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Prognostic prediction ability of postoperative multifocal ERG after vitrectomy for diabetic macular edema

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PURPOSE. *Diabetic macular edema (DME) causes visual loss in diabetic patients. Multifocal electroretinograms (mfERGs) have been used to assess macular function pre- and postvitrectomy for DME.*

METHODS. *A standard three-port pars plana vitrectomy with peeling of inner limiting membrane was performed in 25 eyes of 21 patients (13 male, 8 female) with DME. For each patient, visual acuity examination, measure of retinal thickness (using optical coherence tomography), and mfERGs were performed before and 1 week, 1 month, 3 months, and 6 months after vitrectomy.*

RESULTS. *Mean postoperative visual acuity was significantly improved ($p<0.05$, t test), with mean increase of 0.17 logMAR units; mean retinal thickness was significantly ($p<0.001$) decreased after surgery (from 537 µm to 298 µm). The increase of normalized amplitude of central ring was not significant; the mean P1 wave-amplitude increased from 0.33 to 0.40 mV; mean P1 wave-implicit time decreased 2.88 ms. We divided the patients into two groups: Group 1 (13 eyes), in which the visual recovery was less than 0.20 logMAR, and Group 2 (12 eyes), in which the visual recovery was greater than 0.20 logMAR. ERG results were statistically significantly different between the groups ($p<0.025$), when we consider the response recorded from the central ring. In Group 2 there is a marked reduction in implicit time of both ERGs waves, which was statistically significant for N1 wave ($p=0.01$). The changes of parameters of mfERG observed 6 months after surgery were consistent with those recorded just 1 week after surgery.*

CONCLUSIONS. *Multifocal electroretinogram can be useful to predict functional prognosis in patients with diabetes who underwent vitrectomy for diabetic macular edema. (Eur J Ophthalmol 2008; 18: 609-13)*

KEY WORDS. *Diabetic macular edema, Multifocal ERG, Vitrectomy*

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INTRODUCTION

Diabetic macula edema (DME) is the most common cause of visual loss in diabetic
patients. DME results from a series of biochemical and cellular changes, causing progressive leakage and exudation (1).

Multifocal electroretinograms (mfERGs) have been used to assess macular function and to compare anatomic findings to electrophysiologic results.

The ERG was used to study several conditions related to diabetic retinopathy. In diabetic patients, abnormalities of full-field ERG have been reported, e.g., reductions in the amplitude and delayed implicit times of the a- and b-waves and reduced oscillatory
potentials. These anomalies are related to the severity of retinopathy (2, 3).

Diabetic retinopathy is associated with changes of focal

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TABLE I - PREOPERATIVE DATA OF 25 EYES OF 21 EXAMINED PATIENTS, INCLUDING VISUAL ACUITY (VA), RETINAL THICKNESS (Optical Coherence Tomography measure), AND REGISTERED VALUES OF MULTIFOCAL ELECTRORETINOGRAM

Patients	VA (logMAR)	Retinal thickness (µm)	NA, nV/deg²	P1 A (mV)	P1 L (ms)	N1 A (mV)	N1 L (ms)
A.P.	0.30	512	46.3	0.48	45	0.48	16
A.P.	1.00	525	53.5	0.52	33	0.29	23
A.S.	0.96	560	20.2	0.21	36	0.07	19
B.P.	1.00	543	20.2	0.21	36	0.07	19
C.V.	0.30	498	46.3	0.49	46	0.44	18
D.L.	1.00	556	36	0.37	34	0.12	12
E.R.	1.00	568	48	0.56	31	0.27	23
F.F.	0.96	543	36	0.37	35	0.12	12
L.B.	0.94	576	19.9	0.21	38	0.05	13
L.O.	0.92	544	8.1	0.08	33	0.06	23
L.P.	0.52	540	14.7	0.15	29	0.04	31
M.A.	1.00	583	36	0.37	34	0.12	12
M.T.	1.00	580	54	0.57	32	0.29	23
P.L.	0.54	470	16	0.15	27	0.04	30
P.L.	0.30	480	45	0.48	48	0.48	19
P.T.	0.98	570	21	0.22	40	0.09	13
P.V.	0.90	555	8.1	0.08	34	0.05	22
R.A.	0.30	500	57.8	0.56	41	0.34	23
R.A.	1.00	566	9	0.07	34	0.04	21
R.C.	1.00	548	19.9	0.23	41	0.08	12
R.M	0.94	567	19.4	0.31	37	0.07	18
R.M.	0.34	512	56	0.64	41	0.34	23
S.D.	0.90	573	18.3	0.23	39	0.08	12
T.G.	0.30	450	57.8	0.60	41	0.32	23
T.G.	0.54	524	13.8	0.15	27	0.04	30
AVERAGE	0.76	537.72	31.25	0.33	36.46	0.18	19.18

NA = Normalized amplitude of central ring; P1A = Amplitude of P1 wave; P1L = Implicit time of P1 wave; N1A = Amplitude of N1 wave; N1L = Implicit time of N1 wave

ERGs from the macula; thus this electrophysiologic test is useful to verify changes in macular status in diabetic patients after any type of surgical or parasurgical treatment.

The importance of recording focal ERGs from the macula has been reported (4-6).

Treatment of DME includes systemic glycemic control, weight control, and blood pressure control.

Focal and grid photocoagulation therapy has also been reported to be beneficial (7) and remains the standard care for diabetic maculopathy.

Intravitreal triamcinolone injection has been used for the treatment of persistent diabetic macular edema, with good recovery of the foveal thickness and macular retinal function (8, 9).

Posterior vitreous detachments (PVD) play a critical role through several mechanical or physiologic mechanisms (10, 11).

Vitrectomy with or without inner limiting membrane (ILM) removal seems to be effective in reducing the retinal thickness and improving visual acuity.

The purpose of this study was to evaluate the changes in mfERG components in 25 eyes with DME undergoing a standard three-port pars plana vitrectomy with peeling of ILM, linking electrophysiologic results and the changes of retinal thickness measured by optical coherence tomography (OCT), and demonstrate if early (1 week after surgery) mfERGs could be predictive of final visual recovery.

METHODS

Patients and procedures

A standard three-port pars plana vitrectomy with peeling of ILM was performed in 25 eyes of 21 patients (13 males, 8 females) with DME.

Mean age was 64 years (range 53–75); of 25 eyes, 15 were pseudophakic, 10 were phakic.

Diagnosis of macular edema was made after direct obser-

TABLE II - POSTOPERATIVE DATA OF 25 EXAMINED EYES, INCLUDING THE SAME PARAMETERS EVALUATED BEFORE SURGERY

Patients	VA (logMAR)	Retinal thickness (µm)	NA, nV/deg²	P1 A (mV)	P1 L (ms)	N1 A (mV)	N1 L (ms)
A.P.	0.16	265	11.6	0.40	53.00	0.11	15.00
A.P.	0.90	310	42	0.45	46.00	0.24	19.00
A.S.	0.66	300	23.9	0.35	19.00	0.12	22.00
B.P.	0.76	297	24	0.31	21.00	0.09	22.00
C.V.	0.20	310	12	0.44	55.00	0.10	17.00
D.L.	0.92	322	22	0.45	25.00	0.25	20.60
E.R.	1.00	343	41	0.45	44.00	0.24	19.00
F.F.	0.94	307	29	0.31	26.00	0.22	20.60
L.B.	0.94	317	34	0.36	22.00	0.19	32.00
L.O.	0.54	265	22.5	0.34	20.00	0.02	27.00
L.P.	0.08	255	28.9	0.30	47.00	0.15	9.00
M.A.	0.98	322	29	0.31	25.00	0.25	20.60
M.T.	1.00	331	42	0.52	46.00	0.24	19.00
P.L.	0.12	250	29	0.30	50.00	0.16	9.00
P.L.	0.18	298	11.7	0.36	51.00	0.12	17.00
P.T.	0.96	320	33	0.37	25	0.17	33
P.V.	0.54	305	22.4	0.26	19.00	0.02	27.00
R.A.	0.22	288	40	0.48	29.00	0.03	25.00
R.A.	0.64	298	44	0.52	22.00	0.01	9.80
R.C.	0.96	314	35	0.36	25.00	0.18	30.00
R.M	0.70	295	26	0.38	23.00	0.08	21.00
R.M.	0.12	276	49	0.66	22.00	0.12	9.80
S.D.	0.88	290	37.3	0.43	26.00	0.18	30.00
T.G.	0.10	267	51	0.52	22.00	0.02	9.80
T.G.	0.20	307	29	0.30	50.00	0.16	9.00
AVERAGE	0.59	298.08	30.77	0.40	32.52	0.14	19.18

NA = Normalized amplitude of central ring; P1A = Amplitude of P1 wave; P1L = Implicit time of P1 wave; N1A = Amplitude of N1 wave; N1L = Implicit time of N1 wave

vation by contact lens biomicroscopy, fluorescein angiography, and OCT scanning.

For each patient, visual acuity examination, measure of retinal thickness (using OCT), and mfERGs were performed before and 1 week, 1 month, 3 months. and 6 months after vitrectomy.

The best-corrected visual acuity (BCVA) was measured with ETDRS logMAR chart.

Retinal thickness was measured by OCT (OCT Stratus; Zeiss), performed horizontally and vertically through the fovea, with scan length of 5 mm. Multifocal ERGs were elicited and recorded using Retiscan system (Roland); by use of corneal electrodes; patient's pupils were fully dilated with 0.5% tropicamide; visual stimulus consisted of 103 hexagonal areas. A monitor was positioned at a viewing distance of 32 cm.

All eyes underwent a standard three-port pars plana vitrectomy, with creation of posterior vitreous detachment and peeling of ILM without the use of any type of membrane dye.

None of the phakic patients underwent combined vitrectomy and cataract intervention. In no case was injected triamcinolone endovitreal. Patients with significant cataract and/or epiretinal membranes were excluded from the study (while patients with initial cataract were included).

Mean preoperative visual acuity was 0.77 logMAR (<20/100).

OCT showed preoperative increased values of retinal thickness (compared with normal values); mean total foveal thickness (distance from the inner limiting membrane to the inner border of the retinal pigment epithelium, including the accumulation of subretinal fluid) was 537 µm.

Our analysis of mfERG results was focused on the following parameters, corresponding to the central (foveal) ring (ring 1): normalized amplitude (nV/deg²); amplitude of P1 (µV); P1-wave implicit time (ms); N1-wave amplitude (µV); N1-wave implicit time (ms).

Table I shows preoperative data of 25 examined eyes.

TABLE III - RESULTS OF 1 WEEK AND 6 MONTHS NORMALIZED AMPLITUDE OF CENTRAL RING (NA), IMPLICIT TIME OF P1 WAVE (P1L) , AND IMPLICIT TIME OF N1 WAVE (N1L) OBTAINED IN PATIENTS OF GROUP 2 (better visual recovery)

Patients	NA, nV/deg² (1 wk)	NA, nV/deg² (6 mo)	P1 L (1 wk)	P1 L (6 mo)	N1 L (1 wk)	N1 L (6 mo)
1	52	57.8	43	41	23	23
2	51.2	53	54	42	23	24
3	47.3	57.8	47	41	23	22
4	19.8	21.2	38	36	25	21
5	17	21	41	38	26	19
6	18.6	20.2	36	36	22	18
7	13	15.1	27	27	30	28
8	12	14.7	28	26	35	30
9	11	14.9	29	27	36	32
10	7	8.2	35	34	24	23
11	6.3	8.4	37	33	25	25
12	7.9	8.1	34	31	21	21

NA = Normalized amplitude of central ring; P1A = Amplitude of P1 wave; P1L = Implicit time of P1 wave; N1A = Amplitude of N1 wave; N1L = Implicit time of N1 wave

RESULTS

Mean postoperative visual acuity was significantly improved ($p<0.05$, *t* test), with mean increase of 0.17 logMAR units; retinal thickness measured by OCT is significantly ($p<0.001$) decreased after surgery, from a mean preoperative value of 537 µm to a mean postoperative value of 298 µm (see Tab. II for details).

Multifocal ERG

The increase of normalized amplitude of central ring was not significant; the mean P1 wave-amplitude increased from 0.33 to 0.40 mV; mean P1 wave-implicit time decreased.

Multifocal ERG is an objective electrophysiologic technique that provides information from localized retinal areas. It is repeatable and noninvasive, with high sensitivity and not linked to the operator or the patient. This examination accurately evaluates the electrophysiologic activity in several retinal areas.

In the literature, there are several studies that demonstrate the role of mfERG in various diseases. Some points are unclear, such as the full understanding of electrophysiologic signal.

In our study, we have seen that in patients with DME the amplitudes and the implicit times of waves of mfERG are markedly abnormal.

Yamamoto et al (12) published a work conducted on 19 eyes with DME and cataracts that underwent combined intervention of cataract and vitrectomy. They reported a significant increase of visual acuity, a significant reduction of retinal thickness measured by OCT, and a significant reduction of a- and b- wave implicit times, while there was no significant variation in the normalized central amplitude.

Similar results were obtained by Terasaki et al (13): a significant increase in the b-wave was found in the group of patients who had undergone surgical vitreous posterior detachment for DME.

In our study we found no significant changes of P1- and N1-amplitude.

In terms of visual recovery, the results have been positive, because in 3 cases (12%) there were no changes in postoperative versus preoperative visual acuity, but visual acuity was stable up to 6 months after vitrectomy, while only one case (4%) has shown a reduction of visual acuity after the intervention, related to the development of cataract; all other cases (86%) have a variable rate of visual improvement.

OCT examination showed the beneficial effect of vitrectomy to reducing retinal thickness, directly related to the visual acuity changes and the subjective improvement perceived by the patient.

Multifocal ERG has shown a general trend towards improvement, with increasing amplitudes and reducing implicit time.

More interesting is to consider the possible predictive value of mfERG when performed just 7 days after vitrectomy, because of the absence of significant difference between the values registered at 1 week and 6 months after surgery (Tab. III).

We noted that some parameters, such as the normalized amplitude central (ring 1), and the implicit time of P1 and N1, show a trend (and often sign) different, and directly related to what will be the maximum functional recovery the patient.

We showed functional central values, amplitudes, and decreases of implicit time significantly lower in the cases of poor or modest final recovery than cases with good visual recovery.

Therefore, an evaluation of mfERGs parameters by 1 week after vitrectomy can be useful for the final prognosis, providing information about the functional postoperative response of the macula, directly related to a more or less marked final visual recovery.

Further studies need to be conducted to confirm these results for a higher number of cases. If these data are confirmed, mfERG could be used as an objective technique allowing prediction of the degree of stable recovery immediately after surgery.

Proprietary interest: None.

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