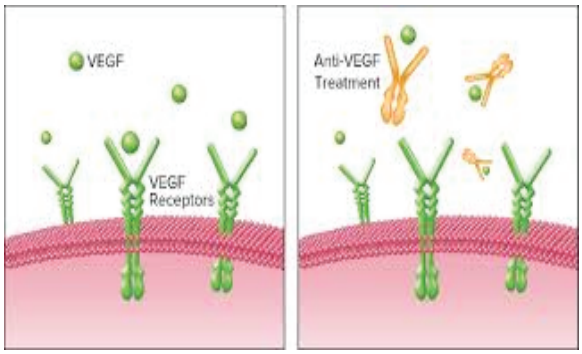
Vascular endothelial growth factor[1] antagonists play an important part in treatment of retinal disorders. To know more about this, a brief explanation of what is vascular endothelial growth factor is necessary. VEGF is a protein which causes vasculogenesis and angiogenesis. Vasculogenesis is important in development of vessels in embryo whereas angiogenesis plays a part in formation of collateral circulation in ischaemia.

VEGF is a type of growth factor. Increased presence in body can lead to diseases. This happens in carcinoma, which leads to increased growth and metastasis. Similarly presence of VEGF causes vascular diseases in retina due to diabetes[2] and Age related macular degeneration. There are five isoforms of VEGF, A, B, C, D and fifth is a placental growth factor. VEGF A is important in angiogenesis after hypoxia. VEGF- B plays an important part in myocardial vasculature, other factors are involved in lymphangiogenesis.



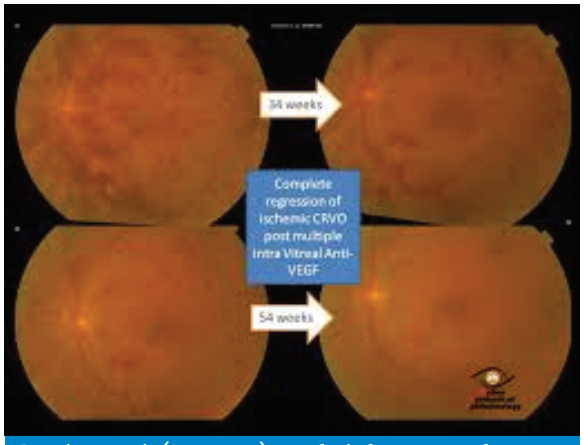
These factors bind to tyrosine kinase receptors on cell surface and become activated by transphosphorylation[3], which causes vasculogenesis, angiogenesis and lymphangiogenesis. Hypoxia stimulates release of VEGF- A which in turn stimulates angiogenesis. In diabetic retinopathy, hypoxia due to retinal ischaemia releases VEGF which leads to neovascularisation of retina leading to vitreous hemorrhage and later tractional retinal detachment. It also plays a part in wet form of Age related macular degeneration.

VEGF antagonists has become a common method of treatment of neovascularisation of retina due to diabetes or other disorders, in vascular occlusion leading to macular edema, Age related degeneration and Neovascular glaucoma[4]. They are also used in macular edema, neovascularisation due to branch retinal vein occlusion, central retinal vein occlusion[5]. Recently they are used in retinopathy of prematurity to prevent progression of retinopathy. They block VEGF and reduce formation of harmful new vessels and there by decrease leakage and retinal edema, It is given as intravitreal injections. There are many anti- VEGF like bevacizumab, Ranibizumab, Pegaptanib, aflibercept, Anecortave acetate. Commonly used drugs are Ranibizumab, Bevacizumab and Aflibercept.

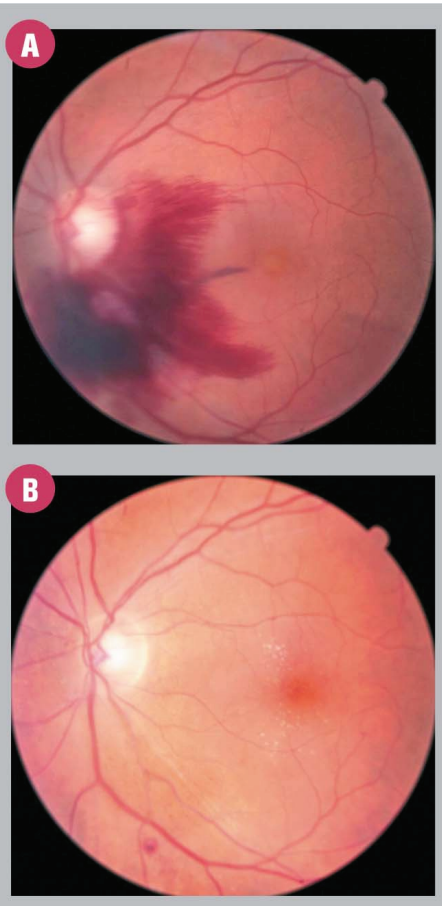
Pegaptanib is a single strand nucleic acid that binds to VEGF 165, which is important in angiogenesis. It is used as 0.3 mg injection once every 6 weeks.

Bevacizumab (Avastin) is a humanized monoclonal antibody to all isoforms of VEGF. It was initially used for colorectal cancer metastasis. It binds directly to VEGF and forms a protein complex which inhibits further action of VEGF. It is used as off label drug in dose of 1.25 mg in 0.05 ml as intravitreal injection every 4-6 weeks. It is not approved by FDA. Intra-vitreal low dose of 0.375mg in 0.03 ml is used in retinopathy of prematurity with good outcome6.

Aflibercept (Trap Eye) is similar to Bevacizumab and Ranizumab. It is a fusionprotein with portion of receptors of VEGF (R-1, R-2). It has FDA approval for use in wet ARMD and is also used in macular edema due to diabetes and vascular occlusions. It is given as 2mg in 0.05 ml every 4 weeks for 3 months and once every 2 months later. All these drugs given by intra-vitreal injections can lead to floaters, increased intra-ocular pressure and rarely lead to endophthalmitis and retinal detachment. Since Bevacizumab half life is more(20 days) compared to Ranibizumab the chance of systemic side effects like stroke was found to higher.



Ranibizumab (Lucentis) is a f-ab fragment of Bevacizumab. It is a monoclonal antibody fragment with strong binding to VEGF-A. it is given as 0.5 mg in 0.05 ml every 4-6 weeks as intra-vitreal injection.



A Fundus photo of the left eye focused at the plane of the RNFL showing striations of blood within that layer of the retina. There is macular swelling, which accounts for the reduced visual acuity.

B Fundus photo of the left eye demonstrating almost complete resolution of the pre-retinal hemorrhage. The visibility of the macula has improved consistent with her improvement in visual acuity. Note the presence of asteroid bodies, as well.

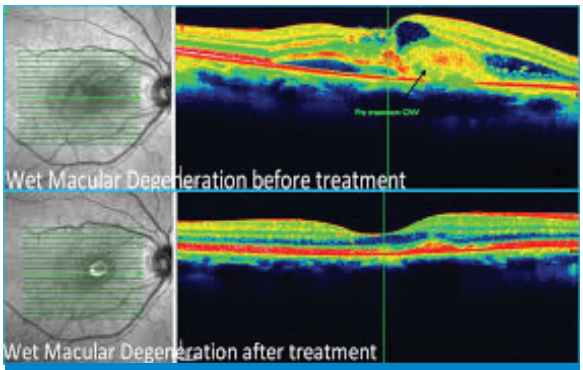


Fig : Age related macular degeneration

Conclusion

In spite of limitations and cost, the advent of anti-VEGF has become a boon for patients to reduce severe visual loss. Newer anti- VEGF are being tested to get better results compared to Ranibizumab and Bevacizumab.

References

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