Assessment of Fixation Stability in Wet Age Related Macular Degeneration Using Microperimetry before and after Intravitreal Anti-VEGF Injection

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Abstract

Background: Wet AMD is considered one of major causes of visual loss above age of fifty, which can be treated by anti-VEGF. Moreover the introduction of Microperimetry for functional evaluation of the macula allows more information about visual prognosis and effect of treatment on macular functions in eyes with AMD.

Aim of Study: To evaluate location/stability of fixation and preferred retinal loci (PRL) before and after bevacizumab injection in wet Age Related Macular degeneration (AMD) using Microperimetry.

Patients and Methods: 30 eyes with wet AMD underwent OCT and microperimetry before receiving bevacizumab and one month after last intravitreal injection of loading dose of bevacizumab (3 consecutive injections one month apart) to assess Location and stability of fixation.

Results: There was improvement in stability of fixation by 30% after treatment with intravitreal bevacizumab in eyes with wet AMD.

Conclusion and Message of the Study: Microperimetry is an important tool in evaluating location/stability of fixation and PRL in wet AMD.

Key Words: *Age related macular degeneration (AMD) – Microperimetry – Bevacizumab – Fixation stability.*

Introduction

IN developed world, age related macular degeneration (AMD) accounts for most cases of severe visual loss above the age of fifty. But the introduction of intravitreal antiangiogenic agents like ranibizumab and bevacizumab, which inhibit the vascular endothelial growth factor (VEGF), added major advance in treatment outcomes of neovascular AMD [1].

Microperimetry is a non-invasive method used to analyse fixation and central visual field defects in atopographic related manner [2]. It also allows for automated assessment of macular function as well as automated correction for eye movements, as unstable fixation [3,4]. It also gives an idea about the fixation pattern and the preferred retinal loci (PRL) of patients. These PRL are mapped in relation to fixed anatomical landmarks, so they can be re-examined in subsequent examinations, a point which allows for future comparisons [4].

The presence of autotracking system technique allows for measuring macular sensitivity for patients with nonfoveal or unstable fixation, which continuously adapts to eccentric fixation or fixation losses during the examination [5].

Moreover fixation stability is categorized into 3 levels (stable, relatively unstable, and unstable) based on the percentage of loci fixation within a circle of 2 and 4 degrees of diameter centered around point of fixation [6].

Fixation is defined as "stable" when 75% of fixations fall within the 2° circle, "relatively unstable" when 75% of fixations fall within the 4° circle, and "unstable" when <75% of fixations fall within the 4° circle [7].

Our study aimed at comparing fixation pattern and stability before and after anti VEGF injection.

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Abbreviations

AMD	: Age related macular degeneration.
CNV	: Choroidal neovascular membrane.
OCT	: Optical coherence tomography.
PRL	: Preferred retinal loci.
SD-OCT	: Spectral domain optical coherence tomography.
VEGF	: Vascular endothelial growth factor.

Patients and Methods

Our study is a non-randomized prospective, interventional study that was carried out between July 2013 and August 2015 at Kasr El-Ainy University Hospital and LASER and ophthalmology research centre. Data collection conformed to all local laws and was compliant with principles of the Declaration of Helsinki. The study was approved by ethical committee of ophthalmology department, Cairo University.

The study included 30 eyes (23 patients) having wet AMD (classic, atypical or occult) scheduled for intravitrea lbevacizumab treatment (at month 0,1,2 and 3).

Only eyes who did not receive previous intravitreal injections were included in the study.

We excluded eyes with AMD that received previous intravitreal injections, eyes with by vitreous hemorrhage or massive exudation leading to exudative retinal detachment, history of diabetes mellitus or a systemic disease affecting the eye, history of previous intra-ocular surgery except uneventful cataract surgery as well as eyes having media opacity interfering with microperimetry.

History was taken to identify the presence of any known risk factors for CNV, Examination was done prior to each intravitreal injection and after four months (one month following the third injection).

All eyes underwent routine ophthalmologic examination in addition to evaluation of AMD in the form of Amsler grid testing (Chart no. 1).

Spectral domain optical coherence tomography (SD-OCT) using OPKO Spectral OCT/SLO combination imaging system; OPKO Instrumentation, LLC, USA, version 1.89 was done for confirmation of diagnosis of wet AMD.

Macular Microperimetry was done using OPKO Spectral OCT/SLO combination imaging system; OPKO Instrumentation, LLC, USA version 1.89 for measurement of retinal sensitivity and assessment of fixation pattern and stability.

The following program was used: Pattern: Square 5x5-90; Target size: Goldmann III yet in cases where it was not seen by the patient, Goldmann IV was used; Strategy: 4-2.

Statistical analysis:

Statistical analysis of data was performed using Statistical Analysis Systems (SPSS ver.16). Summarization of numerical data in the form of means and standard deviations or median & ranges was done. Categorical data was summarized as percentages. Comparison between the groups was done with respect to categorical data sing the chi-square test. p-values <0.05 were considered significant.

Results

Thirty eyes of 23 patient were enrolled in this study, OCT scan and microperimetry were done at baseline and follow-up one month after the end of loading dose (once monthly for three successive months) of intravitreal bevacizumab injection. Location and stability of fixation at baseline were compared to the last follow-up.

The age of the study group ranges from 56 to 76 years with mean age value 63.2 ±8.7 years.

The male to female ratio was (1: 1.875) including 8 males and 15 females.

The location of fixation was categorized into predominantly central, poorly central and eccentric fixation. Baseline locations were compared to follow-up visit as shown in Table (1) and Fig. (1).

Table (1): Statistical values of location of fixation.

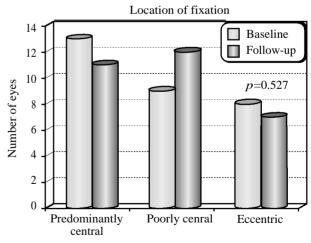| Location of fixation	Predominantly central	Poorly central	Eccentric
Baseline	13	9	8
Follow-up	11	12	7
p-value	0.527		

Fig. (1): Bar chart showing statistical values of location of fixation.

The stability of fixation was categorized into stable, relatively unstable and unstable fixation. Baseline fixations were compared to follow-up visits as shown in Table (2) and Fig. (2).

Table (2): Statistical values of stability of fixation.

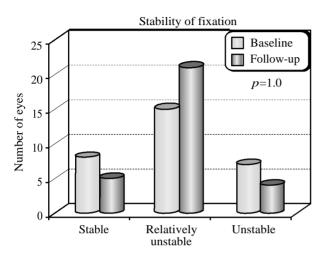| Stability of fixation	Stable	Relatively unstable	Unstable
Baseline	8	15	7
Follow-up	5	21	4
p-value		1.0	

Fig. (2): Bar chart showing statistical values of stability offixation.

Discussion

The current study tackled the change that occur in fixation pattern and stability in wet AMD before and after treatment with intravitreal bevacizumab.

In our study there was improvement of fixation stability from being unstable at baseline in 7 eyes to be only 4 at follow-up and increase of eyes with relatively unstable fixation from 15 eyes at baseline to 21 eyes at follow-up with total improvement of 30%.

Our results concided with that of Parravano et al., that showed improvement in fixation stability in 33.3% of treated eyes after 24 months, Although they found that the effect of treatment peaked at 4 weeks and visual acuity stabilized at 6 month of follow-up [8].

Our results also concides with that of Michalska-Małecka et al., that showed a significant increase of percentage of eyes with stable fixation after 6 months of observation [9], although they refer this improvement to training and development of extrafoveal preferential retinal locus (PRL) on

which eye movements are centered with improvement of visual performance [9].

Conclusion:

Our study concluded that treatment of wet AMD with anti-VEGF improves fixation stability and visual performance.

Conflict of interest:

The authors declare no conflict of interest in the material discussed in this work.

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تقييم ثبات وتمركز اتجاه الابصار فى حالات التحلل العمرى الرطب لماقولة العين قبل وبعد حقن المواد المثبطة لنمو الأوعية الدموية الغير طبيعية

يعد مرض التحلل العمرى الرطب لماقولة العين من أكثر الأسباب التى تؤدى إلى فقدان البصر فوق عمر الخمسين عاما بالدول المتقدمة. كما يعد اكتشاف المواد المثبطة لنمو الأوعية الدموية الغير طبيعية من أهم الأسباب التى أضافت الكثير من الفائده إلى علاج التحلل العمرى الرطب لماقولة العين.

ويعد استخدام جهاز فحص مجال الابصار لماقولة العين من الطرق المتاحة لتقييم وظائف ماقولة العين عن طريق قياس حساسية مقولة العين بالإضافة إلى تقييم ثبات وتمركز اتجاه الابصار مما يساعد فى تقييم تأثير العلاج باستخدام المواد المثبطة لنمو الأوعية الدموية الغير طبيعية لحالات التحلل العمرى الرطب لماقولة العين.

وقد أوضحت الدراسة أن هناك تحسن ملحوظ فى ثبات وتمركز اتجاه النظر بعد العلاج باستخدام المواد المثبطة لنمو الأوعية الدموية الغير طبيعية لحالات التحلل العمرى الرطب لماقولة العين فى ٣٠٪ من العيون التى خضعت للدراسة وهذه النتيجة تتفق مع الدراسات السابقة والتى أوضحت أيضا أن هذا التحسن يستمر بالتطور حتى ٢٤ شهرا من فتره المتابعة لوظائف ماقولة العين بالرغم من أن التحسن فى حده الابصار يستمر فقط حتى ستة أشهر.

وعلية فان هذه الدراسة قد توصلت إلى أن العلاج باستخدام المواد المثبطة لنمو الأوعية الدموية الغير طبيعية لحالات التحلل العمرى الرطب لماقولة العين تحسن من تمركز وثبات اتجاه الابصار مما يؤدى إلى تحسن الأداء البصرى لهؤلاء المرضى.