

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⁾

-Introduction-

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.

Review of Literature

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.