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ABSTRACT

of the dissertation for the degree of Doctor of Philosophy

**APPLICATION OF MULTIFOCAL
ELECTRORETINOGRAPHY IN ASSESSING THE
FUNCTIONAL STATUS OF THE RETINA DURING
DIABETIC MACULAR EDEMA**

Speciality: 3219.01 – eye diseases

Field of science: Medicine

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GENERAL CHARACTERISTICS OF THE RESEARCH

Relevance of the theme. One of the main causes of visual impairment in diabetic retinopathy is diabetic macular edema (DME).

The main goal of treating diabetic macular edema is to prevent complications that may occur in the disease. To achieve this, anti-VEGF therapy, laser coagulation, and vitreoretinal surgery are used^{1,2}. It should be noted that none of these treatment methods are ideal, each has advantages and disadvantages³.

It dictates the development and application of additional diagnostic methods for timely detection of the initial signs of diabetes mellitus, as well as pathogenetic therapy. From this point of view, the search for new and more modern diagnostic methods in the diagnosis of retinal diseases has always been on the agenda⁴. Currently, both traditional and special diagnostic methods are used in the diagnosis of DME, including optical coherence tomography (OCT), microperimetry (MP) and multifocal

¹ Gelişken, Ö. Makula hastalıklarında tedavi prensipleri / Ö.Gelişken, Ö.Yalçınbayır, B.Kaderli // Oftalmologiyanın aktual problemləri, Məqalələr toplusu, – Bakı, – 2010, – s.64-65.

² Kərimov, M.İ. Diabetik retinopatiyanın erkən aşkar edilməsi və müalicə taktikasının təyini. Metodik tövsiyyələr / M.İ.Kərimov, E.Ə.Abdullayeva, A.M.Şahmalıyeva [və b.] – Bakı, – 2006, – 28 s.

³ Бобыкин, Е.В. Современные подходы к лечению диабетического макулярного отека // Офтальмохирургия, – 2019. №1, – с. 67-76.

⁴ Яблоков, М.М. Вариант лечения диабетического макулярного отека, сочетанного с анти-VEGF-терапией / М.М.Яблоков, П.Б.Величко // Современные технологии в офтальмологии, – 2016. №4, – с.270-272.

electroretinography (mf-ERG) ^{5,6} . In recent years, the role of functional examination methods has significantly increased due to the successes achieved by electrophysiological diagnostics in ophthalmology. With the help of clinical electroretinography methods, it is possible to determine the prevalence of pathological processes occurring in the retina, their severity, and at the same time detect pathology in its early stages^{7,8}.

Mf-ERG examination can identify pathological changes in the macula and paramacula, as well as in the mid-periphery⁹. Abnormal mf-ERG usually allows to explain the dysfunction of foveal cones, bipolar cells, as well as the cause of visual impairment. Mf-ERG is valuable in the evaluation of unspecified retinal diseases and in monitoring the progression of the disease^{10,11}.

⁵ Bahadur, M.V. The potential beneficial effects of ethyl pyruvate on diabetic nephropathy: an experimental and ultrastructural study / M.V.Bahadur, V.Vildirim, O.P.Baran [et al.] // *Pol. J. Pathol.*, – 2016. 67(3), – p.250-257.

⁶ Bearse, M.A. Multifocal electroretinography in diabetic retinopathy and diabetic macular edema / M.A.Bearse, G.Y.Orawa // *Current Diabetes Reports*, – 2014. 14(9), – p.526-533.

⁷ Farahvash, M-S. Multifocal electroretinogram in clinically significant diabetic macular edema / Farahvash M-S., S.M.Pharm // *Archives of Iranian Medicine*, – 2006. 9(3), – p.261-265.

⁸ Han, Y. Multifocal electroretinogram delays predict onset of subsequent diabetic retinopathy / Y.Han, M.A.Bearse, M.E.Schneck [et al.] // *Invest. Ophthalmol. Vis. Sci.*, – 2004. 45, – p.948-954.

⁹ Harrison, W.W. Multifocal electroretinograms predict onset of diabetic retinopathy in adult patients with diabetes / W.W.Harrison, M.A.Bearse, M.P.Jevell [et al.] // *Invest. Ophthalmol. Vis. Sci.*, – 2011. 52(2), – p.772-777.

¹⁰ Hoffman, M.B. JSCEV standard for clinical multifocal electroretinopathy (mf-ERG) / M.B.Hoffman, M.Bach, M.Kondo [et al.] // *Doc. Ophthalmol.*, – 2021. 142, – p.5-16.

¹¹ Lung, J.C.Y. Global flash multifocal electroretinogram: early detection of local functional changes and its correlations with optical coherence tomography and visual field tests in diabetic eyes / J.C.Y.Lung, P.G.Swann, D.E.Wong [et al.] // *In Documenta Ophthalmologica*, – 2012. 125(2), – p.123-135.

In patients with DME, the amplitude indicators of the mf-ERG components are significantly lower¹². These changes reflect the presence of gross, irreversible pathological processes, while the presence of negative changes confirms the presence of functional deficiencies in the retina as a negative prognostic sign^{13,14}.

Mf-ERG can be used to predict possible future abnormalities in diabetic patients with diabetic retinopathy. However, insufficient studies have been conducted in this direction^{15,16,17}.

The object of the study. In the current study, 105 eyes of 105 diabetic patients who underwent examinations in 2016-2023 at the "Ocular complications of diabetes" department of the National Ophthalmology Center named after academician Zarifa Aliyeva were

¹² Ma, S. Assessment of macular by multifocal electroretinogram in diabetic macular edema before and after vitrectomy / S.Ma, K.Yao, J.Jiang [et al.] // Doc. Ophthalmol., – 2004. 109(2), – p.131-137.

¹³ Hood, D. JSEV guidelines for clinical multifocal electroretinography – 2007 edition / D.Hood, M.Bach, M.Bridell [et al.] // Doc. Ophthalmol., – 2008. 116(1), – p.1-11.

¹⁴ Horton, M.B. Operational components of telemedicine programs for diabetic retinopathy / M.B.Horton, P.S.Silva, J.D.Cavallerano [et al.] – Text: electronic // Curr. Diabetes Rep., – 2016. 16(12), – p.128.

¹⁵ Khojasteh, H. Multifocal electroretinogram in diabetic macular edema and its correlation with different optical coherence tomography features / H. Khojasteh, H-Riazi-Esfani, E.Khalili Pour [et al.] // Int. Ophthalmol., – 2020. 40, – p.571-581.

¹⁶ Lim, J.W. Assessment of macular function by multifocal electroretinography following epiretinal membrane surgery with internal limiting membrane peeling / J.W.Lim, J.H.Cho, H.K.Kim // Clin. Ophthalmol., – 2010. 30(3), – p.689-694.

¹⁷ Leozappa, M. Prognostic prediction ability of postoperative multifocal ERG after vitrectomy for diabetic macular edema / M.Leozappa, Micelli, T.Ferrari, T.Gross [et al.] // Eur. J. Ophthalmol., – 2008. 18(4), – p.609-613.

included. Patients consisted of 49 men (46.7%) and 56 women (53.3%) according to their gender.

Inclusion criteria for the study: presence of diabetic retinopathy, presence of macular edema, presence of vitreomacular traction.

Exclusion criteria: the presence of a complicated cataract that prevents examinations, the presence of hemorrhage in the vitreous body, thrombosis of the retinal vessels or occlusion of its arteries, and the neovascular glaucoma.

Purpose of the study.

To study changes in the functional activity of the retina and the functional results of treatment in various forms of diabetic macular edema using multifocal electroretinography.

Research objectives:

1. Assessment of the functional status of the macular region using multifocal electroretinography in patients with non-tractional diabetic macular edema.
2. Assessment of the functional status of the macular region using multifocal electroretinography in patients with tractional diabetic macular edema.
3. To study the correlation between multifocal electroretinography and optical coherence tomography data in different types of diabetic macular edema.
4. To study the correlation between multifocal electroretinography and microperimetry data in different types of diabetic macular edema.
5. To calculate predictors of treatment results of various forms of diabetic macular edema based on multifocal electroretinography data and to develop recommendations for treatment.

Research methods used: To achieve the set goals and objectives, both traditional methods, including biomicroscopy, ophthalmoscopy, visometry, tonometry, and special auxiliary methods - optical coherence tomography, microperimetry, and multifocal electroretinography - were used in the examined patients.

Statistical calculations were carried out using the IBM® SPSS® Statistics 27.0 program and appropriate diagrams and graphs were constructed. Since all types of results in the dissertation have a normal distribution, only parametric tests were performed. The distribution of the data was checked using both the Shapiro-Wilk method and the measurement of the skewness and kurtosis coefficients. Since the distribution of the data according to the test results is normal in the comparison of the results between independent groups, an independent t-test was performed. Since the distribution of the data according to the test results within the group is normal, a paired t-test was performed. To determine the relationship between two different variables, the Pearson correlation (r) test was applied. To perform this test, the normal distribution of the results and the linearity of the dependence between them were checked. At this time, the interval of the r coefficient obtained and the significance level of the p coefficient were examined. For prediction, multiple linear regression analysis was performed. In all cases, the results were considered valid if the statistical significance level (p) was below 0,05, as accepted in medical research.

Main provisions submitted for defense:

1. Multifocal electroretinography allows topographical and quantitative study of the extent of pathological processes that occur in the macula during diabetic macular edema.
2. Changes detected in multifocal electroretinography components during diabetic macular edema are correlated with the topographical and light sensitivity indicators of that pathology.

3. Multifocal electroretinography is able to reveal the changes in the outer retina in diabetic macular edema, when ophthalmoscopic examination fails to detect them.

Scientific novelty:

1. For the first time, the indicators of multifocal electroretinography in various forms of macular edema in eyes with diabetic retinopathy were analyzed and it was shown that they have a reliable correlation with the results of optical coherence tomography and microperimetry examination.
2. It has been shown that pre-treatment P1 amplitude variable has a reliable power to predict post-treatment visual acuity during non-tractional and tractional macular edema in eyes with diabetic retinopathy.
3. Using multifocal electroretinography study, it was shown objectively that, after vitreoretinal surgical intervention in eyes with diabetic retinopathy, functional recovery of the outer layers of the retina occurs later than the anatomical recovery.

Theoretical and practical significance of the research:

The multifocal electroretinography method will help in studying the bioelectric activity of the retina in patients with diabetic macular edema, as well as in predicting the functional results of treatment and in dynamic observation of patients.

Approbation of the work:

The main provisions of the dissertation work were reported at the 1st Congress of Young Ophthalmologists (Baku 2007), EURETINA XVI Congress (Copenhagen, Denmark, 2016), EURETINA XVII Congress (Barcelona, Spain 2018), ESCRS 40th Congress (Milan, Italy, 2022), EURETINA XXIII Congress (Amsterdam, Netherlands), 1st, 2nd, 3rd and 8th (Lankaran, Baku) Conferences of Azerbaijani Retinologists.

The initial discussion of the scientific work was held at a scientific meeting (20.12.2024; protocol No. 8) with the participation of employees of the National Ophthalmology Center named after Academician Zarifa Aliyeva. It was discussed at the Scientific Seminar of the FD 1.03 Dissertation Council operating under the National Ophthalmology Center named after Academician Zarifa Aliyeva (12.03.2025; protocol No. 4).

Publications of the main conclusions of the dissertation:

The main results of the work were published in 18 scientific works, of which 10 articles and 8 theses (10 regional and 8 foreign journals).

Name of the organization in which the dissertation work was carried out:

The research work was conducted at the Department of “Laser Surgery”, “Vitreoretinal Surgery” and “Ocular Complications of Diabetes” of the National Center Ophthalmology named after academician Zarifa Aliyeva (2016-2023). The work is part of the scientific plan of the same medical center “Improvement of diagnostic and treatment methods in acquired retinal diseases” (2021-2025) (state registration No. 01134008).

Volume and structure of the dissertation:

The dissertation presented in computer type setting on 169 pages (218226 characters) and is structured as an introduction (11537 characters), a literature review (53683), a materials and methods chapter (26814 characters), a personal research chapter (29879 characters), a final section, conclusions, practical recommendations (57544 characters) and a list of references consisting of 189 sources. 39 pictures and 43 tables are included in the dissertation.

MATERIALS AND METHODS OF RESEARCH

Mf-ERG examination was performed in 105 eyes of 105 patients with diabetes mellitus in the departments of “Laser surgery”, “Vitreoretinal surgery” and “Ocular complications of diabetes mellitus” of the National Ophthalmology Center named after Academician Zarifa Aliyeva, in 2016-2023. Fifty-six of the patients were women (53.3%), 49 (46.7%) were men, the average age was 58.46 ± 8.11 (min. 26, max. 77). The known duration of DM was 13.41 ± 7.07 years (range 0-31 years). 85.9% of the patients (90 people) received insulin treatment, 14.8% (15 people) used oral medications to regulate blood sugar levels. The mean glycosylated hemoglobin (HbA1c) was 7.79 ± 1.04 (range 5.3-10.5%), and the mean visual acuity was 1.0 ± 0.36 (in LogMAR units) (Table 1).

Table 1.

Age, gender, visual acuity and HbA1c characteristics of the
examined patients

Characteristics of patients		Average indicator	Min.	Max.
Age		58.46 ± 8.11	26	77
Gender	Men	49 (46.7%)		
	Woman	56 (53.3%)		
Visual acuity		1.0 ± 0.36	0.3	2.0
HbA1c		7.79 ± 1.04		

According to the study design, the patients to be treated were divided into two main and one control groups:

- With non-tractional macular edema - 41 patients (41 eyes, I group)
- With tractional macular edema - 41 patients (41 eyes, II group)
- 23 patients without diabetic macular edema (23 eyes, control group).

During the conservative treatment of non-tractional macular edema, intravitreal 1,25 mg/ 0,05 ml anti-VEGF bevacizumab (Avastin) injection was used, and repeated examination were performed 2 weeks after the injection.

Pars plana vitrectomy surgical method was used in the treatment of tractional macular edema. Repeated examinations were performed 1,3 and 6 months after the operation.

Examination methods

Comprehensive ophthalmological examinations included traditional standard and special auxiliary examinations. The subjects underwent visometry, tonometry, biomicroscopy, ophthalmoscopy, as well as multifocal electroretinography (mf-ERG), optical coherence tomography (OCT) and microperimetry.

During the OCT examination, 2 protocols Macular Cube 512×128 (measuring retinal thickness in 9 zones) and 5-line HD raster protocols were used.

For statistical analysis 1 indicator was used – central (within a 1 mm ring). In doubtful cases, the retinal thickness was measured manually.

Microperimetry examination was performed on the MAIA microperimetry (CenterVue, Italy) in the 10° central zone before and after treatment according to the Expert exam protocol, and was compared with the normative base in the device. The normative indicators indicated a light sensitivity threshold of 23-25 dB.

Mf-ERG was performed on a Retiscan, Roland Consult (Germany) device.

Description of the improved examination method

This examination method is applied according to the ISCEV (International Society of Electrophysiology of Vision) standard. When recording mf-ERG indicators, multiple local ERG signals are separated from the central part of the visual field. When applying the mf-ERG examination, a 103 hexagonal stimulus pattern stimulation protocol was used. After 10 min. of light adaptation, mf-ERG indicators of grade I are

recorded. Mf-ERG registration is performed monocularly. Electrodes are placed on the cornea and skin under the eye, and thus the response of the retina is measured. The analysis of the obtained images was carried out based on 5 ring indicators from the central zone to the periphery. In our study, the P1 amplitude and P1 implicit time indicators of mf-ERG took the main place.

P1 amplitude – the maximum electrical response (voltage) of the various retinal cells to light. The mf-ERG amplitude is the wave measured from the N1 trough to the P1 peak. Responses within a ring can then be calculated as amplitude/unit area, whereby the responses summed in each ring are divided by the total area of the hexagons in the ring and plotted as nV/deg². The P1 amplitude was measured in each ring and compared with the normative base. According to the normative base, the P1 amplitude in 1 ring is 66.6-130.4 nV/deg²; 30.9-77.7 nV/deg² in 2 rings; 21.7-59.4 nV/deg² in 3 rings; 12.9-37.1 nV/deg² in 4 rings; 10-28.2 nV/deg² in 5 rings.

Implicit time – the time it takes for the electrical response to reach its maximum amplitude. The latent time is measured from the onset of the stimulus to the peak of the corresponding wave component and reflects the rate of signal transmission, and is plotted in ms.

RESULTS OF THE STUDY

Chapter III presents the general characteristics of patients with various forms of DME, as well as the results of OCT and microperimetry examinations and their comparative analysis.

Group I included 41 patients (41 eyes) with diabetic macular edema. Of these, 17 were male (41.5%), 24 were female (58.5%), and their ages were 60.95±6.53. The mean visual acuity was 0.87±0.29 in LogMAR units, and the mean intraocular pressure was 16.9±0.2 mm Hg. Patients received intravitreal injection of anti-VEGF bevacizumab and were re-examined 2 weeks after the injection. Visual acuity after intravitreal injection was 0.58±0.30 LogMAR units, an increase in visual acuity of

33.1%. After intravitreal injection, visual acuity increased in 28 patients (68%), decreased in 7 patients (17%), and remained unchanged in 6 patients (15%). The mean central macular thickness (CMT) in the examined eyes before treatment was $530.12 \pm 82.23 \mu\text{m}$. After treatment, the central macular thickness decreased by $249.34 \pm 41.55 \mu\text{m}$ (-47%) to $280.78 \pm 49.59 \mu\text{m}$ ($p < 0.001$).

According to microperimetry, the average light sensitivity of the central zone of the retina in patients with non-tractional macular edema was $14.05 \pm 4.76 \text{ dB}$. 2 weeks after the intravitreal injection, the average light sensitivity of the central zone of the retina was $16.60 \pm 5.59 \text{ dB}$ (an increase of 18.1%). Light sensitivity in the central zone increased by $2.54 \pm 2.43 \text{ dB}$ in 40 patients (97.6%), and MP indicators decreased in 1 patient (2.4%). The results obtained were statistically significant ($p < 0.001$).

Posterior vitrectomy was performed in patients with diabetic retinopathy complicated by vitreomacular traction (41 eyes), also included in the study. The functional state of the eye and macular thickness indicators were examined before surgery, in 1, 3 and 6 months after surgery. In group II patients, the mean visual acuity before vitrectomy was 1.12 ± 0.39 (LogMAR). After the vitrectomy, the mean visual acuity improved to 0.64 ± 0.34 (LogMAR) (difference -42.7%). The increase in visual acuity after vitrectomy was 42.7%. Visual acuity increased in 37 patients, decreased in 2 patients, and remained unchanged in 2 patients. The central thickness of the macula before vitrectomy was $486.15 \pm 90.69 \mu\text{m}$. 1 month after vitrectomy, the central thickness of the macula decreased and was $292.3 \pm 14.8 \mu\text{m}$ (-40.6%), $277.9 \pm 15.9 \mu\text{m}$ (-39.7%) after 3 months, and $267.68 \pm 49.05 \mu\text{m}$ (-44.9%) after 6 months. According to microperimetry examination in group II patients, light sensitivity increased from preoperative $14.08 \pm 5.9 \text{ dB}$ to $17.01 \pm 5.86 \text{ dB}$ after 1 month, to $17.08 \pm 7.4 \text{ dB}$ after 3 months, and to $18.01 \pm 5.30 \text{ dB}$ after 6 months. The increase was $2.93 \pm 2.34 \text{ dB}$ (20.8%). Photosensitivity scores increased from preoperative scores in 39 patients (95.1%) and decreased in 2 patients (4.9%, $p < 0.001$).

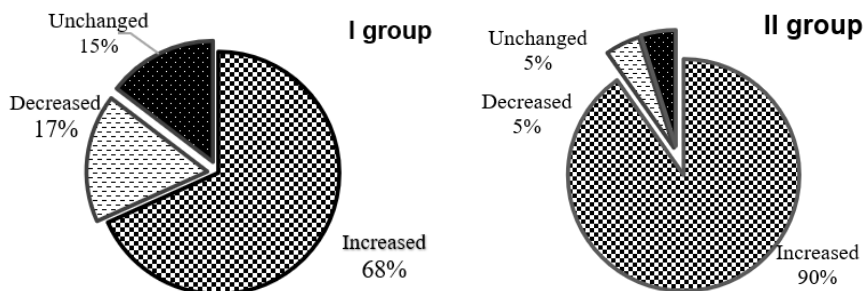


Figure 1. On the left – a diagram of changes in visual acuity after intravitreal injection, on the right – a diagram of changes in visual acuity after vitrectomy.

The control group consisted of 23 patients (23 eyes) without macular edema. Of these, 13 were male (54%), 10 were female (46%), aged 57.74 ± 5.38 . We compared the results obtained in the control group with the results obtained in the main groups (table 2, 3).

Table 2
Comparison of mean MP and OCT values in patients in different groups

	Groups	N	Average indicator	Average difference	P
				(compared to group III)	
MP (dB)	I	41	$14,05 \pm 4,76$	11,58	<0,001
	II	41	$14,08 \pm 5,91$	11,55	<0,001
	III	23	$25,64 \pm 2,50$		
OKT (μm)	I	41	$530,12 \pm 82,23$	-286,9	<0,001
	II	41	$486,15 \pm 90,69$	-242,93	<0,001
	III	23	$243,22 \pm 29,49$		

Multifocal ERG examination showed that in I group, the average bioelectric response of the macular area of the retina decreased sharply, and P1 averaged = 37.48 ± 7.62 nV/deg2 (norm P1 = 66.6 ± 130.87 nV/deg2). In the post-injection period, an improvement was noted in the P1 amplitude, P1 averaged 55.70 ± 21.00 nV/deg2 (+48.6%). The observed increase was statistically significant in the 1st, 4th and 5th rings ($p < 0.001$); in the 2nd and 5th rings, a slight decrease in the P1 amplitude was observed after treatment (Fig. 2 a). The implicit time indicator increased in all rings, only in the 3rd ring the implicit time indicators decrease, in the 1st ring it increased from 40.06 ± 10.31 ms to - 45.11 ± 16.52 ms (+12.6%), in the 2nd and 4th rings the increase was statistically significant ($p < 0.05$) (Figure 2 b).

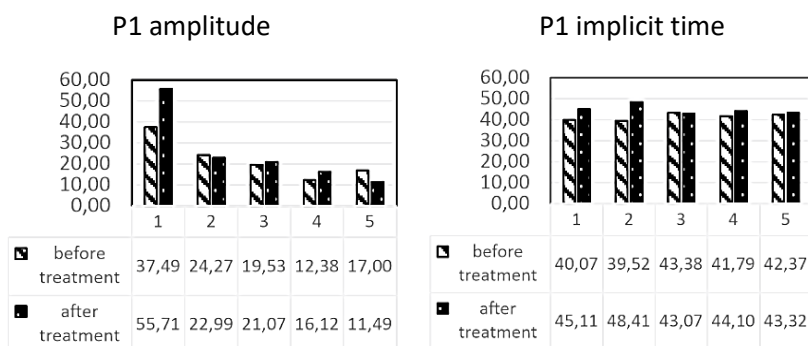


Figure 2. Dynamics of mf-ERG parameters in eyes with non-tractional macular edema. On the left – average P1 amplitude in 5 rings before and 2 weeks after intravitreal injection, on the right – average P1 implicit time before and 2 weeks after intravitreal injection

During tractional macular edema, the average P1 amplitude decreased sharply and P1 average= 38.45 ± 8.631 nV/deg2 (norm P1= 66.6 ± 130.87 nV/deg2). The examination was repeated at 1 month, 3 months and 6 months after the vitrectomy operation and an increase in P1 amplitude and implicit time indicators was noted after the operation, the

most noticeable changes were observed 6 months after the operation. The P1 amplitude was 58.97 ± 27.00 nV/deg² (+53.4%) 1 month after the operation, 59.54 ± 26.97 nV/deg² (+54.6%) 3 months after the operation, and 60.10 ± 26.29 nV/deg² (+56.3%) 6 months after the operation. The changes in P1 amplitude were statistically significant in all rings ($p < 0.001$).

The mean P1 implicit time was 41.16 ± 10.03 ms before surgery, 39.96 ± 10.67 ms (-2.9%) 1 month after surgery, 40.84 ± 9.80 ms (-0.8%) 3 months after surgery, and 40.64 ± 10.68 ms (-1.3%) 6 months after surgery. The change in implicit time was statistically insignificant ($p > 0.001$).

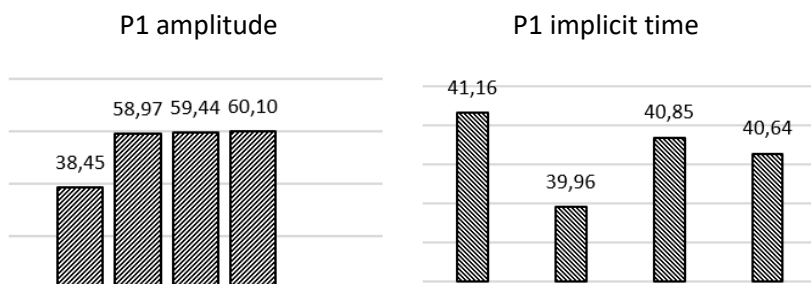


Figure 3. Dynamics of mf-ERG indicators in eyes with tractional macular edema. On the left – P1 amplitude in the 1st ring before surgery and 1, 3, 6 months after surgery, on the right – P1 implicit time in the 1st ring before surgery and 1, 3, 6 months after surgery

In Chapter IV, we studied the prognostic significance of multifocal electroretinography in various forms of diabetic macular edema. For this purpose, functional indicators obtained from the central zone of the retina in patients with DME using the mf-ERG method, structural and quantitative indicators obtained from OCT, as well as qualitative and quantitative indicators obtained from microperimetry (MP) and visual acuity, were analyzed and a correlation analysis was performed.

Pearson correlation analysis showed that in non-tractional macular edema, a strong, negative ($r = -0.813$) and highly significant correlation was found between the central thickness of the macula and the amplitude of P1

($p < 0.01$). There was a weak positive and significant correlation between the central macula thickness and the P1 “implicit time” indicators ($r = 0.036$) ($p < 0.05$). Pearson correlation analysis in group II patients showed that a strong negative ($r = -0.759$) and highly significant ($p < 0.01$) correlation was found between the central macula thickness (CMT) and the amplitude of P1. There was a weak negative and significant ($p < 0.05$) correlation between the central macula thickness and the P1 “implicit time” indicators ($r = -0.140$).

In our scientific study, a strong positive and statistically significant correlation was found between visual acuity and P1 amplitude during DME accompanied by vitreomacular traction ($r = 0.821$), ($p < 0.05$). There is a weak negative and unreliable correlation between the central thickness of the macula and P1 implicit time indicators ($r = -0.140$, $p > 0.05$). There is also a weak positive and reliable correlation between P1 amplitude and light sensitivity parameters ($r = 0.149$, $p < 0.05$). There is a weak positive and reliable correlation between P1 implicit time and light sensitivity parameters ($r = 0.034$, $p < 0.05$). In macular edema accompanied by vitreomacular traction, a strong positive and statistically reliable correlation between visual acuity and P1 amplitude ($r = 0.821$, $p < 0.05$), and a weak and unreliable correlation between visual acuity and P1 implicit time ($r = 0.203$, $p > 0.05$).

In order to predict post-treatment visual acuity of multifocal ERQ values obtained before treatment in patients with various forms of diabetic macular edema, linear regression analysis was performed between both P1 amplitude and P1 implicit time and mean visual acuity (in LogMAR units). At this time, in the linear regression analysis performed with P1 amplitude before treatment in patients with both non-tractional and tractional macular edema, a statistically significant relationship was determined only for the 1st and 2nd rings, and a statistically insignificant relationship was determined for the other rings.

In eyes with non-tractional macular edema (group I), an analysis of variance (ANOVA) was performed to test the overall fit and statistical validity of the population model used for P1 amplitude, and the fit of the

models for both rings 1 and 2 was shown to be statistically significant ($p < 0.001$ for ring 1, $p < 0.05$ for ring 2). The results of the regression model in the first ring were found to have an R^2 value of 0.580, indicating that the power of explaining pre-treatment P1 amplitude to post-treatment visual acuity was 58.0% (regression coefficient -0.021, $p < 0.001$, Figure 4).

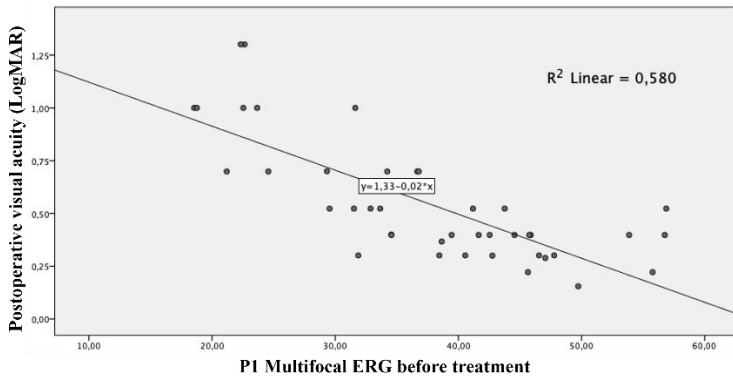


Figure 4. Prognostic role of P1 amplitude in ring 1 on multifocal ERG examination before intravitreal injection in non-tractional macular edema.

The obtained result can be expressed mathematically by the following equation:

Y (postoperative visual acuity, LogMAR) = $1.33 - 0.02 * X$ (P1, before treatment).

That is, each unit increase in the amplitude of P1 before treatment by nV/deg² corresponds to a decrease in the visual acuity indicator by 0.02 units of LogMAR (i.e., an increase in vision).

In group II patients, the strongest correlation was found for ring 1 ($p < 0.001$). The results of the regression model in this ring show that the R value is 0.839, which means that the correlation of this model is strong. The R^2 value was found to be 0.703, which indicates that the power of explaining the P1 amplitude before treatment to the visual acuity after treatment is 70.3% (regression coefficient -0.026, $p < 0.001$, Figure 5).

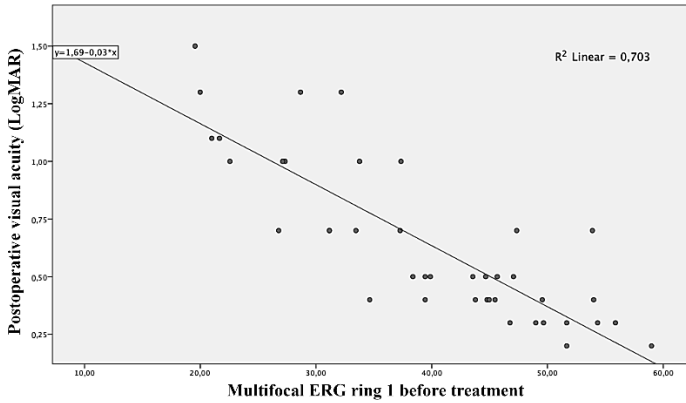


Figure 5. Prognostic role of P1 amplitude in ring 1 on preoperative multifocal ERG examination in tractional macular edema.

The obtained result can be expressed mathematically in the following equation:

Y (*postoperative visual acuity, LogMAR*) = $1.69 - 0.02 * X$ ($P1$, *before treatment*).

That is, each unit increase in the amplitude of P1 before treatment by nV/deg² corresponds to a decrease in the visual acuity indicator by 0.02 units of LogMAR (i.e., an increase in vision).

CONCLUSIONS:

1. In patients with non-tractional macular edema, mf-ERG examination showed a significant decrease in the average bioelectric response of the macular area of the retina. In these eyes, P1 was 37.48 ± 7.62 nV/deg. compared to the average normal $P1 = 66.6 \pm 130.87$ nV/deg. The amplitude of P1 in patients with non-tractional macular edema was statistically significantly lower in the 1st ring – 92.6%; in the 2nd ring – 38.5%; in the 3rd ring – 42.0%, in the 4th ring – 70.6%, in the 5th ring – 1.9% compared to the control group ($p < 0.01$).
2. In patients with tractional macular edema, the average bioelectric response of the macular area of the retina during mf-ERG examination was markedly reduced – P1 average was 38.45 ± 8.63 nV/deg. (normal $P1 = 66.6 \pm 130.87$ nV/deg.). In patients with tractional macular edema, the P1 amplitude was statistically significantly lower than in the control group: in the 1st ring – 87.8%; in the 2nd ring – 75.3%; in the 3rd ring – 34.1%, in the 4th ring – 34.7%, in the 5th ring – 50.8% ($p < 0.01$).
3. A strong negative ($r = -0.813$) and statistically highly significant correlation was found between mf-ERG parameters and mean central macular thickness in non-tractional diabetic macular edema ($p < 0.01$). A strong negative ($r = -0.759$) and statistically significant ($p < 0.01$) correlation was found between P1 amplitude and central macular thickness in tractional macular edema.
4. In patients with non-tractional diabetic macular edema, there was a weak positive and significant correlation between the P1 amplitude and the light sensitivity parameters obtained from microperimetry examination ($r = 0.183$), ($p > 0.05$). In tractional macular edema, a weak positive and significant correlation was observed between the P1 amplitude and the light sensitivity parameters ($r = 0.149$, $p > 0.05$).

5. Multifocal electroretinography, performed in eyes, which underwent vitrectomy, showed that electrogenesis in the retina was restored in a longer period. P1 amplitude in the 1st ring increased by 53.4% in 1 month, by 54.6% in 3 months and by 56.3% in 6 months after the surgery. In non-tractional macular edema, the P1 amplitude increased by 48.6% after the intravitreal injection.
6. Multifocal electroretinography P1 amplitude indicators have been shown to predict functional outcomes of diabetic macular edema treatment. In non-tractional macular edema, the power of the P1 amplitude indicator in the 1st ring before treatment to predict post-treatment visual acuity was 58.0% (regression coefficient -0.021, $p < 0.001$), and in tractional macular edema, the power of the P1 indicator in the 1st ring before surgery to predict post-operative visual acuity was determined to be 70.3% (regression coefficient -0.026, $p < 0.001$)

PRACTICAL RECOMMENDATIONS

1. Multifocal electroretinography is recommended to more accurately determine the functional activity of the macula, the extent of the pathological process and the severity of the disease in various forms of diabetic macular edema.
2. Multifocal electroretinography is recommended to explain the controversial functional results during the treatment of diabetic macular edema (unsuccessful treatment results, or when visual acuity is not corresponding to structural changes in the macula).
3. It is advisable to use multifocal electroretinography to predict the functional results of treatment and the expected visual acuity before starting treatment of various forms of diabetic macular edema.

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LIST OF ABBREVIATIONS

DR	– diabetic retinopathy
DM	– diabetes mellitus
DME	– diabetic macular edema
ILM	– internal limiting membrane
VEGF	– Vascular Endothelial Growth Factor
IDF	– International Diabetes Federation
ETDRS	– Early Treatment Diabetic Retinopathy Study
Mf-ERG	– Multifocal electroretinography
OCT	– optic coherence tomography
MP	– microperimetry
PE	– pigment epithelium
ISCEV	– International Society for Clinical Electrophysiology of Vision

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