The Egyptian Journal of Hospital Medicine (April 2018) Vol. 71 (4), Page 2956-2959

Evaluation of Outer Retinal Layers Changes before and after Intervention in Diabetic Macular Edema

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ABSTRACT

Aim of the work: this study aimed to evaluate changes in photoreceptors, inner segment/outer segment (IS/OS) junction and external limiting membrane (ELM) following grid argon laser versus intravitreal injection of antivgef (Ranibizumab) in diabetic type2 patients affected by clinically significant macular edema.

Methods: forty eyes of diabetic type2 patients who were affected by clinically significant macular edema were randomly categorized into two groups(Group treated by argon grid laser and group treated by intravitreal injection of antivgef for the first time) both groups were investigated for best corrected visual acuity (BCVA) and the integrity of the photoreceptors, IS/OS and ELM as being (Continuous(+), interrupted(±) or Absent (-)) by spectral-domain optical coherence tomography (SD-OCT)(CIRRUS HD-OCT) before treatment , 1month, 2months and 3months after treatment . Other variables, included central macular thickness (CMT) and central macular volume (CMV) were evaluated. **Results:** significant difference was found between [photoreceptor, is/os] (+), photorecptor, is/os (+,-) and photoreceptor, is/os (-) groups in BCVA at baseline; it was 0.61,0.73,and 1 and after 6 months it was 0.48,0.73 and 1 . Results were similar for ELM groups. Signiant difference was found between ELM (+), ELM (+,-) and ELM (-) groups in BCVA at baseline it was 0.59,0.72,and 1 and after 6 months it was 0.46,0.68 and 1 in lucentis group and signiant difference was found between photoreceptor, is/os (+) and photorecptor ,is/os (+,-) groups in BCVA at baseline was(0.32and 0.3 and after 6 months it was 0.27and 0.3 . Results were similar for ELM groups. Signiant difference was found between ELM (+) and ELM (+,-) groups in BCVA at baseline it was 0.29 and 0.5 and after 6 months it was 0.25 and 0.4 in argon laser group

Conclusion: the more damage of outer retinal layers at the time of DME the lower visual acuity following DME resolution and the presence of intact of these layers is an important factor in determining final visual acuity.

Keywords: diabetic macular edema, external limiting membrane, inner segment-outer segment junction, integrity of photoreceptor layer, optical coherence tomography.

Abbreviations:

BCVA: Best corrected visual acuity, **CMT:** Central macular thickness, **CMV:** Central macular volume, **CSME:** Clinically significant macular edema, **DR:** Diabetic retinopathy, **ELM:** External limiting membrane, **ETDRS:** Early treatment diabetic retinopathy study, **IS/OS:** Inner segment outer segment, **ONL:** Outer nuclear layer, **SD-OCT:** Spectral domain optical coherence tomography, **VEGF:** Vascular endothelial growth factor.

INTRODUCTION

Diabetic retinopathy (DR) and diabetic macular edema(DME) are the major causes of loss of vision and blindness in diabetic patients. The pathogenesis of DME has not been fully explained since it is caused by complex pathological process with many contributing factors [1,2]. 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 integral part of the diagnosis and management of this condition with improved visualization of retinal architecture offered by OCT[3].Several recent studies of DME had described new assessment modalities, including optical coherence tomography (OCT), for microstructural visualization of the integrity of the inner segment-outer segment (IS/OS) junction, integrity of the external limiting membrane (ELM) and length of the outer nuclear layer (ONL) [3-5].OCT is a non-invasive imaging modality that produces cross-sectional images with high-resolution of ocular tissues[6]. Spectral-domain OCT (SD-OCT) yields a higher degree of axial resolution and provides more details of intraretinal structures, the IS/OS junction and ELM in particular [7].Such detailed views are critical, as disturbances of these layers reflect anatomical disruptions of the retinal photoreceptors[8].

MATERIALS AND METHODS

Patients

This study was conducted according to tenets of declaration of Helsinki and received the approvals of ethical and scientific committees of the concerned institutions.

Received:20 /3 /2018
Accepted30: /3 /2018

DOI**: 10.12816/0046164**

A total of 45 DME patients (50 eyes) were enrolled for this analysis. All participants of this prospective study were recruited from the outpatient clinic of El Mahrosa Eye Center at Suez. Patients included in this study were with evidence of clinically significant macular edema (CSME) defined according to the ETDRS . Excluded from this study were patients who had corneal opacities or any media opacity, moderate to dense lens opacities , history of intraocular inflammation such as anterior or posterior uveitis and eyes with other conditions that can cause macular thickening such as venous occlusion, epiretinal membrane and/or vitreomacular traction. All patients underwent comprehensive ophthalmologic examinations, including measurement of BCVA, intraocular pressure, macular status evaluation by slit-lamp biomicroscopy, fundus examination using indirect ophthalmoscope and SD-OCT. Patient's ages, gender, insulin dependency, duration of diabetes, duration of DME and any prior treatments for DME were recorded. BCVA was measured by using Decimal Notation Scale(converted to Log MAR)

OCT

OCT scans were obtained by using spectral-domain optical coherence tomography (SD-OCT) (CIRRUS HD-OCT). Eyes were dilated before OCT examination. All OCT scans were centered on the fovea, using a centrally oriented internal fixation mark. OCT scans were conducted by the same operator. CMT and central macular volume (CMV) were calculated automatically by the instrument and the integrity of the photoreceptors, IS/OS and ELM were assessed as follow **:** Continuous (+) Interrupted (+,-) or Absent (-). One experieced grader was masked to the BCVA status of each patient and classified the eyes independently

Post intervention Evaluation:

Patients were treated according to the type of the edema and macular thickness whether by argon laser or intravitreal injection (Ranibizumab) after which the patients were evaluated by history taking: asking about any recent complaints and ocular examination including by Slit lamp examination ,slit lamp biomicroscopy, BCVA expressed in Decimal Notation Scale(converted to Log MAR) and SD-OCT. This was done 1 month after management then at 3 and 6 months in which macular thickness and central macular volume were assessed with assessment of the integrity of the photoreceptor, IS/OS and ELM layers.

Statistical analysis

Data management and analysis were performed using Statistical Analysis Systems. Numerical data were summarized using means and standard deviations, categorical data were summarized as percentages.

Numerical Data were analyzed by one-way analysis of variance (ANOVA) when parametric analysis was possible. Comparisons between groups with respect to numeric variables were done by Tukey-Kramer Multiple comparisons Test and the fisher exact test was performed for non numerical data.All p-values were two-sided. P-values < 0.05 were considered significant.

RESULTS

This study included 50 eyes from 45 diabetic patients (24women, 21 men) who had diabetic macular edema with a mean age of 53.2 year (range: 45–60 years) .

CMV in ranibizumab versus argon laser:

Comparing CMV in lucentis versus argon laser, we found that the mean CMV in pre injection of lucentis was 11.475 and in argon laser was 10.755, mean CMV after 1 month of follow-up in lucentis was 11.19 and in argon laser was 10.625, mean CMV after 3 months of follow-up in lucentis was 11.12 and in argon laser 10.67 and after 6 months of follow-up in lucentis was 11.12 and in argon laser was 10.68. **P value** of CMV in lucentis was 0.0390, considered significant and in argon laser was 0.4591, considered not significant **(Figure 1).**

CMT in ranibizumab versus argon laser:-

comparing CMT in lucentis versus argon laser, we found that the mean CMT in pre injection of lucentis was 342.15 and in argon laser was 285.95, mean CMT after 1 month of follow-up in lucentis was 323.65 and in argon laser was 275.35, mean CMT after 3 months of follow-up in lucentis was 323.4 and in argon laser 276.7 and after 6 months of follow-up in lucentis was 321.5 and in argon laser was 276.8. the **p value** of CMT in lucentis was 0.0311, considered significant and in argon laser was 0.0369, considered significant**(Figure 2).**

BCVA in ranibizumab versus argon laser:-

comparing BCVA in lucentis versus argon laser, we found that the mean BCVA in pre injection of lucentis was 0.645 and in argon laser was 0.315, mean BCVA after 1 month of follow-up in lucentis was 0.55 and in argon laser was 0.285, mean BCVA after 3 months of follow-up in lucentis was 0.53 and in argon laser 0.27 and after 6 months of follow-up in lucentis was 0.54 and in argon laser was 0.27. the **p value** of BCVA in lucentis was 0.0068, considered very significant and in argon laser it was 0.0395 and considered significant**(Figure 3).**

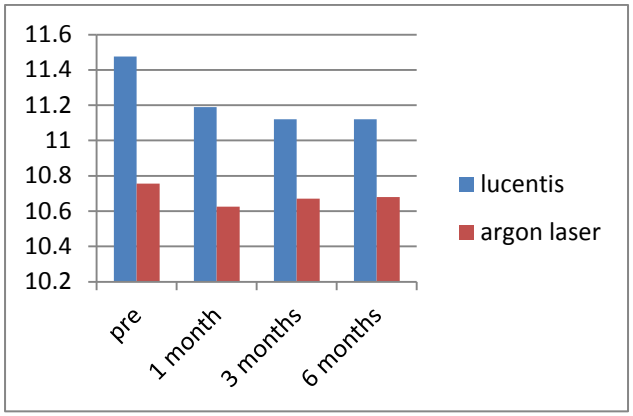

Figure1: CMV in ranibizumab versus argon laser

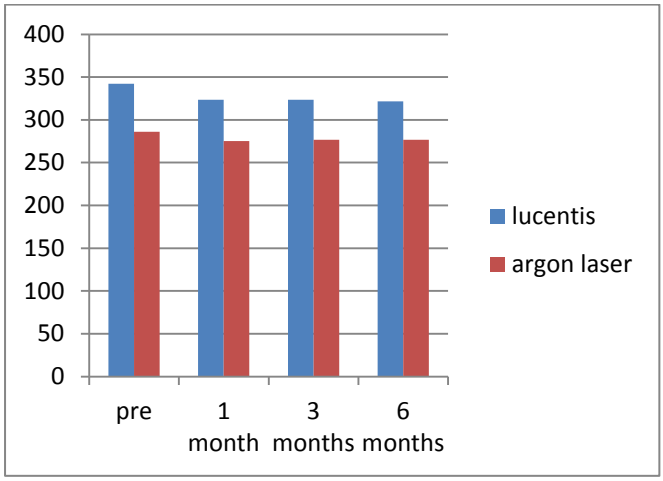

Figure 2: CMT in ranibizumab versus argon laser

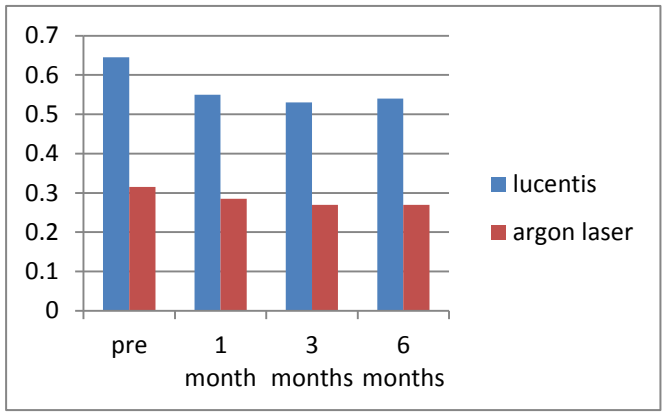

Figure 3: BCVA in ranibizumab versus argon laser

In ranibizumab group significant difference was found between photoreceptor, is/os (+) , photorecptor ,is/os (+,-) and photoreceptor, is/os (-) groups in BCVA at baseline it was 0.61,0.73 and 1 and after 6 months it was 0.48,0.73 and 1 . Results were similar for ELM groups. Significant difference was found between ELM (+) ,ELM (+,-) and ELM (-) groups in BCVA at baseline it was 0.59,0.72,and 1 and after 6 months it was 0.46,0.68 and 1 **(Table 1).**

Table 1 : BCVA at baseline and after 6 months in ranibizumab group

	BCVA	
	At base line	After 6 months
Photo,is/os (+)	0.61	0.48
Photo,is/os (+,-)	0.73	0.73
Photo,is/os (-)	1	1
ELM (+)	0.59	0.46
ELM (+,-)	0.72	0.68
ELM (-)	1	1

In argon group a significant difference was found between photoreceptor, is/os (+) and photorecptor ,is/os (+,-) groups in BCVA at baseline it was 0.32and 0.3 and after 6 months it was 0.27and 0.3 . Results were similar for ELM groups. Significant difference was found after 6 months and it was 0.25 and 0.4 **(Table 2).**

Table 2: BCVA at baseline and after 6 months in argon group

	BCVA	
	At base line	After 6 months
Photo,is/os (+)	0.32	0.27
Photo,is/os (+,-)	0.3	0.3
ELM (+)	0.29	0.25
ELM (+,-)	0.5	0.4

No clinical or statistical difference was found by intergroup comparison of photoreceptor, is/os junction and ELM layers before and after intervention during follow up

DISCUSSION

Diabetic macular edema (DME) is the leading cause of visual loss in diabetic individuals. The use of the OCT was incorporated in the routine work of the ophthalmologists after studies demonstrated its collaboration on the detection of the disease. Besides confirming diagnostic impressions, the OCT monitors the pharmacological treatment of the macular edema and follows its progression [9]. Several recent studies of DME described new assessment modalities, including optical coherence tomography (OCT), for microstructural

visualization of the integrity of the inner segment-outer segment (IS/OS) junction, integrity of the external limiting membrane (ELM) and length of the outer nuclear layer (ONL) [10-18].

Integrity of the photoreceptor, inner segment–outer segment (IS/OS) junction and external limiting membrane(ELM) have been handled in different

cross sectional studies of patients with diabetic macular edema with its correlation with visual acuity[10-18].In our prospective study OCT scanning of 50 eyes with diabetic macular edema was done by using SD-OCT (CIRRUS HD-OCT), the photoreceptor, IS/OS line and ELM were evaluated at base line, one month, three months and 6 months after treatment . The treatments used in our study were argon laser and intravitreal injection by lucentis . At base line in ranibizumab group, we found that the mean value of visual acuity in the continuous group of photo,is/os (+) was better than the interrupted group photo,is/os (+,-)) and also better than the absent groupphoto,is/os (-) .

Similar results were found in ELM. After 6 months in ranibizumab group, we found that the mean value of visual acuity in the continous group of photo,is/os (+) was better than the interrupted group photo,is/os (+,-)) and also better than the absent group photo,is/os (-) .

Similar results were found in ELM.On the other hand, in argon laser group at bsase line, we found that the mean value of visual acuity in the continous group of photo,is/os (+) was better than the interrupted group photo,is/os (+,-)).Similar results were found in ELM.After 6 months In argon laser group, we found that the mean value of visual acuity in the continous group of (photo,is/os (+)) was better than the interrupted group photo,is/os (+,-)), Similar results were found in ELM.

CONCLUSION

We can consider that the more damage of outer retinal layers at the time of DME the lower visual acuity following DME resolution, and the presence of intact of these layers is an important factor in determining final visual acuity.

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