

Evaluation of Macular Function after Vitrectomy in Diabetic Macular Edema

Mona Abdelkader*, Mohamed Mamdouh and Ayman Fawzy

Ophthalmology Center, Faculty of Medicine, Mansoura University, Egypt

Abstract: *Purpose:* To document the effects of successful vitrectomy on retinal function and anatomy in diabetic patients.

Methods: Three-port pars plana vitrectomy with detachment of posterior vitreous face was performed in 30 eyes of 25 patients with diabetic macular oedema DME (11 male, 14 Female). For each patient, visual acuity (VA) examination, measurement of retinal thickness using optical coherence tomography (OCT), full field electro-retinogram (ERG) and multifocal electroretinogram (MF-ERG) were performed before and 1 week, 1 month and 3 months after vitrectomy.

Results: Mean postoperative visual acuity was significantly improved ($P < 0.05$); mean retinal thickness was significantly ($P = 0.001$) decreased after 3 months of surgery (from 450 ± 150 into 220 ± 50 micron). b-wave amplitudes of all cone and rod responses of ERG were significantly decreased in all vitrectomized eyes after 1 week. At one month, rod response was still unimproved but improved after 3 months. Reduction in foveal function as well as in para-foveal areas detected in the MF-ERG within 1st month. Then, mean P₁ wave amplitude of MF-ERG of central ring increased and mean P₁ wave implicit time decreased. These changes of MF-ERG parameters observed 3 months after vitrectomy.

Conclusion: Multifocal electroretinogram can be useful to provide objective criteria for functional evaluation before and after vitrectomy in diabetic oedema.

INTRODUCTION

Pars plana vitrectomy has become the treatment of choice for a variety of vitreoretinal disorders. When separating the vitreous cortex from the inner most retinal, transient and/ or permanent damage to retinal structures may occur as a result from mechanical trauma as well as from postoperative inflammation [1,2]. As a result of clinical side effects from pars plana vitrectomy including retinal breaks, retinal detachment and visual field defects are not uncommon [3,4].

Clinically, retinal function has been reported to be reduced preoperatively by vitrectomy procedure but less is known about postoperative changes [5]. After successful operation, most patients gain improvement of visual acuity with reduction of metamorphopsia [6]. However, the VA level represents only a part of the impaired visual function which also includes metamorphopsia and blurred vision. There have been few methods to evaluate these visual disturbances. Focal electroretinography is one of them [7].

However, this method requires prolonged recording time and varying signal to noise ratios. In addition, focal ERG was designed to assess the macular area within 10 degree. So it is impossible to evaluate the electrophysiologic response in the perimacular area by this method. Using MF-ERG, it is possible to study

simultaneously not only the macular area but also the retina extending 30 degrees around the macula [8]. To assess the general as well as the local effect of vitrectomy, full field electroretinogram and MF-ERG were done in cases of DME in this study.

PATIENTS AND METHODS

Twenty-five (25 eyes) of twenty-five (25) patients with diabetic macular edema underwent pars plana vitrectomy (PPV) with detachment of posterior vitreous face at Mansoura Ophthalmic Center during period from January 2015 to November 2019. All patients were carried out in accordance with the tenets of the Declaration of Helsinki (1989) of the world medical association. The study was approved by Mansoura University Hospital trust ethics committee.

All patients had type II diabetes mellitus. Informed consent was obtained from each participant after the nature and possible consequences of the procedure had been explained.

Patients were included in the study if they had: **1-** macular oedema (DME) with attached posterior hyaloids caused by diabetic retinopathy as documents by slit-lamp biomicroscopy with contact lens, direct ophthalmoscopy and indirect ophthalmoscopy and fluorescein leakage on angiography **2-** a best corrected visual acuity on Snellen chart $\leq 20/70$ and

3- A minimum follow up period of 3 months, Exclusion criteria were: 1-a thickened and taut vitreous

*Address correspondence to this author at the Ophthalmology Center, Faculty of Medicine, Mansoura University, Egypt; Tel 002-050-2216440; Fax 002-050-2256104; E-mail: monaabdelkader78@yahoo.com

membrane or posterior vitreous detachment diagnosed by OCT or the presence of Weiss ring 2- Cataract surgery or intra-vitreous injection within 6 months before surgery 3- laser treatment including pan retinal photocoagulation (PRP), grid macular photocoagulation or posterior capsulotomy within 6 months before surgery 4- presence of dense refractive media opacity before or after surgery including vitreous hemorrhage, pre-retinal hemorrhage, tractional retinal detachment, cataract, active neovascularization, pre-macular membrane or vitreous cavity filled with irrigational fluid, silicon oil or air postoperatively.

A complete ophthalmic examination including visual acuity, applanation tonometer, slit lamp biomicroscopy using a +90D non contact lens and 3 mirror contact lens, colour fundus photography, Fluorescein angiography, Optical coherence tomography, full field electroretinogram and multi-Focal electroretinogram were performed on every patient at baseline, 1 week, 1 month, 3 months after surgery.

Fluorescein angiography was done using Topcon Corporation 2000, TRC, 50x, Japan. OCT was performed on every patient using (Topcon, three dimensional OCT, -1000, -USA). After dilation of the pupil, the macula was scanned in the horizontal and vertical meridians using the standard, linear cross hair pattern with a scan length of 6 mm centered through the fovea as determined by simultaneous evaluation of the red-free image on the computer monitor of the OCT scanner. The central macular thickness was measured automatically by software.

All ERG data were recorded using (Roland Consult, Brandenburg, Germany) Full Field ERG were performed after dark adaptation for 20 minutes then (3) steps were recorded rod response, maximal combined response and oscillatory potential response then light adaptation for 10 minutes then 2 steps were recorded cone response & 30 Hz flicker response. Stimulation and recording of MF-ERG responses were performed using the ISCFV guidelines [6]. The stimulus, consisting of 61 hexagons covering a visual field of 30° was presented at a frame rate of 75 Hz on a monitor 30 cm from the patient's eye. The luminance (97% contrast) of each hexagon independently alternated between black and white. The amplifier gain was set at 100,000, the lower cutoff frequency was 5 Hz and the upper frequency was 100 Hz. After maximum dilation of the pupil, Dawson Trick Iltskow (DTL) electrodes were applied to topically anaesthetized

cornea with one ground electrode in the forehead and two temporal reference electrodes and the opposite eye occluded. The eyes were optically corrected for near vision in order to see clearly the small fixation spot in the center of the stimulus matrix. For patients with poor vision such as there in this study, a Spoke-shaped (filled cross) fixation target was used and the patients were instructed to fixate at the intersection of the spokes. The recording period was comprised of eight segments of 30 seconds, providing a total recording time of 4 minutes.

The First-order component of MF-ERG was analyzed with reference to mean response density of P_1 amplitude (amplitude per unit of retinal area (nv/deg^2) and the mean implicit time (in milliseconds). The quality of the recording was controlled by real-time display and contaminated segments were discarded & repeated the values over foveae (1st 2 rings) and (other 3 rings). The surgical technique was standard three-port pars plana vitrectomy. All operations were performed by single surgeon. In all eyes, the posterior vitreous was separated from the retinal surface by applying suction from vitreous cutter.

Statistical Analysis

It was performed using SPSS version 17 on a windows platform. Mann-Whitney method was used to compare mean amplitudes and latencies of P_1 wave before & after surgery, the paired t-test was used for foveal thickness comparison.

RESULTS

The study included 30 eyes of 25 patients. The age & sex & clinical characteristics were included in Table 1 and 2. All patients were treated with pars plana vitrectomy with detachment of posterior vitreous without any intraoperative complication. No serious vision threatening complication such as vitreous hemorrhage, retinal detachment, sclera perforation or infectious endophthalmitis were found during the follow-up period.

Best Corrected Visual Acuity (BCVA)

The baseline of V.A was (mean 0.2 ± 0.05 SD). Compared with the preoperative level, the postoperative BCVA improved gradually with the passage of follow up.

Table 1: Clinical Features of Patients

Clinical Features	Number of Eyes	%
Classification of D.M		
PDR	20	83.3%
NPDR	5	16.6%
Type of oedema		
Diffuse	15	66.6%
Cystoid	10	33.3%
Previous laser photo coagulation		
Grid patter	5	16.6%
PRP	10	50%
No laser	10	33.3%
Previous intravitreal Trimacinolon injection	5	16.6%
Previous intravitreal Avastin injection	3	10%

Table 2: Changes of Visual Acuity (p=0.001)

Time points	Visual acuity	
	No change	Improved
	Number of eyes(%)	1 Snellen line 2 lines Number %
1 week	24(96.6%)	1(0.033%) -
1 month	20(66.6%)	5(33.3%) -
2 month	14(0.50%)	10(46.6%) 1(0.03%)
3 month	3(16.6%)	20(76.6%) 2(0.06%)

Table 3: Changes in Foveal Thickness in Micron by OCT

Duration	Foveal Thickness Range	Mean \pm SD
Preoperative	380-700	450 \pm 150
1 week	350-600	300 \pm 130
1 month	300-520	280 \pm 110
2 month	270-480	230 \pm 55
3 month	265-420	220 \pm 50
P	P=0.001	P=0.005

Foveal Thickness

The preoperative foveal thickness was 380-700 μ . After surgery, the mean foveal thickness were 350-600 μ at first week, 300-520 μ at the first month 270-480 μ at the second month, 265-420 μ at the third month. Macular oedema have been gradually absorbed 2 months postoperatively.

Table 4: Full Field ERG of Pre and Post Operative Values

Scotopic Rod Amplitude	Photopic Cone Amplitude	Oscillatory Potential amp implicit time	30Hz flicker amp implicit time
Preoperative 25 \pm 10	15 \pm 7.5	12 \pm 2.2 35 \pm 9	30 \pm 15 70 \pm 13
1 week 20 \pm 9	12 \pm 6.1	9 \pm 3.5 39 \pm 10	23 \pm 10 72 \pm 10
1 month 21 \pm 11	13 \pm 7.0	11 \pm 5.2 37 \pm 11	25 \pm 9 71 \pm 8
2 month 23 \pm 13	15 \pm 7.4	12 \pm 4.9 36 \pm 12	31 \pm 16 70 \pm 9
3 month 35 \pm 17	22 \pm 11	15 \pm 5.5 30 \pm 5	44 \pm 5.5 65 \pm 5.1
P 0.009	0.001	0.004 0.002	0.005 0.008

Standard ERG

At postoperative examination, all eyes displayed clear media, well detectable and reproducible responses were obtained from all eyes and the signal to noise ratio was high. In operated eyes examined 1 week postoperatively, the b-wave amplitudes of full field ERG in all dark-as well as light – adapted conditions were significantly reduced but very slight when compared to pre-operative values. At one month postoperatively, a significant reduction of rod was still evident in most eyes. At 2 month, amplitude responses were restored to preoperative – values. At 3 month, the amplitude responses were increased compared to preoperative value.

Table 5: Changes of Amplitude and Implicit Time of MF ERG

	Mean Value of R1,2	Value of R3,R4,R5
Changes of amplitude Preoperative	40 \pm 11.1	33 \pm 12.0
1 week	35 \pm 10.5	25 \pm 9
1 month	38 \pm 12	28 \pm 11
2 month	40 \pm 11	32 \pm 10
3 month	45 \pm 15	36 \pm 8.8
Changes of implicit times Preoperative	66 \pm 3.5	65 \pm 3.1
1 week	70 \pm 3.6	71 \pm 3.9
1 month	68 \pm 3.7	69 \pm 3.2
2 month	66 \pm 2.8	65 \pm 2.9
3 month	60 \pm 2.2	61 \pm 3.3
P	0.005	0.005

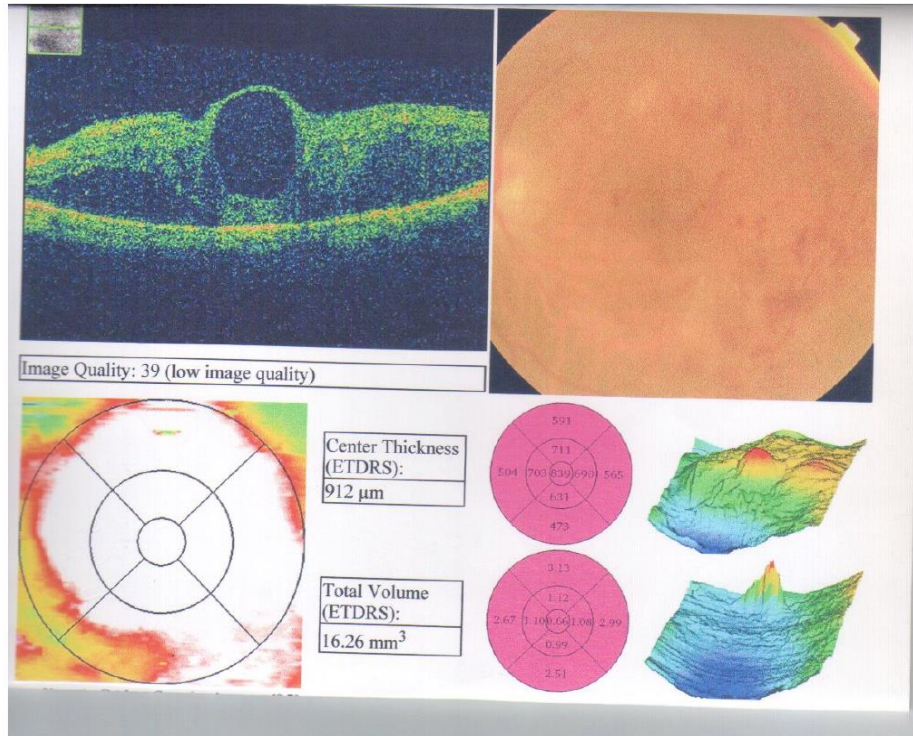


Figure 1: OCT of Diabetic patient before vitrectomy.

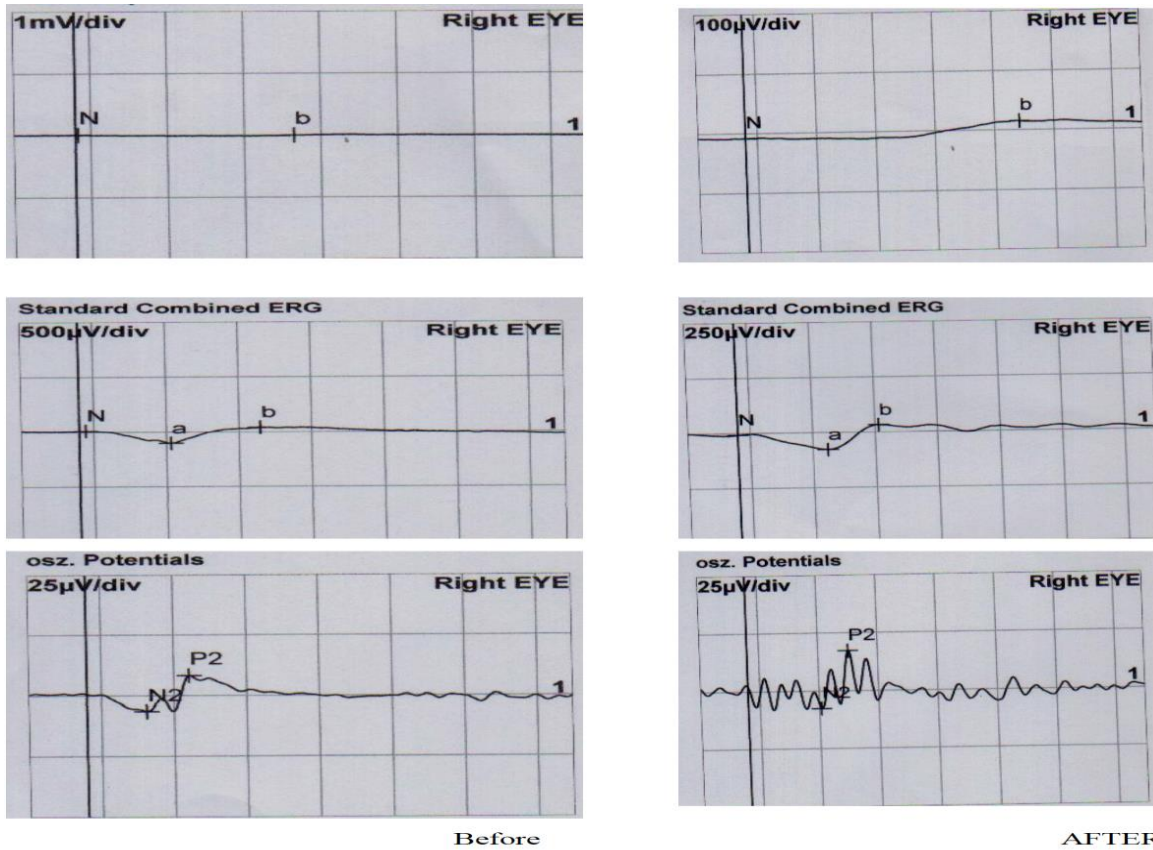


Figure 2(a): Scotopic ERG before and after vitrectomy (there was improvement of ERG parameters before & after vitrectomy).

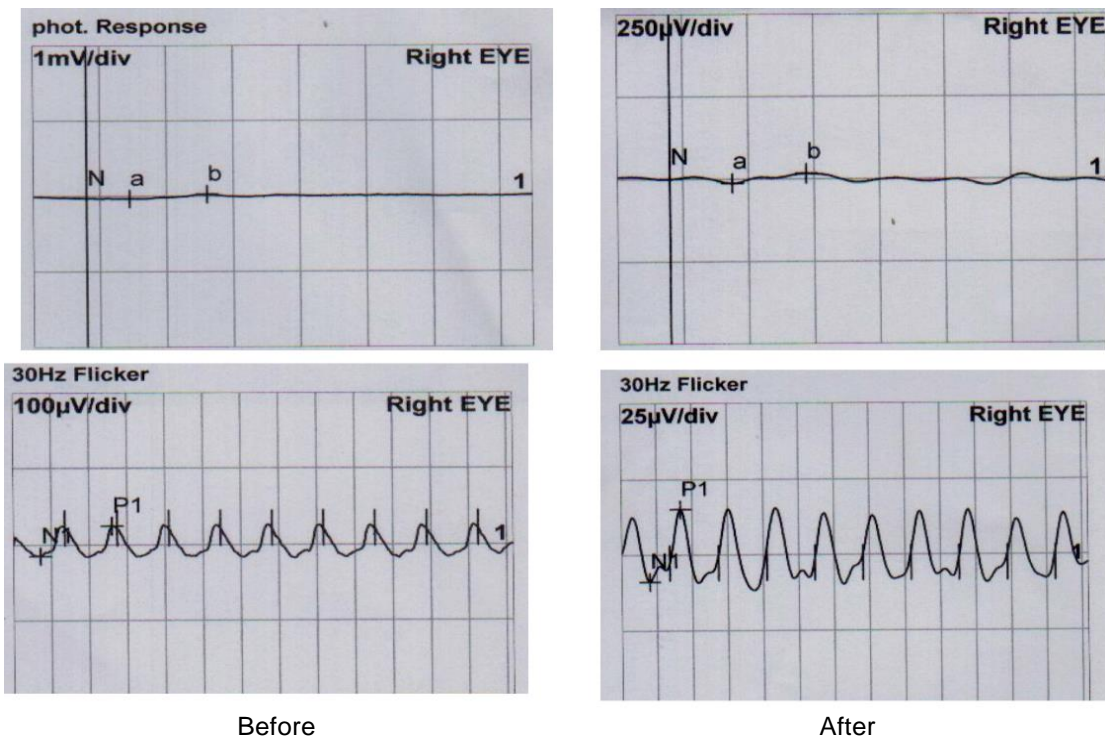


Figure 2(b): Photopic ERG before and after vitrectomy (There was increase in amplitude and reduction in latency after vitrectomy).

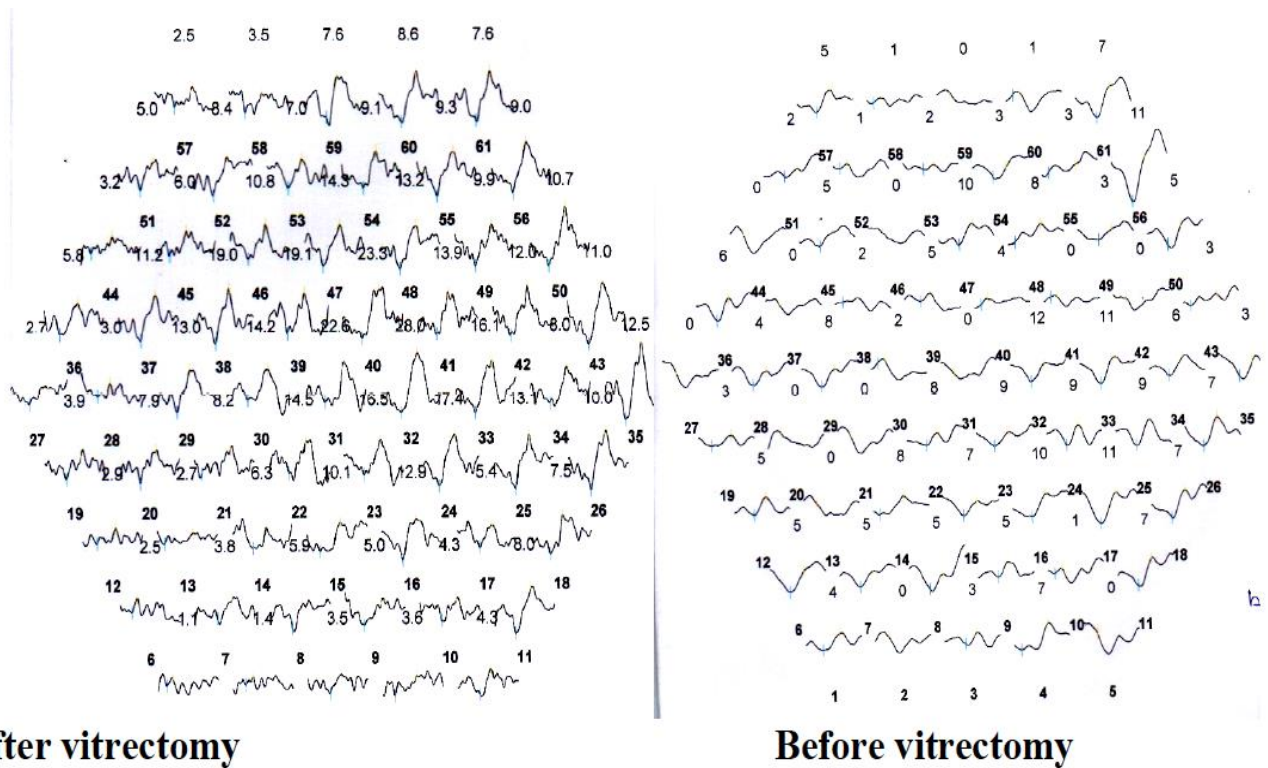
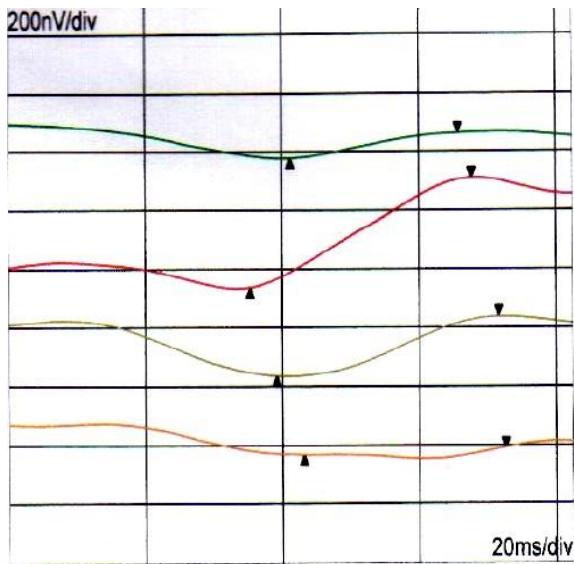
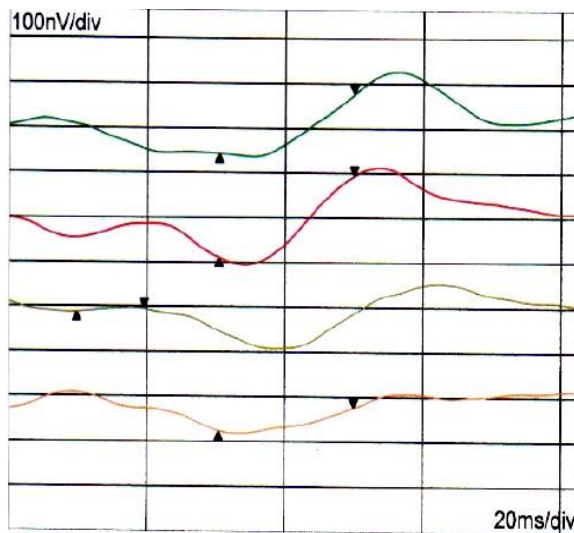


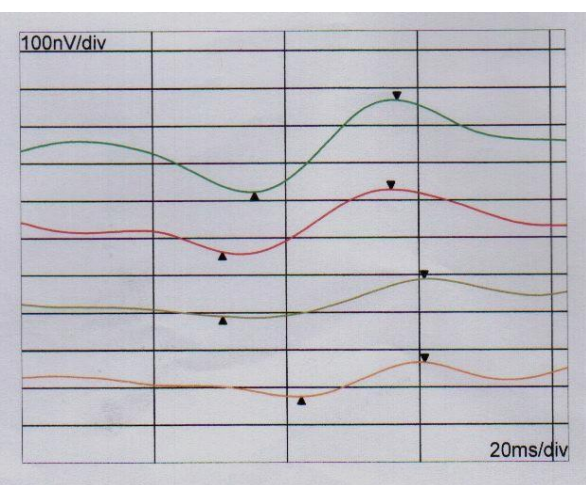
Figure 3(a): Trace array MFERG before and after vitrectomy. There was irregularity of curves & no apparent peak or trough before vitrectomy and 3 months after vitrectomy, there was well defined peak and trough with improvement of amplitude and latency).



Before vitrectomy (There was delay in latency)



2 month After vitrectomy (There was improve in amplitude and latency).



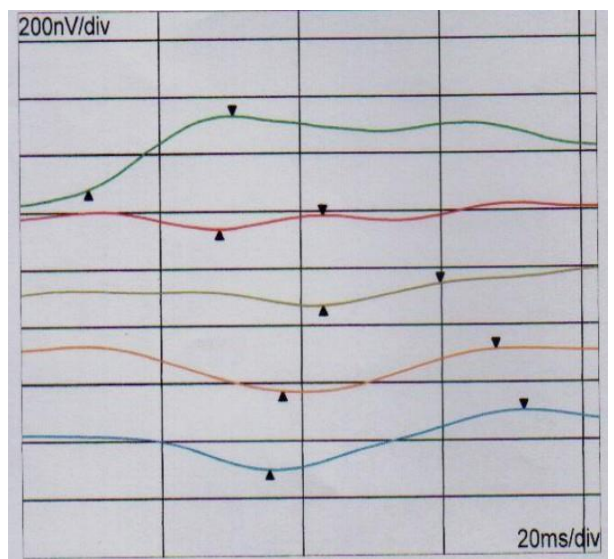
3 months after vitrectomy (there was more increase in amplitude and reduction in latency)

Figure 3(b): Four Quadrants form of MFER before and after vitrectomy operation.

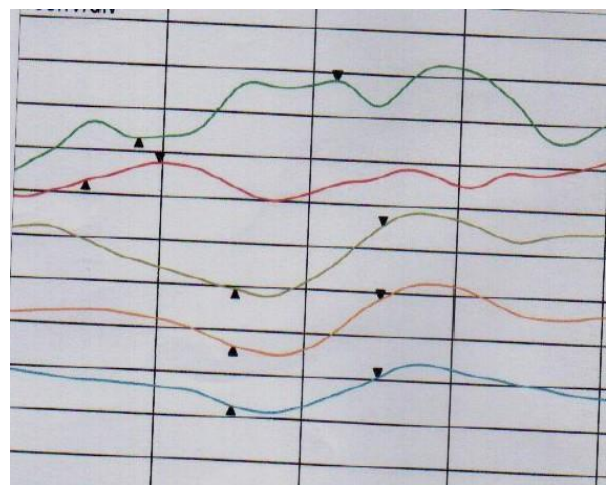
Multifocal ERG

There is reduction in macular function after vitrectomy compared to preoperative value at 1 week and 1 month. At 2 month the value increase to return to preoperative value & at 3 month the value increased & improved than preoperative values.

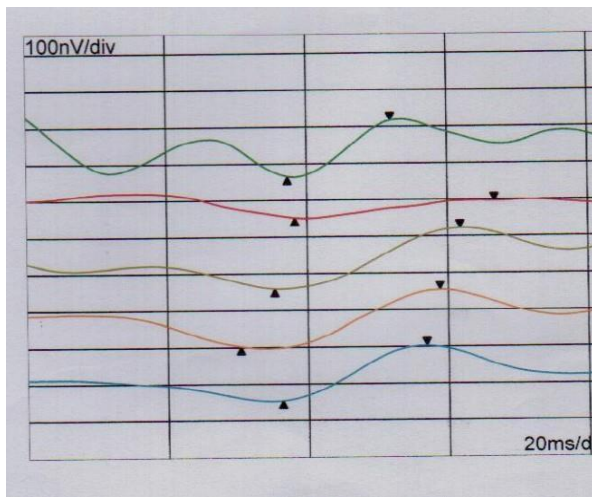
There was weak correlation between foveal thickness and visual acuity ($R=0.1$ & $P=0.02$) Also, there was weak correlation between ME ERG parameters and foveal thickness and visual acuity. ($R=0.2$ & $P=0.005$ & $R=0.22$ & $P=0.002$ respectively).



Ring form of MF ERG before operation (there was reduction in amplitude in all rings).



Ring form of MFERG after 2 month of vitrectomy (There was improvement of amplitude & latency in peripheral rings).



Ring form of MFERG 3 months after vitrectomy (There was more improvement in amplitude & latency).

Figure 3(c): Ring form of MFEG before and after vitrectomy.

DISCUSSION

Diabetic macular oedema is a main cause of visual impairment in patient with diabetic retinopathy [9,10]. The condition is characterized by increased vascular permeability and the deposition of hard exudates in the central retina. A hypothesis put forth on the pathophysiology of DMO: the oedema results from a traction of the posterior vitreous on the macula. Several studies have reported that removal of a thick and taut premacular posterior hyaloids membrane is effective in reducing the macular oedema and improving visual acuity in diabetic eyes [11-13].

Also, this study demonstrated that vitrectomy reduced the macular oedema and improved the visual acuity significantly. In order to make further investigation on the efficacy of vitrectomy, MF ERG was used to evaluate surgical outcomes on macular visual function. It has proven to be a powerful tool in various congenital and acquired retinal diseases as it reflects retinal function under photopic condition [14,15].

Thus, this technique has been used not only for retinal diseases with localized lesions, but also for macular diseases such as macular oedema and holes. Yomamoto, *et al* believed that the MF-ERG may be a helpful technique in evaluating surgery effects for DMO [16].

Leozappa, *et al* found increase in MFERG amplitudes and improvement in MFERG latencies. It was found that the changes of parameters of MF-ERG

observed 6 months after surgery were consistent with those recorded just 1 week after surgery [17]. Ma, *et al* recorded that MFERG response increase gradually in macular and para macular area after vitrectomy for DMO.

Both latency and amplitude were improved after surgery, but latency was more affected. p_1 latency started to decrease at second postoperative month; p_1 amplitude started to increase at the third postoperative month [18]. While, Yamamoto, *et al* found non significant change in MFERG amplitude while there was significant decrease in implicit time postoperative [19].

Also, Kim *et al* found that the MF-ERG implicit time changes was significant. It was found that preoperative MF-ERG parameters, especially the implicit time can be useful indicators for predicting functional visual prognosis after vitrectomy in DMO [20]. While Wallenten, *et al* found reduction of b-wave amplitudes of all cone & rod responses of the ERG at three day postoperative, also at 28 day but returned to normal by 58 day. There was no reduction in the central cone function detected by MF-ERG [21].

In this study, there was reduction of rod & cone response detected by full field ERG at 1 week & 1 month then increased than preoperative value at third month. Also, There were reduction in MF-ERG parameters at 1 week & 1 month then improved than preoperative value at the third month. The causes of reduction of retinal function at 1week were low temperature of the infusion fluid used during vitrectomy and elevated intraocular pressures. Also, the use of unbuffered infusion solution, and light exposure from an end illuminating light source [20,21], may be causes of reduction of retinal function in the early postoperative period.

In this study, there were reduction in macular oedema from first week & there were no correlation between MFERG parameters & foveal thickness & visual acuity improvement. The same as Kim *et al* found that MFERG response at peripheral rings and central macular thickness did not show significant association with visual prognosis [20,22,23].

Also, Kumar & colleagues reported that visual improvement after vitrectomy in DME patients was limited, despite a reduction of macular thickness [24]. While Ma, *et al* found that the tendency in the change of macular function is coincident with that of macular morphology [18,25].

In summary, pars plana vitrectomy is helpful not only in reducing macular oedema and improving visual acuity but also in reinforcing the resume of macular and para macular visual function. The macular responses recorded with full field & multifocal ERG system is a useful tool to evaluate the effect of vitrectomy for DME objectively.

REFERENCES

- [1] Avery R. L., Castellarin A. A, Steinle N. C. "Systemic pharmacokinetics following intravitreal injections of ranibizumab, bevacizumab or aflibercept in patients with neovascular AMD," *British Journal of Ophthalmology* 2014 ,98 , (12) 1636–1641.
<https://doi.org/10.1136/bjophthalmol-2014-305252>
- [2] Bonnin, O. Sandali, S. Bonnel, C. Monin, and. El Sanharawi M .Vitrectomy with internal limiting membrane peeling for tractional and nontractional diabetic macular edema," *Retina*,2015;35(5) 921–928,
<https://doi.org/10.1097/iae.0000000000000433>
- [3] Morizane Y. Kimura S., Hosokawa M. Planned foveal detachment technique for the resolution of diffuse diabetic macular edema," *Japanese Journal of Ophthalmology* 2015, 59;5:279–287.
<https://doi.org/10.1007/s10384-015-0390-4>
- [4] Yonemura N, Hirata A, Hasumura T. Fundus changes corresponding to visual field defects after vitrectomy for macular hole . *ophthalmology* 2001;108,1638-43.
[https://doi.org/10.1016/s0161-6420\(01\)00677-7](https://doi.org/10.1016/s0161-6420(01)00677-7)
- [5] Miyake y, Horiguchi M. Electro-retinographic alterations during vitrectomy in human eyes. *Graefes Arch clin Exp ophthalmol* 1998; 236:13-17.
<https://doi.org/10.1007/s004170050036>
- [6] Shinoda K, Ishida S, Kawashima A. New method For quantification of metamorphopsia in patients with epiretinal membrane . *Jpn J ophthalmol* 2000,44:424-27.
[https://doi.org/10.1016/s0021-5155\(00\)00173-8](https://doi.org/10.1016/s0021-5155(00)00173-8)
- [7] Takinowa A, Horiguchi M, Kondo M. Focal macular electroretinograms in eyes with idiopathic epimacular membrane. *Am J ophthalmol* 1999; 127:559-64.
[https://doi.org/10.1016/s0002-9394\(98\)00447-4](https://doi.org/10.1016/s0002-9394(98)00447-4)
- [8] Marmor MF,Hood DC, Keating D Guidelines for basic multifocal electretinography (MFERG) .*Doc ophthalmol* 2003;106:105-15.
- [9] Pelzek C, Lim JI. Diabetic macular aedema : review and update *ophthalmol clin North Am*, 2002;15:522-63.
[https://doi.org/10.1016/s0896-1549\(02\)00043-3](https://doi.org/10.1016/s0896-1549(02)00043-3)
- [10] Klein R, Klein BE, Moss SE. The Epidemiologic Study of Diabetic Retinopathy XVII: the 14-year incidence and progression of diabetic retinopathy and associated risk factors in type 1 diabetes. *Ophthalmology* 1996; 105:1801-15.
[https://doi.org/10.1016/s0161-6420\(98\)91020-x](https://doi.org/10.1016/s0161-6420(98)91020-x)
- [11] E, Moisseiev J and Loewenstein A Surgical treatment for diabetic macular edema *Journal Expert Review of Ophthalmology* 2016,11(3),173-9.
<https://doi.org/10.1080/17469899.2016.1182864>
- [12] Kumagai K,Furukawa M,Ogino N. Long- term Follow up of vitrectomy for diffuse non tractional diabetic macular aedema . *Retina* 2009; 29: 464-72.
<https://doi.org/10.1097/iae.0b013e31819c632f>
- [13] Kim YM, Chung EJ, Byeon SH, Pars plana vitrectomy with internal limiting membrane Peeling compared with intravitreal triamcinolone injection in the treatment of diabetic macular oedema . *ophthalmologia* 2009; 223:17-23.
<https://doi.org/10.1159/000161878>
- [14] Chan HHL, Broum B. Pilot study of the multifocal electretinogram in ocular hypertension. *Br. J. ophthalmol* 2000; 84:1147-53.
<https://doi.org/10.1136/bjo.84.10.1147>
- [15] Hasegawa S, Oshima A, Hayakawa Y. Multifocal electroretinograms in patients with branch retinal artery occlusion . *Invest ophthalmol VIS Sci* . 2001; 42:298-4.
<https://doi.org/10.1167/iovs.03-0083>
- [16] Yamamoto S,Yamamoto T,Hayashi M . Morphological & functional analyses of diabetic macular oedema by optical coherence tomography and multifocal electro- retinograms. *Graefe's Arch clin Exp ophthalmal* 2001; 239:96-1.
<https://doi.org/10.1007/s004170000238>
- [17] Leozappa M, Micelli Ferrari T, Grossi T. Prognostic prediction ability of postoperative multifocal ERG after vitrectomy for diabetic macular oedema . *Eur. J ophthalmal* 2008; 18(4) : 609-13.
<https://doi.org/10.1177/112067210801800418>
- [18] Ma J, yaokjiang J. Assessment of macular function by multifocal electroretinogram in diabetic macular oedema before and after vitrectomy. *Doc ophthalmol* 2004; 109:134-7.
<https://doi.org/10.1007/s10633-004-2890-2>
- [19] Yamamoto S, Yamamoto T, Ogata K. Morphological and functional changes of the macula after vitrectomy and creation of posterior vitreous detachment in eyes with diabetic macular oedema . *DOC ophthalmol* 2004; 109:249-53.
<https://doi.org/10.1007/s10633-004-8056-4>
- [20] Kim YM, Lee SY Koh Ht. Prediction of postoperative multifocal electroretinography in eyes with diabetic macular oedema . *Graefes Arch clin Exp ophthalmol* 2010; 248:1387-93.
<https://doi.org/10.1007/s00417-010-1398-6>
- [21] Wallenten KG, Andreasson S, Ghosh F. Retinal Function after vitrectomy . *Retina* 2008;28(4) : 558-63 . de Raod S, Szczesny PJ , Munz K . light damage in the rat retina : gill filrillary acidic protein accumulates in correlation with photoreceptor damage . *Ophthalmic Res* 1996; 28:99-7.
<https://doi.org/10.1097/iae.0b013e31815e9890>
- [22] Van den Biesen PR, Berenschot T, verdaasdonk RM. Endoillumination during vitrectomy and photo toxicity threshold . *Br J ophthalmal* 2000; 84:1372.
<https://doi.org/10.1136/bjo.84.12.1372>
- [23] Kumar A; Sinha S, Azad R. Comparative evaluation of vitrectong & dye enhanced ILM peel with grid Laser in diffuse diabetic macular oedema. *Graefes Arch Clin EXP Ophthalmol* 2007; 245: 360-68.
<https://doi.org/10.1007/s00417-006-0456-6>
- [24] Samir M. E, Ahmed M. A and Mahmoud A. A .Submacular Injection of Ranibizumab as a New Surgical Treatment for Refractory Diabetic Macular Edema. *Hindawi Journal of Ophthalmology*,2019:1-8.
<https://doi.org/10.1155/2019/6274209>

Received on 20-10-2019

Accepted on 03-11-2019

Published on 28-12-2019

DOI: <https://doi.org/10.31907/2414-2093.2019.05.04>

© 2019 Kader *et al.*; Licensee Green Publishers.

This is an open access article licensed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0/>) which permits unrestricted, non-commercial use, distribution and reproduction in any medium, provided the work is properly cited.