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Multifocal Electroretinogram in Retinitis Pigmentosa

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Abstract

Purpose: To evaluate the role and sensitivity of multifocal electroretinogram in patients with retinitis pigmentosa (RP).

Subjects and Method: The study included 75 subjects (150 eyes); 25 subjects (50 eyes) were normal, 25 patients (50 eyes) suffered from retinitis pigmentosa without macular edema; 25 retintis pigmentosa patients (50 eyes) with macular edema. All patients underwent full ophthalmological examination, full field electroretinogram (ERG) and multifocal electroretinogram (MF-ERG). MFERG is repeated twice in the same day and in the next day.

Results: The amplitudes of P1in all rings were reduced in retinitis pigmentosa compared with normal .The amplitude of P1 was reduced in ring 1,2,3 more with RP associated with macular adema compared with patients without macular edema. There were delay in rings4,5 only in RP without macular edema compared with normal, Whereas there were delay in all rings in retintis pigmentosa associated with edema.

Conclusion: MFERG is simple easy objective tool valuable for evaluating the macula in RP

Keywords: Retinitis Pigmentosa; Retinal Disorders; Analog or Digital filters; Optical Coherence Tomography; Residual receptors

Abbreviations: RP: Retinitis Pigmentosa; ERG: Electroretinogram; MFERG: Multifocal ERG; OCT: Optical Coherence Tomography

Introduction

Retinitis pigmentosa (RP) is progressive primary degeneration of rod associated with secondary degeneration of cones [1]. The visual reduction affected mainly at nights with gradual deterioration of central visual acuity [2]. The pathogenesis of RP is tangled; first, loss of rods and cones associated with abnormality in the retinal pigment epithelium and retinal glia. Then, the inner retinal neurons, blood vessels, and optic nerve head are affected [3,4]. Multifocal ERG (MFERG) evaluates the innermost 30 of the retina and is useful in detection localized retinal function defects [5,6]. MFERG is useful in detection outer retinal disorders. It is used to quantify the remaining cone-mediated function in RP patients especially in advanced stages of the disease [7,8]. While; Full Field ERG reflects total retinal area. It estimates small residual responses in advanced RP patients in combination with computer averaging and use of analog or digital filters, but without this technique, a recordable response cannot be obtained from advanced RP patients [9]. MF ERG monitors macular cone system function in RP [10]. The aim of this study is evaluate the of role of MFERG in patients with retinitis pigmentosa.

Subjects and Methods

This study was a retrospective study. The study was performed in Mansoura Ophthalmic center from January 2023 to July 2024 in accordance with the Declaration of Helsinki, after Written informed consents were obtained from all participates. The diagnosis of RP was based on funduscopic examination and on results of the full-field ERG and family history. Patients with previous ocular surgery ,ocular media opacities that affect the test results, coexisting ocular disease (retinal pathology other than RP, glaucoma, uveitis, strabismus, nystagmus), any systemic diseases (diabetes, neurological diseases, hypertension) that affect the results were excluded from the study.

The study included three groups; group 1 control group (normal group); group 2 retinitis pigmentosa without macular edema, group 3 retintis pigmentosa with edema. Complete medical history , detailed ophthalmic examination were done including BCVA and intraocular pressure measurements, anterior segment evaluation with slit-lamp bio-microscopy, color fundus

photography, Optical Coherence Tomography (OCT), full field ERG and MFERG. BCVA was recorded with a Snellen chart and convert to log Mar. The severity of RP assessed with VA testing, electroretinography.

Electrophysiological Tests

Full field ERG and Multifocal ERG were performed according to the International Society for Clinical Electrophysiology of Vision (ISCEV) guidelines [11]. Full field ERG and Multifocal ERG were done using Roland Consult (Roland Consult Electrophysiological Diagnostic System. RETI port 21, Brandenburg, Germany). Dawson Trick -Litzkow (DTL) thread electrode which was positioned on the inferior cornea along the lid margin and fixed temporarily. The pupils were dilated with tropicamide 1%. Gold-Cup reference and surface electrodes were applied to the subject's temple and forehead, respectively.

During the MFERG , 61 hexagons of the individual MFERG responses were generated, and these hexagons were grouped into five concentric rings (15˚) centered on the fovea. The average amplitude and implicit time of the first positive wave (P1) in the five rings were measured. MFERG repeated twice in the same day and in the next day in all patients. The same electrode was used for each subject for all recordings to decrease change of electrode resistance difference. To assess the diagnostic ability of MFERG; Receiver operating characteristic curves (ROC) was analyzing in group 2,3.

Optical Coherence Tomography

OCT was performed with the 3-dimensional OCT-1000 (Topcon Corp., Tokyo, Japan). OCT measurements were performed using a fiberoptic optically integrated Michelson interferometer with short coherence length super luminescent Diode.

Statistical Analysis

Statistical analyses were performed using statistical package for social science (SPSS version 20 statistical package program, IBM Corp. in Armonk, NY). Descriptive data are presented as mean ±SD and as percentage for categorical variables. Kolmogorov-Smirnov test was used to evaluate the distribution of the numeric data. Pearson's Chi-Square test and One-Way ANOVA test were used for comparing the numeric data. $p < 0.05$ was considered as statistically significant level.

All correlation were assessed by the Pearson Correlation Coefficients, Receiver operating characteristic (ROC) curves were used to describe the ability of each parameter to differentiate between normal and retinitis pigmentosa. A perfect test would have (100% sensitivity &100% specificity) whereas a test with no diagnostic value would have ROC of 0.5 [12]. Sensitivity of MFERG was defined as the percentage of diseased eyes that had an abnormality on the test. Specificity was defined as the percentage of normal eye that had normal test

Results

150 eyes of 75 patients were studied. The study included three groups; group1: control group 25 patients(50 eyes) mean age was 40.5 (ranged from 20 to 69) years and 15 subjects (60 %) were male. Group 2: retinitis pigmentosa without macular edema ; 50 eyes of 25 patients; The mean age was 39.5 (19.5 -70) years .The mean age at onset of disease was 19.5 years and the mean disease duration was 20.3 (between 7 - 40) years; 13 patients (52%) were male; There was a family history in 52 % of the patients. Group 3; 50 eyes of 25 patients had retinitis pigmentosa with macular edema; The mean age was 37.5 (19.5 -60) years .The mean age at onset of disease was 20.5 years and the mean disease duration was 25.5 (between 15 - 40) years; 12 patients (48%) were male; There was a family history in 10 patients (40 %) of the patients.

The mean value of the VA of the study patients were 0.9 ±0.1 in group 1, 0.55±0.2 in group 2 and 0.12±0.29 in group 3. The mean CMT were 121.6 ± 51.3 µm in group 1, 130 ±49.9 µ in group 2 and 300±105.9µ in group 3. Regarding full field ERG, there were reduction of all parameters of full field-ERG in both group 2,3 compared with normal Table 1.

Table 1: Full field ERG parameters among groups.

ERG parameters	Group 1	Group 2	Group 3	p
Scotopic b-wave amplitude	95±23nv	25±23nv	5±13nv	0.001
Combined b-wave amplitude	240 ±50nv	90 ±30nv	20 ±10nv	0.005
Ops Implicit time	23±5ms	34±15ms	43±9ms	0.008
Ops Amplitude	27±3nv	17±13nv	7±3nv	0.006
Photopic b-wave amplitude	45±9nv	25±12nv	20±5nv	0.05
30 Hz flicker amplitude	50±5ms	59±5ms	70±10ms	0.0007
30 Hz flicker Implicit time	55±16nv	35±6nv	15±12nv	0.009

Note: There were reduction in all parameters of ERG in group 2,3 compared with normal group.

Table 2: MFERG parameters changes.

MFERG parameters	Group 1	Group2	Group3	P
R1				
Amplitude µv	90.5±10.9	55.9±6.9	35.9±5.9	0.001
Latency ms	40±3.4	41.1±1.9	61.1±1.9	0.1
R2				
Amplitude	75.5±9.5	48.9±7.7	28.9±5.7	0.001
latency	41.4 ±2.1	41.1±1.5	61.5±2.5	0.9
R3				
Amplitude	65.6 ±13.4	41.6±6.9	28.9±7.2	0.001
latency	42.2±3.1	40.9±2.2	65.1±1.5	0.71
R4				

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Amplitude	43.6±11.7	35.5±7.8	14.9±6.7.	0.001
latency	42.3±4.1	50.9±5.1	61.1±1.5	0.051
R5				
Amplitude	35.1±8.9	25.9±4.9	18.9±7.1	0.001
latency	41.3±2.21	53.5±3.7	61.9±1.8	0.001

Note: This table shows significant reduction in amplitudes in all rings in both groups 2,3 compared with group1with statistical significant delay in all rings in group 3.

Concerning MF-ERG, there were reduction of amplitude in all rings (moderate reduction in the rings 1,2,3 and sever reduction in rings 4,5) and quadrants in most patients (22 patients) with delay in latencies in peripheral rings (4,5 rings) only while the center rings had normal latencies in group 2, (Table 2) and (Figure 1,2). While, in group 3; there were reduction in amplitudes and delay in latencies in most of patients (23 patients) in all rings and quadrants.

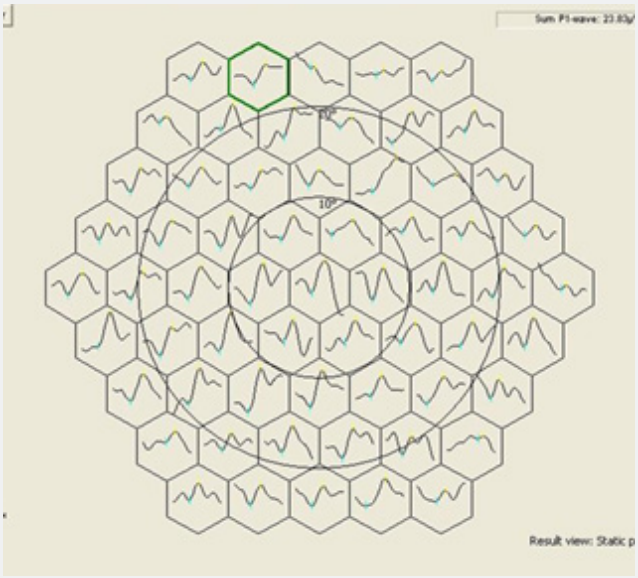

Figure 1A: Trace array in group 1 shows normal wave with normal peak and trough ,normal latency and amplitude.

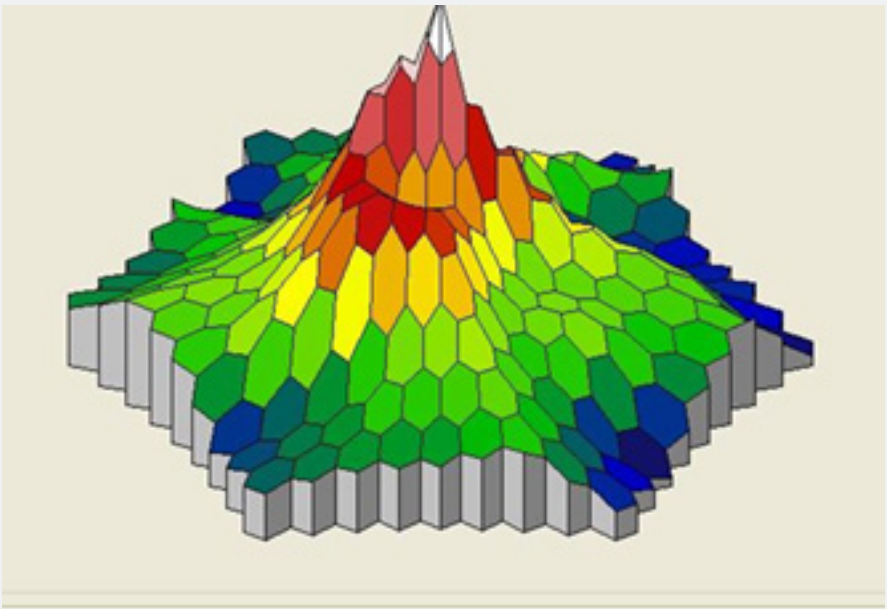

Figure 1B: Three dimension map in group 1 shows normal peak.

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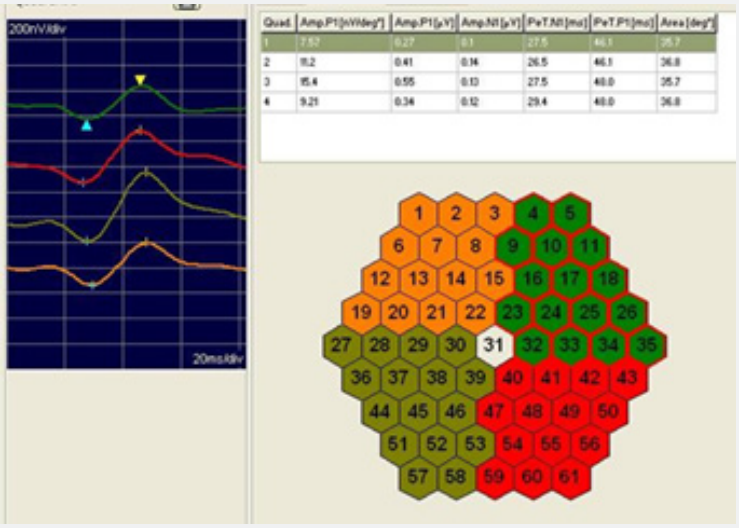

Figure 1C: Quadrant form in group 1 shows normal amplitude and latency.

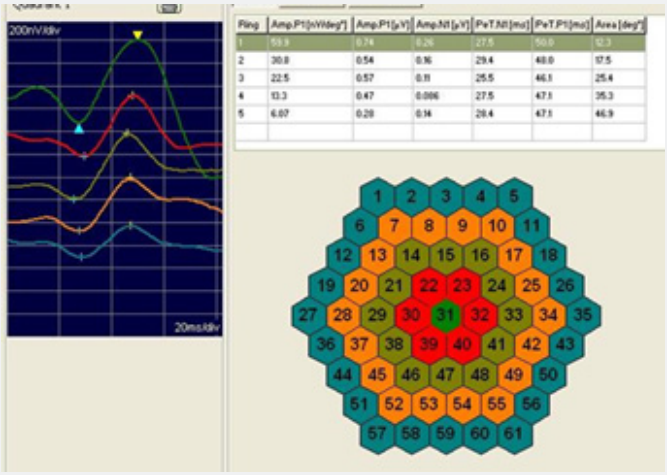

Figure 1D: Ring form in group 1 shows normal amplitude and latency.
Figure 1: MFERG IN GROUP1.

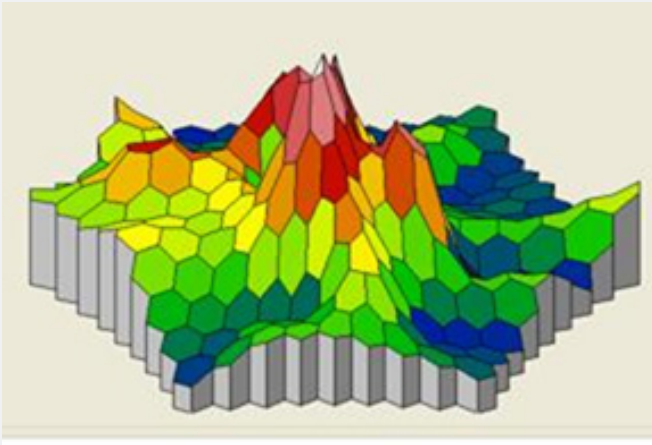

Figure 2A: Three dimension map in group 3 shows abnormal peak.

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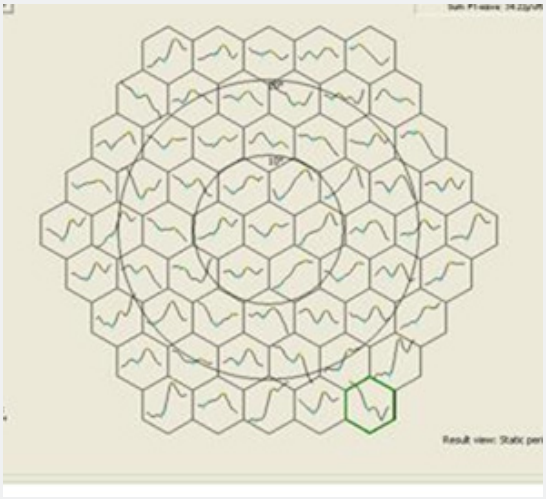

Figure 2B: Trace array in group 3 shows abnormal wave just irregular line no apparent peak and trough.

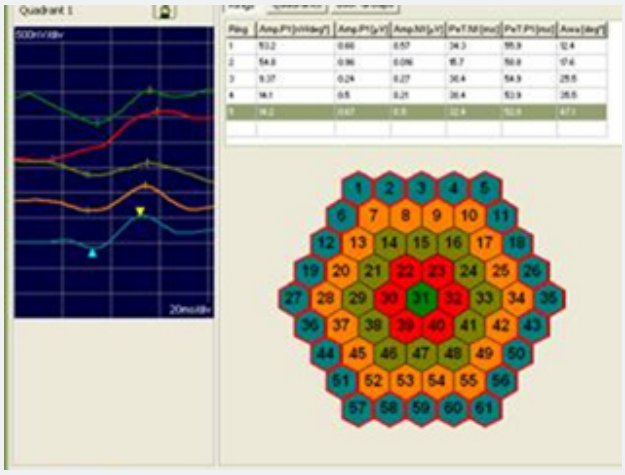

Figure 2C: Ring form in group 3 shows abnormal amplitude and latency.

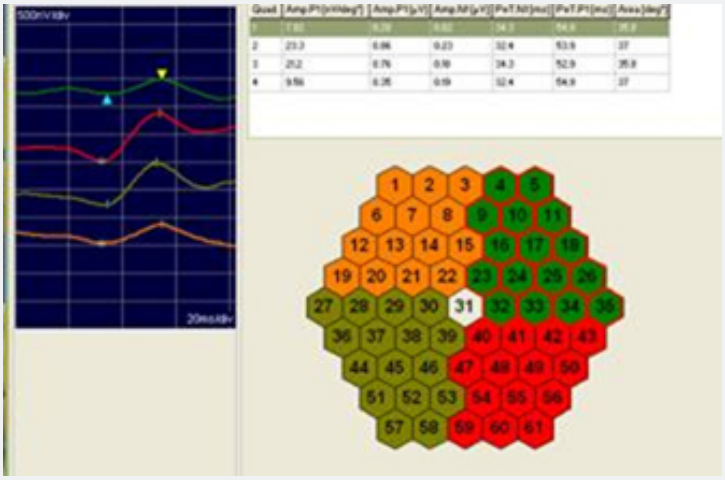

Figure 2D: Quadrant form in group 3 shows abnormal amplitude and latency.
Figure 2: MFERG IN GROUP 3.

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Regarding , which parameter is characteristic affected in RP was latency of ring 4. In group 2, widest ROC curves were related to peripheral rings 4(0.811). Also, in group 3, widest ROC curves were related to peripheral rings 4 (0.898) (Table 3). Regarding, the reproducibility of the MFERG responses in the same day and next day; mean coefficient of repeatability was 2.2 %in group 1, 6.8% in group 2 and 9.7 % in group 3. A criterion with an estimated specificity of MFERG in normal subjects of 91% result in 96% (2 eyes). Visual acuity correlated well with the amplitude of the central ring 1 (R1) of the MF-ERG in this study (R=0.7,P=0.001). Also, only Ring 5 amplitudes of the MFERG strongly correlated with the scotopic Ganzfeld ERG mixed cone-rod response amplitude (R= +0.6, P = 0.05), while, there were insignificant correlation between the center 3 rings and scotopic ERG (R= +0.3, P = 0.5).

Table 3: ROC Curve areas of MFERG.

MFERG	ROC areas of group 2	ROC areas of group3
Ring 1	0.5	0.56
Ring 2	0.6	0.63
Ring 3	0.65	0.67
Ring 4	0.811	0.898
Ring 5	0.712	0.722

Discussion

Electrophysiological tests ; full field ERG and multifocal ERG provide an objective, functional measurement of the retinal function [13]. They are useful in diagnosing RP and monitoring the prognosis. Full field ERG assesses nonselective global responses of the retina But may be extinguished in the early stage of RP; it is not able to detect small progression; especially in the end stage of RP and not sensitive enough to indicate the function of the central retina [14]. Multifocal ERG measures the innermost 30° of the retina [15].

In this study ,there is reduction in amplitude in all rings of MFERG in RP (group 2,3) compared with normal (group 1). Regarding latency, there were delay in latencies in peripheral rings (4,5 rings) only while the center rings had normal latencies in group 2, (Table 2). While, in group 3; there were delay in latencies in most of patients (23 patients) in all rings and quadrants. Similarly, Woisley et al, reported reduction of MFERG amplitude in all regions with significant delay in retinal eccentricity of 6-12 only [16]. Also, Felius ,et al said that there were delay in latencies in temporal with normal latencies in the center retina [17]. While, Seeliger et al. and Holopigian et al found reduction in amplitude with preserved latency within normal in all rings [18,19]. The reduction of amplitude without delay could be explained the difference in the origin of each parameter; amplitude reflects losses in the number of cones, whereas timing reflects the function of the residual receptors.

In this study, Full field ERG is marked reduced in retinitis pigmentosa; in contrast to MFERG parameters remained detectable. Similarly, Gerth, et al. reported that mfERG responses were recordable in all patients with advanced RP and non-recordable Full Field ERGs [20]. Also, Granse et al. observed severe reduction of all full field ERG values in all patients of advanced RP with reliable detectable responses of MF-ERG in most of the patients of RP and concluded that MFERG is important for monitoring the residual central retinal function in RP [14].

Regarding the reliability of the MFERG responses; in this study there were insignificant differences of MFERG latency and amplitude in the same and next day in group 1. Similarly, Zhang and Zhao [21] reported no significant differences between MF-ERG amplitude on the two visits among eleven control subjects [21]. Parks et al. found coefficient of repeatability for MF_ERG amplitude averaged over 10 visits ranged from 6.2% to 14.5% for three control subjects [22]. Aoyagi et al. reported a CV of 22% for nine control subjects tested on four visits [23]. Mohidin et al. compared mfERG reliability among twelve control subjects on three visits and said that the CV were 15%; 19%; 23% for a jet contact lens electrode, for the gold foil electrode, and for the DTL electrode, respectively [24]. Seiple et al. observed CRs of eight control subjects for the MFERG amplitude averaged 10.1%; this value is within the lower range reported by these other studies [25].

There was correlation between visual acuity and amplitude of the central ring1 (R1) of the MF-ERG in this study (R=0.7, P=0.001); There was also, correlation between only Ring 5 amplitudes of the MFERG and the scotopic Ganzfeld ERG mixed cone-rod response amplitude (R = +0.6, P = 0.05), while, there were insignificant correlation between the center 3rings and scotopic ERG (R = +0.3, P = 0.5). Similarly; Seiple, et al. found correlation between Ring 5 amplitudes of the MFERG and the scotopic Ganzfeld ERG mixed cone-rod response amplitude [25]. Summary, MFERG allows mapping of the macula with high resolution and detects of the remaining foveal cone function even in advanced stage of the disease. There were reduction in MFERG amplitudes and delays in all rings in all cases associated with macular edema.

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