Correlation of Macular Thickness Changes and Microperimetric Values in Wet Age Related Macular Degeneration (AMD) Before and After Anti-VEGF Injection

A thesis submitted for partial fulfillment of

MD Degree in Ophthalmology

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2016

Abstract

Purpose: The aim of our study is to evaluate the effect of intravitreal bevacizumab on macular anatomical structure and macular function in eyes with wet age related macular degeneration (AMD)

Methods: 30 eyes with wet AMD underwent full ophthalmological examination, Amsler grid testing, macular OCT as well as macular microperimetry before receiving loading dose of bevacizumab and after one month of treatment. Topography and Microperimetry overlay was used. The location and stability of fixation were assessed.

Results: There was a statistically significant improvement of macular thickness map as well as the best corrected visual acuity (BCVA) but the improvement of macular sensitivity was not significant. There was a significant positive correlation between the baseline visual acuity (VA) of 0.05 or less and the change occurred in VA .There was no significant correlation between the improvement in macular thickness and the change in macular sensitivity. There was no significant correlation between the improvement in visual acuity and the improvement in macular sensitivity**.**

Conclusion: although early diagnosis and proper treatment are essential for the best outcome regarding both structural improvement and restoration of functional vision, there is still a chance for low vision eyes to restore a reasonable vision.

Key words: Age related macular degeneration (AMD), Microperimetry, optical coherence tomography (OCT), retinal sensitivity, Anti –VEGF, macular thickness.

Acknowledgement

First and foremost, I thank ALLAH, the most gracious and merciful for HIS infinite gifts.

I would like to express my sincere appreciation and gratitude to **Prof.Dr. Ali Mohamed Taha,** Professor of Ophthalmology, Faculty of Medicine**,** Cairo University, for his great co-operation,unlimited help and contiuous guidance during this work; I am deeply touched by his help and concern.

I am deeply gratefull to **Prof.Dr. Omaima Khaled Eyada, Professor of ophthalmology, Faculty of Medicine, Cairo University**, for her great effort and supervision through out this work.

No words can describe the enormous efforts of **Dr. Iman Magdy Eissa, Lecturer of Ophthalmology, Faculty of Medicine,Cairo University** ,for her honest assistance which made the achievement of this work possible.

I am deeply gratefull to **Dr. Riham Samy Hanafy Mahmoud Allam, Lecturer of Ophthalmology, Faculty of medicine, Cairo University**, for her continous supervision and help which made the achievement of this work possible.

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List of abbreviations

ARM	Age related maculopathy
AMD	Age-related Macular Degeneration
BCVA	best corrected visual acuity
BCEA	bicurve ellipse area
CFT	central foveal thickness
CNV	choroidal neovascularization
dB	decibel
BF	Factor B
FDA	Food and drug administration
FRLs	functional retinal loci
IOP	Intraocular pressure
MP	microperimetry
NSAIDs	Non steroidal anti inflammatory drugs
OCT	optical coherence tomography
PDT	photodynamic therapy
PED	Pigment epithelial detachement
PRLs	preferred retinal loci
RPE	retinal pigment epithelium

SNPs	single nucleotide polymorphism
SD-OCT	Spectral domain-optical coherence tomography
VEGF	vascular endothelial growth factor
VA	visual acuity

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Aim of the work

The aim of this study is to demonstrate the effect of the Anti-VEGF bevacizumab on macular functions represented as macular sensitivity measured by microperimetry as well as macular anatomical structure assessed by Optical Coherence Tomography (OCT) in wet age related macular degeneration (AMD).

Age Related Macular Degeneration

Definition

Age-related Macular Degeneration (AMD) is a progressive, degenerative disease of the macula, which is responsible for sharp vision. When the macula is damaged, the ability to see fine details and colors is threatened. If not treated, the damage may be permanent, and the visual loss may be irreversible; in other words, the untreated patient may become legally blind (According to the American Foundation for the blind legal blindness is a visual acuity of 20/200 or less, according to Snellen Eye Chart, in the better-seeing eye with best conventional correction or a visual field of 20 degrees in the better-seeing eye). **(Nguyen et al., 2013)**

Incidence and Prevalence

AMD is the leading cause of irreversible loss of visual acuity in patients over the age of 50 in the United States. About 1.75 million United States residents had advanced AMD with associated visual loss at 2004, and that number is expected to grow to almost 3 million by 2020. **(Friedman et al., 2004)**

Risk factors

While aging is the major risk factor for AMD, other systemic risk factors such as tobacco smoking, obesity, and sunlight exposure have also been found to be common in the development of AMD. In addition, studies of the genetic basis of AMD have revealed variations in landmark genes such as *HTRA1* and *CFH* that account for as much as 50% of the genetic risk of AMD **(Zhang *et al.*, 2012).**

Disease progression

There are two forms of AMD: dry and wet (neovascular). While dry AMD is most common, wet AMD is associated with more sudden and severe visual loss. Approximately 10-15% of dry AMD cases progress to wet AMD. Wet AMD is known clinically as choroidal neovascularization (CNV). **(Wang et al., 2010)**

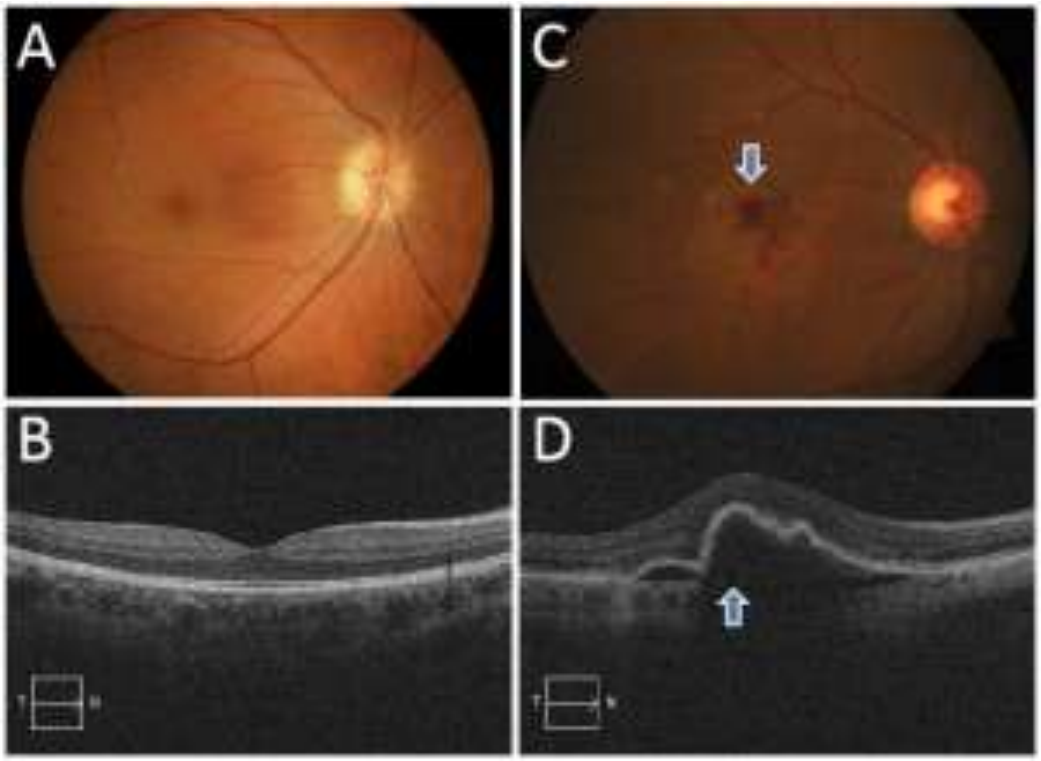

Fig. (1): Neovascular AMD. A healthy eye without AMD (Panels **A**, **B**) has a normal retina without signs of bleeding on color fundus photograph (A). On optical coherence tomography (OCT) image, the anatomical structure of a healthy retina is intact (B). In neovascular AMD, bleeding under the retina due to choroidal neovascularization (blue arrows) disrupts the retinal anatomy (**D**) and can lead to hemorrhage under the macula (**C**) that can cause dramatic sudden loss of sharp vision. **(Nguyen et al., 2013)**

Pathogenesis:

An important association of the complement cascade with AMD has recently been made but we still do not understand the pathogenesis of

the disease which is characterized by loss of the retinal pigment epithelium (RPE) within the macula and in turn loss of the overlying foveal photoreceptors. **(Wang et al., 2010)** therefore there are many theories that tried to explain how this happens. Of these, the fibrotic theory, the inflammatory and the genetic are the most commonly discussed.

Fibrotic Theory

Wang 2010 believes that the onset of dry AMD is started by aging changes in Bruch's membrane and subsequent death of many RPE cells in the macula and overlying photoreceptor cells. Progression of dry AMD to wet AMD is marked by the development of neovascularization within Bruch's membrane and sub retinal space. This neovascular formation is linked to a fibrotic response leading to scar tissue and further damage to Bruch's membrane, and the photoreceptor cells. **(Wang et al., 2010)**

Inflammatory Theory

In 1994 histopathological studies have shown inflammatory cells, including macrophages and lymphocytes, in AMD lesions **(Dastgheib and Green, 1994)**. By 2002 drusen have been shown to contain C3 and C3a fragments of complement, and complement deposition has been identified in the Bruch's membrane of AMD patients **(Anderson et al., 2002).** However, it remains unclear whether such inflammatory reactions are causative or secondary to the disease. Later on several studies suggest that the complement cascade is involved in the pathogenesis of AMD, and that polymorphisms in complement H are genetically linked to AMD **(Edwards et al., 2005).** Recently, intraocular expression of CCR3,

which is a chemokine, was implicated in the development of CNV **(Takeda et al., 2009)**.

However, the population-based cohort Blue Mountain Eye study, found no association between the use of systemic anti-inflammatory drugs (NSAIDs or corticosteroids) and either the cross-sectional prevalence or the longitudinal incidence of AMD **(Wang et al., 2003).** Nevertheless, there is significant evidence linking AMD to inflammatory pathways. **(Wang et al., 2010)**

Genetic Theory

Meyers et al., 1995 suggested Genetic contributions in at least 25% of AMD patients. Indeed, single nucleotide polymorphism (SNPs) in the gene encoding complement Factor H (CFH) have been linked to susceptibility to AMD, and allelic variants in two other complement related genes, Factor B (BF) and complement component C2, have also been linked to AMD **(Gold et al., 2006).** Other candidate genes have also been reported to link to AMD, including ELOVL4, VLDLR, and LRP6 **(Haines et al., 2006)**.