Role of Anti-VEGF in Treatment of Corneal Neovascularization

Essay
Submitted for partial fulfillment of the MCs degree in
Ophthalmology

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2014


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صدق الله العظيم
سورة طه: آية (114)

ACKNOWLEDGEMENT

I would like to express my deepest gratitude to *Professor Dr. Fikry Zaher* who meticulously supervised every minor and major detail in this work with concern and with a lot of patience and valuable time.

My deepest gratitude is to *Lecturer Dr. Nashwa Ezzat,* for supervising this work and supporting me all through the different stages of this essay.

I would like to thank my dear parents, brother and sisters as they supported me with ongoing care throughout this work.

Mohamed Refaat

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List of Abbreviations

AMD .....Age-related Macular Degeneration
Anti-VEGF.....Anti Vascular Endothelial Growth Factors
bFGF .....basic Fibroblast Growth Factor
BRVO .....Branch Retinal Vein Occlusion
BVs.....Blood vessels
CNV.....Choroidal Neovascularisation
Corneal NV.....Corneal Neovascularization
CRVO .....Central Retinal Vein Occlusion
CsA.....Cyclosporin A
DALK.....Deep anterior Lamellar Keratoplasty
ECM .....Extracellular matrix
FDA.....Food and Drug Administration
FGF .....Fibroblast Growth Factor
FND .....Fine needle diathermy
IL.....Interleukin
mAB .....Monoclonal Antibody
MMPs .....Matrix Metalloproteinase
mRNA.....Messenger RNA
NV .....Neovascularization
PDGF.....Platelet-derived Growth Factor
PDT .....Photodynamic Therapy
PEDF .....Pigment Epithelium-Derived Factor
PK .....Penetrating Keratoplasty
PlGF .....Placental Growth Factor
RNAi.....RNA interference
ROP.....Retinopathy of Prematurity
RPE .....Retinal Pigment Epithelium

List of Abbreviations (Cont.)

RVO.....Retinal Vein Occlusion

siRNA.....small interfering RNA

TA.....Triamcinolone Acetonide

TGF.....Tumour Growth Factor

TKIs.....Tyrosine Kinase Inhibitors

TNF.....Tumour Necrosis Factor

TSP.....Thrombospondin

VEGF.....Vascular endothelial growth factor

Introduction

Ocular neovascularization may affect the retina, choroid, iris and cornea and is commonly seen in some of our most common sight-threatening eye diseases including diabetic retinopathy, age-related macular degeneration, retinopathy of prematurity (ROP) and ischemic retinal vein occlusions ***(Gogat, 2004).***

The cornea has the unique feature (except for cartilage) of being normally avascular, but under pathologic conditions, vessels invade the cornea from the limbal vascular plexus. A wide variety of insults including infection, inflammation, ischemia, degeneration, trauma, loss of the limbal stem cell barrier, reaction to corneal transplantation and extended contact lens wear can cause corneal neovascularization (corneal NV) ***(Chang et al., 2001).***

Although corneal NV can occasionally serve a beneficial role in the clearing of infections, wound healing and arresting stromal melts, its disadvantages are numerous as corneal NV often leads to tissue scarring, edema, lipid deposition, and persistent inflammation that may significantly alter visual acuity ***(Augustin et al., 2010).***

It is controlled by inducers and inhibitors that modulate the formation and regression of the abnormal vessels. The major positive regulators appear to be vascular endothelial

growth factor A (VEGF-A), basic fibroblast growth factor, angiopoietins, transforming growth factor-alpha and beta, hepatocyte growth factor, connective tissue growth factor, and interleukin-8 ***(Ferrara, 2004).***

Downregulation of VEGF retards corneal NV, suggesting a role for anti-VEGF therapy in the management of corneal NV ***(Cursiefen et al., 2006).***

Multiple treatment modalities have been used to indirectly or directly occlude corneal vessels including steroids, cyclosporine A, photodynamic therapy (PDT), argon laser photocoagulation, fine-needle diathermy (FND) and electrolysis needle cauterization. However, these methods have limited clinical value because of potential associated complications such as glaucoma, cataracts, iris atrophy, accidental retinal photocoagulation, and intracorneal bleeding ***(Wertheim et al., 2007).***

The advent of anti-VEGF treatments marks a major advancement in the treatment of angiogenic eye diseases ***(Hubschman et al., 2009).***

Recently, many reports have demonstrated the efficacy of topical or subconjunctival anti-VEGF in corneal NV with variable etiologies ***(Papathanassiou et al., 2013).***

Although there is a high risk of hypertension, cerebrovascular accidents and myocardial infarcts with systemic administration of anti-VEGF & local complications of intravitreal injection of anti-VEGF therapy such as endophthalmitis, retinal detachment, cataract and uveitis, the topical and subconjunctival administration of anti-VEGF showed no systemic or local toxic effects ***(Wu et al., 2009), (Chalam et al., 2009).***

Aim of the Work

Is to high lighten role of anti-VEGF in treatment of corneal neovascularization in comparison with other treatment modalities.

Chapter (I): Corneal Anatomy

The cornea is a unique portion of the outer, fibrous ocular tunic that is transparent and serves a refractive function while maintaining a mechanically tough and chemically impermeable barrier between the eye and the environment ***(Klyce et al., 1972)***.

In concert with the evolutionary development of vision, the cornea became structurally and functionally specialized to achieve the required optical properties. It evolved as an avascular structure that meets its oxygen requirements largely from the atmosphere via the anterior corneal surface and most of its additional nutritional requirements from the aqueous humor via the posterior corneal surface ***(Beuerman et al., 1987).***

Gross Anatomy:

The cornea forms the anterior one-sixth of the eyeball. It is transparent and avascular with a smooth, convex surface and concave inner surface. The diopteric power of the cornea is 42 diopters, and refractive index is 1.38. The average corneal diameter is 11.5mm vertical and 12mm horizontal. It is thinnest at its center, measuring about 0.5 to 0.6 mm, and thicker at the periphery, measuring about 0.7 mm. The cornea is the main structure responsible for the refraction of light entering the eye ***(Hughes, 2008).***