Role of Anti Vascular Endothelial Growth Factor (Anti-VEGF) in anterior segment disorders

Essay
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Abbreviations list

• AMD	• Age related macular degeneration
• BCVA	• Best corrected visual acuity
• BFGF	• Basic fibroblast growth factor
• BRB	• Blood retinal barrier
• BRVO	• Branch retinal vein occlusion
• °C	• Celsius
• CME	• Cystoid macular edema
• CNV	• Choroidal neovascularization
• CRVO	• Central retinal vein occlution
• DME	• Diabetic macular edema
• DR	• Diabetic retinopathy
• ECs	• Endothelial cells
• ECM	• Extracellular matrix
• E.Coli	• Escherichia coli
• EGF	• Epidermal growth factor
• ELISA	• Enzyme linked immune sorbent assay
• EPC	• Endothelial progenitor cells
• °F	• Fahrenheit
• FDA	• Food and Drug Administration
• 5-FU	• 5 –Flurouracil
• HCRVO	• Hemi-central retinal vein occlusion
• HIF	• Hypoxia induced factor
• IGF-1	• Insulin like growth factor-1

• IgG	• Immunoglobulin G
• IgM	• Immunoglobulin M
• IOP	• Intra-ocular pressure
• IV	• Intravenous
• IVB	• Intravitreal bevacizumab
• IVR	• Intravitreal ranibizumab
• KDa	• Kilodalton
• mg	• Milligram
• MMC	• Mitomycin C
• mmHg	• Millimeter mercury
• MMPs	• Matrix metalloproteinases
• NO	• Nitric oxide
• NOS	• Nitric oxide synthases
• NPDR	• Non-proliferative diabetic retinopathy
• NV	• Neovascularization
• NVA	• Neovascularization of anterior chamber angle
• NVG	• Neovascular glaucoma
• NVI	• Neovascularization of iris
• OCT	• Optical coherence tomography
• PDGF	• Platelet derived growth factor
• PDR	• Proliferative diabetic retinopathy
• PEDF	• Pigment epithelium derived factor
• Pg/ml	• Picogram per milliliter
• PH	• Power of hydrogen

• PKP	• Penetrating keratoplasty
• PlGF	• Placental growth factor
• PRP	• Panretinal photocoagulation
• PT	• Prothrombin time
• PTT	• Partial thromboplastin time
• RhuFAbV2	• Recombinant humanized monoclonal anti-VEGF
• RVO	• Retinal vein occlusion
• Serpin	• Serine protinase inhibitor
• TGF-B	• Transforming growth factor-B
• ug/ml	• Microgram per milliliter
• UV	• Ultraviolet radiation
• VA	• Visual acuity
• VEGF	• Vascular endothelial growth factor
• VEGF-R1	• Vascular endothelial growth facfor receptor 1
• VEGF-R2	• Vascular endothelial growth factor receptor 2
• VEGF-R3	• Vascular endothelial growth factor receptor 3
• VPF	• Vascular permeability factor

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INTRODUCTION

The eye contains highly vascularized and completely avascular tissues in close apposition. This specialized anatomy requires tight regulation of the balance between vascular quiescence and vascular growth. Growth normally occurs in ocular embryonic development, but is virtually absent from the eye in adult life (Ferrara et al., 1995).

Normal visual function requires transparency in certain avascular compartments of the eye, such as the cornea, lens and vitreous. However, transparency of the light pathway is compromised when blood vessels grow into these avascular compartments. Moreover, the pathological vessels often have abnormal structures such as pericyte density and basement membrane, which can lead to leaking vasculature and hemorrhage, affecting visual acuity (Zhang et al., 2007).

The exact mechanism for the pathogenesis of ocular neovascularization is not well understood yet. In the normal adult eye, homeostasis of angiogenesis regulation is essential for maintaining the structural and functional integrity of the ocular vascular system. A disturbed balance between pro-angiogenic and anti-angiogenic factors is believed to play an important role in pathological ocular neovascularization (Ma et al., 2005).

Extensive studies were conducted to investigate the roles of increased levels of pro-angiogenic factors, such as vascular endothelial growth factor (VEGF), and decreased levels of anti-angiogenic factors, such as pigment epithelium-derived factor (PEDF), in ocular neovascularization (Ma et al., 2005).

Vascular endothelial growth factor (VEGF) binds to specific receptors on the endothelial cells lining blood vessels, leads to the formation of new capillaries (Stefanini et al., 2009). During the last few years, several members of the VEGF family have been described namely the VEGF-A, B, C, D, E and placenta growth factor (PlGF) among which VEGF-A plays a role of prime importance in angiogenesis (Shinkaruk et al., 2003).

Angiogenesis or neovascularization, the formation of neo-vessels, is a physiological phenomenon endued in vasculature, but is involved in various pathological conditions including cancers and ocular diseases (Sato et al., 2010).

VEGF plays a role in anterior segment diseases. Newly grown vessels in the cornea can lead to an impairment of transparency and visual acuity. Neovascularization of the iris (rubeosis iridis) and the anterior chamber angle may lead to elevated IOP (Scholl et al., 2010). Also there is marked elevation of VEGF in pterygium (Mauro et al., 2009).

The anti-VEGF antibody bevacizumab has been approved for treatment of various solid cancers including colorectal, lung, and breast cancers as well as glioblastoma and renal cell carcinoma (Hsu et al., 2009). In the last decade, it is used in ocular diseases as for the treatment of choroidal neovascularization in age-related macular degeneration (Sener et al., 2011), macular edema, neovascular glaucoma (Sato et al., 2010) and central retinal vein occlusion (Rensch et al., 2008).

The monoclonal antibodies can selectively target specific molecules, proteins or receptors in the body responsible for pathogenesis of a particular disorder (Biswas et al., 2010).

Monoclonal antibodies against VEGF such as bevacizumab, ranibizumab and pegaptanib, were found effective for the inhibition of corneal neovascularization and the most effective agent was bevacizumab (Sener et al., 2011).

Bevacizumab is used off-label, in topical form or as an intracameral injection, to treat anterior segment neovascularization with encouraging results (Scholl et al., 2010). Subconjunctival injection of bevacizumab reduced bleb vascularity and may provide an adjunct to current antifibrosis therapy (Coote et al., 2008).

Eye drops can sufficiently penetrate the corneal stroma and anterior chamber. It has significant effect on inhibition of alkali burn-induced corneal neovascularization (Hosseini et al., 2007), reduce corneal damage (Yoeruek et al., 2008), and lead to a reduction of the vessel diameter. It was generally well-tolerated for up to 12 months (Koenig et al., 2009).

Topical neutralization of VEGF-A at the corneal surface does not have significant side effects on normal corneal epithelial wound healing, normal corneal integrity, or normal nerve fiber density. Therefore, anti-VEGF eye drops seem to be a relatively safe option to treat corneal neovascularization (Bock et al., 2009).

Aim of the study

This essay will review the various types of anti VEGF and their use in the eye with special stress on anterior segment diseases regarding their efficacy and potential complications.