Multifocal Electroretinogram Changes after Vitrectomy in Patients with Diabetic Macular Edema

Fathy Elsalhy (fathyelsalhy2010@gmail.com)
Al-Azhar University Faculty of Medicine

Hisham Fawzy Khalil
Al-Azhar University Faculty of Medicine

Mohamed Mohamed-Aly Ibrahim
Al-Azhar University Faculty of Medicine

Research Article

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Abstract

Purpose: was to assess the results of vitrectomy with and without internal limiting membrane (ILM) peeling on retinal function and anatomy in patients with diabetic macular edema (DME).

Methods: Pars plana vitrectomy (PPV) was done in 40 eyes of 40 patients with DME (15 male, 25 female). Patients were enrolled randomly into two different groups. Group A- comprised (20) eyes who underwent vitrectomy without ILM peeling. Group B- comprised (20) eyes who underwent vitrectomy with ILM peeling. For each patient, visual acuity (VA) examination (in decimal charts), assessment of central macular thickness (CMT) with optical coherence tomography (OCT) and multifocal eletroretinogram (MF-ERG) were done before and 3 months post vitrectomy.

Results: Postoperative mean VA increased significantly (from 0.17 to 0.27 in group A and from 0.21 to 0.38 in group B). Mean CMT decreased significantly after surgery (from 493 µm to 315 µm in group A and from 502 µm to 299 µm in group B). Mean P1 wave amplitude (nV/ deg2) in the macular area increased after surgery (from 32.15 to 41.10 in group A and from 35.5 to 40.8 in group B). Mean P1 wave latency (millisecond) in the macular area decreased after surgery (from 50.30 to 36.40 in group A and from 49.5 to 39.2 in group B).

Conclusion: Vitrectomy with and without ILM peeling improve VA and macular edema in diabetic patients moreover an increase of amplitude and reduction of the latency of the macular mf-ERGs indicated an improvement of the macular visual function.

Introduction

With increasing prevalence of diabetes mellitus (DM) across the globe, DME has become a major source of vision loss necessitating management by ophthalmologists. A meta analysis in 2010 expected that nearly 93 million persons may suffer from diabetic retinopathy (DR) also 28 million may have vision threatening retinopathy [1].

Mf-ERG is an objective electrophysiologic technique that measures the electrical changes in the central retinal area. This technique accurately assess the electrophysiologic activity in multiple retinal areas, and gives us a topographic charting of retinal function [2–4].

The role of vitrectomy for treatment of DME has been discussed in many clinical studies but it hasn't been completely assessed in literature [5, 6].

Vitrectomy is indicated in cases of tractional epiretinal membrane (ERM) or vitreomacular traction (VMT) [7].

A number of studies have reported favorable results for vitrectomy in DME even in the absence of macular traction [8–10].

Different mechanisms have been supposed to clarify the positive effects of vitrectomy in DME one of which is increase oxygenation to the internal retina; increasing perifoveal capillary blood flow. In addition, increased oxygen tension is likely to reduce vascular endothelial growth factor (VEGF) [11, 12].

The purpose of this work was to assess the results of vitrectomy with and without peeling of the ILM on retinal function and anatomy in patients with DME.

Subjects And Methods

Subjects

40 eyes of 40 patients with DME underwent a standard three-port 23 gauge PPV with detachment of posterior vitreous face (in group B additional ILM peeling was done). All patients were type II DM.

All surgical procedures and fellow up were done in the departments of ophthalmology at Al Azhar University hospitals between January 2019 and April 2021.

This study was approved by Al-Azhar Medical Research Ethical Committee

A clear printed approval was taken from each participant before entering the study.

Subjects were included in the study if they had:**1-** Persistent DME as documented by direct observation by slit-lamp biomicroscopy, fluorescein leakage on angiography and OCT scanning (CMT) ≥ 300 μm) **2-** Best corrected visual acuity (BCVA) ≥ 6/60 (recorded with Snellen chart). **3-**No media opacity before surgical procedure as dense cataract, vitreous haemorrhage and so on. **4-**No evidence of tractional macular detachment by ERM or Angiographic evidence of macular ischemia.

For each participant, VA assessment, measurement of CMT (using OCT), and mf-ERGs were done before and 3 months post vitrectomy.

BCVA was measured in decimal charts.

CMT was measured by OCT (DRI OCT TRITON PLUS, TOPCON, Japan), performed vertically and horizontally through the central fovea (scan length 5 mm).

Stimulation and recording of MF-ERG responses were done using Retiscan system (Roland Consult, Brandenburg, Germany); by the use of H-K loops; dilatation of the patient's pupil were done with the use tropicamide 0.5%; the monitor displays 61 hexagons arranged concentrically and covering a visual field of approximately 30°.The hexagons size was scaled with eccentricity to produce nearly the same amplitude responses at all sites. The display flickers because each hexagon follow a pseudo-random binary m-Sequence of white and black presentation at a rate of 75 Hz. After correction of refractive error (viewing distance from monitor is 30 cm) patients were asked to fixate on the mark in the center of the monitor. for those with poor VA, signals were amplified with a gain of 100,000 and filtered with a

bandpass filter (10–300 Hz). The recording sessions were broken into eight trials each measure 30 seconds giving a total recording time of about 4 minutes. in many diabetic patients the responses from ring 1 (central hexagon) were very weak and not detectable so, we sum the responses from ring 1 and ring 2 (central seven hexagons) and used as the macular response covering a visual field of 10° approximately. The amplitude and latency of the first positive wave (P1) of the first order kernel were analyzed.

Method:

40 patients were enrolled in the study in 2 groups: each comprised 20 patients

- Group (A): included (20) eyes where PPV was done without ILM peeling.
- Group (B): included (20) eyes where PPV was done with ILM peeling.

All procedures were done by the same well experienced vitreoretinal surgeon. The surgical procedure was standard three-port 23-gauge PPV. In all patients, detachment of the posterior vitreous was done by active suction with vitrectomy probe.

In group B: ILM was stained with brilliant blue G (Membrane Blue Dual, D.O.R.C. International) followed by ILM peeling using ILM forceps (D.O.R.C. international).

Panretinal laser photocoagulation (PRP) and direct laser photocoagulation to macular microaneurysms had been done in all patients but grid laser macular photocoagulation hadn't been done in any patient before entering the study.

All patients were left on air postoperatively.

All patients were phakic: combined phacovitrectomy was done in 9 cases (cataract extraction with implantation of intraocular lens in the bag). 3 eyes in group A and 6 eyes in Group B

Statistical analysis:

Data were investigated and analyzed using SPSS V-20. Quantitative values were reported in the form of mean ± SD (standard deviation).Qualitative data were reported in the form of numbers and percentage.

These tests were done:

♣ Parametric independent T-sample test for comparisons of the means of two independent groups and Mann Whitney U test(z) for comparisons of two groups in non-parametric data.

♣ Paired sample t-test for comparison between related sample.

♣ Pearson's correlation coefficient (r) test to study the possible association between two sets of variables

♣ Scatter plot: a graph of two variables plotted along two axes, the pattern of the resulting points show the correlation present.

♣ Percentage change% (Delta change): to calculate the percent of improvement after intervention. It equals the difference between 2nd reading- 1st reading/ 1st reading x 100.

♣ Mean Difference: to calculate the mean improvement after intervention. It equals the difference between 2nd reading- 1st reading.

♣ Probability value (p-value) was considered significant if < 0.05 and considered highly significant if < 0.001.

Results

The mean age of the studied cases was 57.16 ± 6.81 years ranging from 44–66 year in group A and 61 ± 6.87 years ranging from 56–71 year in group B. The studied cases included 8 males (40%) and 12 females (60%) in group A and 7 males (35%) and 13 females (65%) in group B.

The mean diabetes duration was 13.23 ± 4.47 ranging from 7–21 year in group A and 10.71 ± 5.69 ranging from 4–24 year in group B.

The mean preoperative HbA1c level was 7.98 ± 0.92 ranging from 6.1–9.2 in group A and 8.36 ± 1.17 ranging from 5.6–9.7. in group B.

The mean preoperative IOP in group A was 15.36 ± 3.17 ranging from 12–21 mm.Hg. and 16.44 ± 2.18 ranging from 11–20 mm.Hg. in group B.

The differences among the studied groups regarding baseline characteristics were statistically insignificant.

BCVA

The mean preoperative BCVA in our patients was 0.17 ± 0.08 (range, 0.1–0.4) in group A and 0.21 ± 0.10 (range, 0.1–0.4) in group B (table 1).

The mean postoperative BCVA was 0.27 ± 0.14 (range, 0.1–0.4) (Delta change 58.8 ± 51.21) in group A and 0.38 ± 0.21 (range, 0.2–0.5). (Delta change 81.0 ± 73.6) in group B.

The postoperative BCVA significantly increased compared with preoperative one in both groups. (p-value = 0.002 in group A and < 0.001 in group B)..

The differences among the studied groups in pre and post BCVA were statistically insignificant.

By the end of our study, we had 13 eyes (65%) improved in BCVA in group A compared to 14 eyes (70%) in group B while there was 6 eyes (30%) in group A did not improve compared to 3 eyes (15%) in group B, only 1 eye (5%) in group A worsened compared to 3 eyes (15%) in group B

Table (1)

Comparison between Group A and Group B according to BCVA.

BCVA	Group A (n = 20)	Group B (n = 20)	Test	p-value
Pre				
Mean ± SD	0.17 ± 0.08	0.21 ± 0.10	T=-1.448	0.156
Range	0.1–0.4	0.1–0.4		
Post				
Mean ± SD	0.27 ± 0.14	0.38 ± 0.21	T = 1.949	0.059
Range	0.1–0.4	0.2–0.5		
Paired t-test	4.059	5.627		
p-value	0.002*	< 0.001**		
Mean Diff.	0.10 ± 0.11	0.17 ± 0.14	Z = 1.758	0.087
Delta Change%	58.8 ± 51.21	81.0 ± 73.6	Z = 1.107	0.275
Using: t-Independent Sample t-test; z-Mann Whitney test; p-value > 0.05 NS				

CMT

The mean preoperative CMT in our patients was 493.50 ± 124.27 µm ranging from 309 µm to 803 µm in group A and 502.35 ± 103.31 µm ranging from 334 µm to 748 µm in group B.

The mean postoperative CMT was 315.90 ± 67.31 µm ranging from 219 µm to 499 µm in (Delta change – 36.0 ± 11.13) group A and 299.10 ± 58.46 µm ranging from 184 µm to 422 µm (Delta change – 40.5 ± 9.8) in group B.

There was a significant reduction of CMT postoperatively compared with preoperative values in both groups (p-value < 0.001).

The differences among the studied groups in pre and post CMT were statistically insignificant.

Table (2)

Comparison between Group A and Group B according to CMT.

CMT	Group A (n = 20)	Group B (n = 20)	Independent t-test	p-value
Pre				
Mean ± SD	493.50 ± 124.27	502.35 ± 103.31	-0.245	0.808
Range	309–803	334–784		
Post				
Mean ± SD	315.90 ± 67.31	299.10 ± 58.46	0.843	0.405
Range	219–499	148–422		
Paired t-test	-9.368	-12.256		
p-value	< 0.001**	< 0.001**		
Mean Diff.	-177.60 ± 84.78	-203.25 ± 74.2	-1.018	0.315
Delta Change%	-36.0 ± 11.13	-40.5 ± 9.8	-1.357	0.183
Using: t-Independent Sample t-test; p-value > 0.05 NS				

MF-ERG

The mean Preoperative P1 amplitude in ring (1 + 2) (nV/degree2) was 32.15 ± 6.86 ranging from 18 to 44 in group A and 35.50 ± 8.15 ranging from 20 to 50 in group B.

The mean postoperative P1 amplitude in ring (1 + 2) was 41.10 ± 7.15 ranging from 30 to 55 (Delta change 27.80 ± 22.67) in group A and 40.85 ± 7.26 ranging from 23 to 51 (Delta change 15.1 ± 13.63) in group B.

Compared to the preoperative P1 amplitude values the difference was significant in both groups (p-value < 0.001)

The mean Preoperative P1 latency (ms) in ring (1 + 2) was 50.30 ± 7.36 ranging from 39 to 68 in group A and 49.55 ± 7.65 ranging from 38 to 66 in group B.

The mean post operative P1 latency (ms) in ring (1 + 2) was 36.40 ± 8.17 ranging from 22 to 50 (Delta change − 27.60 ± 14.64) in group A and 39.25 ± 8.50 ranging from 27 to 61 (Delta change − 20.8 ± 8.93) in group B.

Compared to the preoperative P1 latency values the difference was significant in both groups (p-value < 0.001)

The differences among the studied groups in pre and post amplitude and latency were statistically insignificant.

Table (3)

Comparison between Group A and Group B according to MF-ERG.

MF-ERG	Group A (n = 20)	Group B (n = 20)	Test	p-value
Amplitude				
Pre				
Mean ± SD	32.15 ± 6.86	35.50 ± 8.15	T=-1.407	0.168
Range	18–44	20–50		
Post				
Mean ± SD	41.10 ± 7.15	40.85 ± 7.26	T = 0.110	0.913
Range	30–55	23–51		
Paired t-test	7.035	6.364		
p-value	< 0.001**	< 0.001**		
Mean Diff.	8.95 ± 5.69	5.35 ± 3.76	Z=-2.361	0.024*
Delta Change%	27.80 ± 22.67	15.1 ± 13.63	Z=-2.147	0.038*
Latency				
Pre				
Mean ± SD	50.30 ± 7.36	49.55 ± 7.65	T = 0.316	0.754
Range	39–68	38–66		
Post				
Mean ± SD	36.40 ± 8.17	39.25 ± 8.50	T=-1.081	0.287
Range	22–50	27–61		
Paired t-test	-7.574	-10.760		
p-value	< 0.001**	< 0.001**		
Mean Diff.	-13.90 ± 8.21	-10.30 ± 4.28	Z = 1.739	0.090
Delta Change%	-27.60 ± 14.64	-20.8 ± 8.93	Z = 1.773	0.084
Using: t-Independent Sample t-test; z-Mann Whitney test;				
*p-value > 0.05 NS; *p-value < 0.05 S*				

Significant correlation was found among postoperative changes of the macular thickness, BCVA,

amplitude & latency of the mf-ERGs and HbA1c.

Table (4): Correlation between CMT Change with all parameters, using Pearson Correlation Coefficient in all patients.

Parameters in all patients	CMT Change	
	r-value	p-value
Age (years)	-0.113	0.436
Duration of DM (years)	0.024	0.868
HbA1c	0.865	0.423
IOP	-0.202	0.158
BCVA Change Pre and Post	-0.288	0.043*
MF-ERG [Amplitude] Change Pre and Post	-0.870	< 0.001**
MF-ERG [Latency] Change Pre and Post	0.888	< 0.001**
*r-Pearson Correlation Coefficient, p-value > 0.05 NS; *p-value < 0.05 S; **p-value < 0.001 HS*		

This table shows statistically significant negative correlation between CMT Change with BCVA Change and MF-ERG [Amplitude] Change, while HbA1c and MF-ERG [Latency] Change show significant positive correlation.

Only one eye (0.05%) in group A had an iatrogenic break that was treated intaoperatively by endo-laser photocoagulation with air tamponade post operative without development of postoperative retinal detachment, no iatrogenic breaks occurred in group B.

In terms of postoperative complication, mild vitreous haemorrhage developed in 2 cases. 1 case (0.05%) in group A and 1 case (0.05%) in group B, with spontaneous resolution at 2 month postoperatively.

At the end of study (after 3 months) we had 5 cases developed cataract; 3 out of 17 phakic eyes in group A (17%) and 2 out of 14 phakic eyes in group B (14%).

Discussion

DME is a major source of vision loss in patients with DR. The condition is characterized by retinal vascular hyper permeability which is accompanied by fluorescein leakage on angiography and accumulation of hard exudates within the macula. [13].

DME thought to result from traction of thick pre macular cortical vitreous. Various studies have revealed that removal of this thickned and adherent posterior hyaloids is helpful in decreasing macular oedema and increasing VA in diabetic eyes [14–16].

Many studies have demonstrated postoperative outcomes following PPV in patients with DME regarding anatomical and functional changes of the macula using OCT and mf-ERG [2–4] **Yamamoto and his associates** reported that mf-ERG offered supplementary evidence for improved macular function post vitrectomy, and for the safety of vitrectomy for DME [4].

Many reports have emphasized the role PPV in eyes with DME refractory to traditional focal or grid laser macular photocoagulation. These studies have revealed a significant improvement in VA, and reduction of CMT measured by OCT [15–20].

The role of ILM peeling in DME is not clear in the literature. Some authors suggest better structural and functional results after ILM peeling[21, 18] but others show no significant differences between groups with and without ILM peeling as regard structural and functional results [22, 9].

In non tractional DME, some studies support ILM peeling because it's the only way to eliminate the vitreous remnants which causes continuous traction and provides a scaffold for astrocyte proliferation thus prevent 2ry ERM formation in addition, ILM peeling accelerates absorption of macular edema because it eliminates all tractional forces at the vitreortinal interface [21].

Our results demonstrated that vitrectomy with and without ILM peeling reduce macular edema and increase VA significantly in diabetic patients in both groups (group B much more better and the difference was statistically insignificant between both groups), Mf ERG parameters showed significant improvement regarding amplitude & latency in both groups

Decrease of the macular visual function preoperative may reflect pathological alterations in the inner retina, and the increase of macular function postoperative may reflect the improvement from those pathological alterations.so MF-ERG may be used for prediction of macular visual function post vitrectomy.

Yamamoto et al [5] conducted his study on 19 eyes of 17 patients with DME that underwent combined phaco vitrectomy. They reported a significant improvement of VA (from log MAR VA 0.7 preop to 0.4 post op), significant decrease of macular thickness measured by OCT (from 510 μm preoperatively to 201 μm postoperatively), and a significant decrease of a and b wave latencies (from 30.0 ms preoperatively to 28.3 ms postoperatively), however there was no significant change in the central amplitude (from 6.3 nV/deg2 preoperatively, to 6.1 nV/deg2 postoperatively). Similar findings were obtained by **Terasaki et al** [23].

Leozappa et al has evaluated the mfERG 1 week and 1, 3, and 6 mo after standard three-port PPV with peeling of ILM for 25 eyes of 21 patients with DME: He found improvement in VA (from log MAR VA 0.7 preop to 0.5 post op) and reduction of retinal thickness(from 537 μm to 298 μm) with increase in MFERG

amplitudes and improvement in MF ERG latencies (Mean P1 amplitude improved from 0.33 mV to 0.40 mV; mean P1 latency reduced from 36.4 ms to 32.5 ms), and considered mfERG useful for predicting functional prognosis [24].

Ma et al reported that MF-ERG response improve gradually following vitrectomy for DME in the macular and para macular area (Ring 1 + Ring 2). Both amplitude and latency were improved after surgery, but latency affected more. p1 amplitude began to increase at the 3rd month post vitrectomy. While p1 latency began to reduce at 2nd month post vitrectomy Also Mean BCVA improved from 0.09 pre op to 0.35 at the sixth month post op.mean foveal thickness Decreased from 571.2 ± 146 μm to 327.6 ± 109 μm at the sixth month [4].

Complications of Vitrectomy for PDR includes postoperative vitreous haemorrhage, retinal detachment, neovascular glaucoma (NVG).and cataract progression [25].

Vitreous haemorrhage is the most common complication, **Wakabayashi** and **Ozone** reported the incidence of postoperative vitreous haemorrhage was 25% and 22% respectively [26, 27].

Neovascular glaucoma is the most serious complication. **Kumagai** reported the incidence of NVG post vitrectomy was 3.9% [9].

Jackson et al reported the most frequent complications includes retinal break occurred in (7.1%), increased intraocular pressure in (5.2%), epiretinal membrane formation in (3.3%), and vitreous haemorrhage in (2.4%). Cataract progressed in 68.6% of 121 phakic eyes. [28].

Further studies will be necessary to reinforce these results for a larger number of cases. If these results are established, mf-ERG might be used as an objective method predicting the degree of stable recovery post vitrectomy.

Conclusion

Vitrectomy with and without ILM peeling improve VA and macular edema in diabetic patients moreover an increase of response density and reduction of the latency of the macular mf-ERGs indicated an improvement of the macular visual function. Although improvement was much better in group B the difference was statiscally insignificant between both groups

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Declarations

Funding No funds have been received for the study.

Compliance with ethical standards.

Conflict of interest: All authors declare that they have no conflict of interest.

Ethical approval: All procedures performed in the study were in accordance with Al-Azhar Medical Research Ethics Committee ethical standards and with the 1964 Helsinki declaration and its later amendments.

Informed consent Informed consent was obtained from all individual participants included in the study.

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Figures

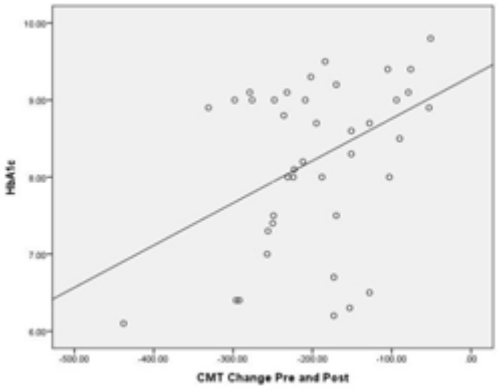

Figure 1

Scatter plot between CMT Change and HbA1c in all patients.

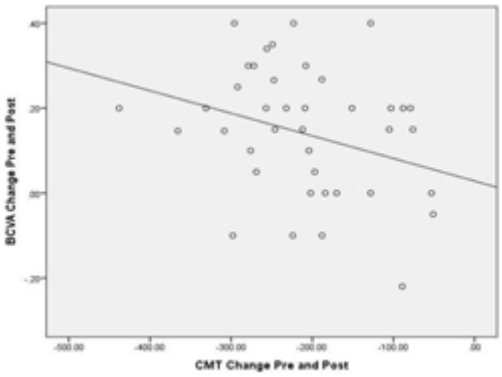

Figure 2

Scatter plot between CMT Change and BCVA change in all patients

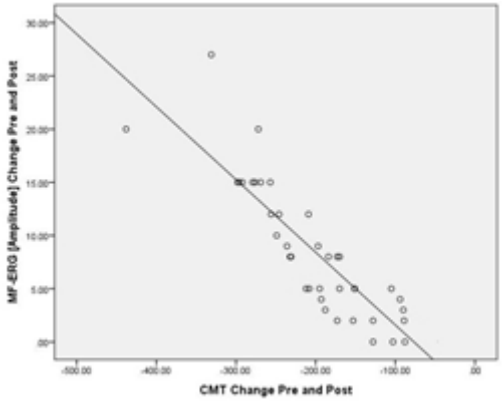

Figure 3

Scatter plot between CMT Change and MF-ERG [Amplitude] Change in all patients.

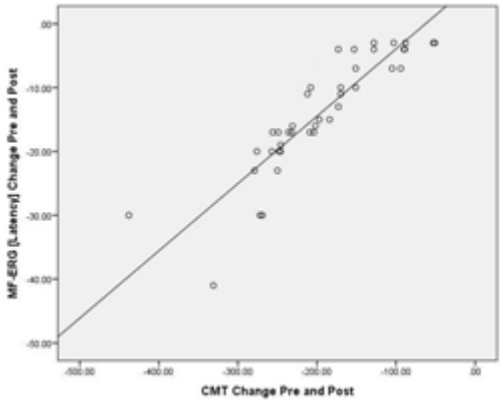

Figure 4

Scatter plot between CMT Change and MF-ERG [Latency] Change in all patients.

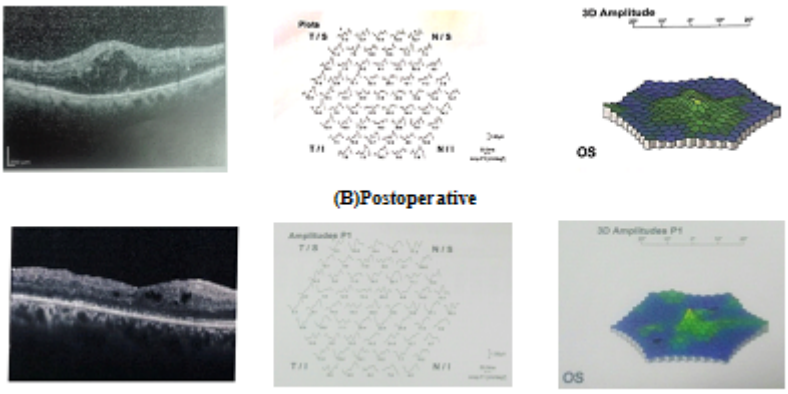

Figure 5

Pre and post vitrectomy with ILM peeling of the same case in group B (the left image (OCT) the middle image (trace array of mf-erg) the right image (3d plotting of mf-erg)) (A) Preoperative:CMT was 566 μm, P1 amplitude was 29.5 nV/deg2 and P1 latency was 46.6 ms BCVA was 0.1 (B) Postoperative (3mo): CMT was 292 μm, P1 amplitude was 38.4 nV/deg2 and P1 latency was 39.7 ms BCVA was 0.3