The Relation Between Inner Segment/ Outer Segment Junction And Visual Acuity Before And After Ranibizumab In Diabetic Macular Edema

Thesis

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List of Abbreviations

ACE .....Angiotensin Converting Enzyme

AGEs.....Advanced Glycation End-Products

BCVA.....Best Corrected Visual Acuity

BFGF .....Basic Fibroblast Growth Factor

CME.....Cystoid Macular Edema

CMT.....Central Macular Thickness

COST.....Cone Outer Segment Tips

CSF.....Central Sub Foveal

DM.....Diabetes Mellitus

DME .....Diabetic Macular Edema

DR .....Diabetic Retinopathy

EGF .....Epidermal Growth Factor

ELM.....External Limiting Membrane

ETDRS.....Early Treatment Diabetic Retinopathy Study

EZ.....Ellipsoid Zone

FFA.....Fundus Fluorescein Angiography

GDNF.....Glial-Cell Derived Neurotropic Factor

ICAM-A.....Intercellular Adhesion Molecule-A

IGF-1 .....Insulin-Like Growth Factor-1

IOP .....Intraocular Pressure

IPL.....Inner Plexiform Layer

IRMA .....Intraretinal Microvascular Abnormalities

IS/OS .....Inner Segment /Outer Segment

IZ.....Interdigitation Zone

Log MAR.....Logarithm of the Minimum Angle of Resolution

NPDR.....Non-Proliferative Diabetic Retinopathy

List of Abbreviations

OPL.....Outer Plexiform Layer

PDGFs .....Platelet-Derived Growth Factors

PDR .....Proliferative Diabetic Retinopathy

PRP.....Pan Retinal Photocoagulation

RD .....Retinal Detachment

ROST.....Rod Outer Segment Tips

RPE .....Retinal Pigment Epithelial

SD-OCT .....Spectral-Domain Optical Coherence Tomography

SRD .....Serous Retinal Detachment

TGF-β2 .....Transforming Growth Factor-Beta 2

TD-OCT .....Time-Domain Optical Coherence Tomography

UV.....Ultra Violet

VA.....Visual Acuity

VEGF .....Vascular Endothelial Growth Factor

VMIA .....Vitreomacular Interface Abnormality

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Introduction

The prevalence of diabetes mellitus (DM) is increasing worldwide, with estimates indicating that DM affected 285 million adults in 2010. This figure is projected to increase to 439 million by 2030.[1]

Diabetic macular edema (DME) is a major cause of vision loss in diabetic patients. It has been accepted that macular edema can develop at all stages of retinopathy. Classically, patients have a gradual onset of blurred vision, and in more advanced cases, the macula becomes thickened and even cystic with profound visual loss.[2]

The pathological process of DME formation has several principal components; a primary event is breakdown of the blood-retinal barrier with a following increase in passive leakage and accumulation of water, salts and lipoproteins in the extra cellular compartment in the macula. One of the causes to the breakdown of the blood-retinal barrier seems to be an increase in vascular endothelial growth factor (VEGF).[3]

Intravitreal pharmacotherapy has significantly improved the treatment of diabetic retinopathy (DR) over the past decade. Drug trials demonstrated that ranibizumab improves visual acuity (VA) in the majority of patients.[4]

Because of the various clinical presentations of DME, specialized techniques such as spectral-domain optical coherence tomography (SD-OCT) have become an important tool and an important part of the diagnosis and management of this condition. The correlation between OCT measured macular thickness and VA. Furthermore, in some cases paradoxical changes in VA occur in response to changes in OCT-measured thickening.[5]

Although OCT can serve as a valuable tool in the clinical evaluation of patients with DME, OCT derived macular thickness measurements may not be appropriate as strong markers of VA. With the improvement of the visualization of retinal architecture offered by SD-OCT, the retinal photoreceptor layer can be evaluated accurately. It is reported that inner segment/outer segment (IS/OS) junction integrity has important value in studying retinal diseases.[6]

Aim of the Work

The aim of this work is to evaluate the relation between the photoreceptor IS/OS, the best corrected visual acuity (BCVA) and color vision before and after the intravitreal injection of anti-vascular endothelial growth factor (anti-VEGF); ranibizumab (Lucentis®) in patients with DME.

Anatomical Background of the Retina

Retina is a light-sensitive layer of tissue. Light striking the retina initiates a cascade of chemical and electrical events. Neural retina typically refers to three layers of neural cells (photo receptor cells, bipolar cells, and ganglion cells) within the retina that ultimately trigger nerve impulses. These are sent to various visual centers of the brain through the fibers of the optic nerve. [7]

The human retina has ten distinct layers (Figure 1). From closest to farthest from the vitreous body as follows:[8]

1. Inner limiting membrane is composed of extensive, expanded terminations of Müller cells (often called footplates) covered by a basement membrane.
2. Nerve fiber layer contains axons of the ganglion cell nuclei which a thin layer of Müller cell footplates exists between this layer and the inner limiting membrane.
3. Ganglion cell layer containing nuclei of ganglion cells, the axons of which become the optic nerve fibers.
4. Inner plexiform layer (IPL) contains the synapses between the bipolar cell axons and the dendrites of the ganglion and amacrine cells.

5. Inner nuclear layer which contains the nuclei and surrounding cell bodies of the amacrine cells, bipolar cells and horizontal cells.
6. Outer plexiform layer (OPL) contains projections of rod endings (rod spherules) and cone endings (cone pedicles). These make synapses with dendrites of bipolar cells.
7. Outer nuclear layer contains cell bodies of rods and cones.
8. External limiting membrane is layer that separates the inner segment portions of the photoreceptors from their cell nucleus.
9. Layer of rods and cones contain rod cells and cone cells.
10. Retinal pigment epithelium (RPE) which is a single layer of cuboidal cells.