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RETINAL AND OPTIC NERVE FUNCTIONAL ACTIVITY AFTER VITRECTOMY FOR VITREOMACULAR TRACTION SYNDROME

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✧ ***Background.*** Impacts of vitrectomy for vitreomacular traction syndrome on retinal and optic nerve functional activity are analyzed.

✧ ***Materials and methods.*** The electrophysiological monitoring was carried out before vitrectomy and on Days 1, 3, 7, 14, 30, 60, 180 after surgery in 59 patients (59 eyes). Patients were divided into three groups depending on the intraocular tamponade type: the first group – air tamponade, the second group – gas (C3F8) tamponade, the third group – BSS (balanced salt solution).

✧ ***Results.*** A significant inhibition of the functional activity of neurons of internal layers of the retina and of the optic nerve was revealed on the Day 1 after surgery compared to baseline data ($p < 0.001$). In groups I and III, the functional activity of inner layers of the retina and of the optic nerve restored twice as actively as that in the second group.

✧ ***Conclusions.*** Vitrectomy causes a reversible and significant inhibition of functional activity of retina and optic nerve. The duration of vitrectomy procedure is a significant negative factor determining the degree of depression of the functional activity of inner layers of the retina and of the optic nerve in the post-op period. The gas tamponade of the vitreous cavity with perfluoropropane-air mixture, compared to air and BSS tamponades, is a significant negative factor influencing the degree of functional activity inhibition of retina and optic nerve after surgery.

✧ ***Keywords:*** vitreomacular traction syndrome; vitrectomy; visual evoked potentials; electrophosphene; electrophysiology testing.

ФУНКЦИОНАЛЬНАЯ АКТИВНОСТЬ СЕТЧАТКИ И ЗРИТЕЛЬНОГО НЕРВА ПОСЛЕ ВИТРЭКТОМИИ ПРИ ВИТРЕОМАКУЛЯРНОМ ТРАКЦИОННОМ СИНДРОМЕ

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✧ ***Введение.*** Проанализированы результаты влияния витрэктомии по поводу витреомакулярного тракционного синдрома на функциональную активность сетчатки, зрительного нерва.

✧ ***Материалы и методы.*** Электрофизиологический мониторинг проведён до витрэктомии и на 1, 3, 7, 14, 30, 60, 180-е сутки после операции у 59 пациентов (59 глаз). В зависимости от вида тампонады стекловидной камеры сформировано три группы пациентов: I —тампонада стерильным воздухом, II — тампонада газовоздушной смесью, III — сбалансированный солевой раствор.

✧ ***Результаты.*** Достоверное угнетение функциональной активности нейронов внутренних слоёв сетчатки, зрительного нерва зарегистрировано на 1-е сутки после операции по сравнению с исходными данными ($p < 0{,}001$). В группах I, III функциональная активность внутренних слоёв сетчатки, зрительного нерва восстанавливалась в два раза активнее, чем во II группе.

✧ ***Выводы.*** Витрэктомия вызывает обратимое значимое угнетение функциональной активности внутренних слоёв сетчатки, зрительного нерва. Длительность витрэктомии — значимый негативный фак-

тор, определяющий степень угнетения функциональной активности данных нейронов после операции. Тампонада стекловидной камеры с перфторпропаном в составе газовоздушной смеси, по сравнению с тампонадой стерильным воздухом и сбалансированным солевым раствором, является значимым негативным фактором, влияющим на степень угнетения функциональной активность сетчатки, зрительного нерва после операции.

✧ ***Ключевые слова:*** витреомакулярный тракционный синдром; витрэктомия; зрительные вызванные потенциалы; электрофосфен; электрофизиологические методы исследования.

INTRODUCTION

Retinal macular diseases are significant causes of pronounced decrease in visual acuity and thus deterioration in the quality of life of patients [1]. Vitreomacular traction syndrome (VMTS) leads to edema, macular hole formation, and dysfunction of the central retinaea [2, 3]. Subtotal vitrectomy (VE), with removal of the posterior hyaloid membrane and the internal limiting membrane, and vitreous cavity tamponade with absorbable gas is the conventional surgical approach [4]. However, despite the success of surgical treatment of VMTS, functional outcomes after VE are often unsatisfactory [5, 6]. This may be due to adverse effects on the optic nerve pathway of physical factors (such as the vibrational effect of the vitreous cutter tip on the retina, and membrane removal) and chemical factors (such as the effect of various stains, and vitreous body substitutes) [7–10]. The aim of our study, therefore, was to conduct an analysis of changes with time in the functional activity of the retina and optic nerve after VE in VMTS cases using detailed electrophysiological examinations.

MATERIALS AND METHODS

Inclusion criteria in the study were:

(1) patients with VMTS requiring surgical treatment using

(2) a standard three-port transciliary 25G VE, and

(3) strict observance of the terms of control examinations and an electrophysiological examination.

Exclusion criteria from the study were:

(1) diseases that affect the functional activity of the retina and the optic nerve (such as partial atrophy of the optic nerve, glaucoma, diabetic retinopathy, or retinal detachment); and

(2) intraoperative complications affecting the functional activity of the retina and the optic nerve (such as acute circulatory failure in the optic nerve, or iatrogenic retinal detachment).

A control group (70 patients, 70 eyes) consisted of patients who underwent standard, uncomplicated cataract removal with intraocular lens implantation. This surgery was confined to the anterior chamber of the eye, not affecting the retina and the optic nerve structure and functions.

All VE patients underwent a three-port 25G VE using the Accurus vitrectomy system (Alcon, USA). During the surgical procedure, the working frequency of cut of the vitreous cutter was on average 2,500 rpm, and the volume of the eyeball was replenished with balanced salt solution (BSS, Alcon, USA). The posterior hyaloid membrane contrasted with triamcinolone acetonide (Kenalog 40 (KRKA, Slovenia)) was removed. The internal limiting membrane stained with Membrane Blue stain (Dorc, Holland) was removed with vitreal tweezers. In 20 patients (20 eyes), surgery was completed with tamponade of the vitreal cavity with sterile air, in 20 patients (20 eyes), — with gas-air mixture (C3F8 and sterile air in a 1 : 4 ratio), and in 19 patients (19 eyes), — with BSS.

Visual acuity was examined in all patients, and electrophysiological testing was performed. Visometry was performed using Sivtsev visual acuity charts according to the standard method. The functional activity of neurons in inner retinal layers was evaluated by electrical sensitivity (ES) threshold and the critical frequency of phosphene disappearance (CFPD). ES and CFPD were examined on an Esophy-01 electro ophthalmic stimulator (Spetsmedpribor, Russia). The functional state of the optic nerve was determined estimating flash visual evoked potentials (FVEP) using Tomey EP-1000 Multifocal electrophysiological instrument (Tomey Corporation, Japan).

The following electrophysiological parameters were analyzed:

- FVEP: latency of the P2 component (ms), relative (%) change in the P2 component latency;
- electrophosphene: ES threshold (μA), relative (%) change in the ES threshold, CFPD values (Hz), relative (%) change in CFPD values.

The visual acuity testing and the electrophysiological examination were performed before surgery and on Days 1, 3, 7, 14, 30, 60, and 180 after the surgery.

For statistical analysis, MedCalc Software v 18.4.1 was used. The normality of the sample distribution was estimated using the Kolmogorov-Smirnov criterion. All data were presented as mean ± standard deviation. The statistical significance of differences between the groups was determined, and pair-wise comparison of groups was made using one-way analysis of variance with Bonferroni correction ($p < 0.0125$). Spearman's correlation coefficient and its significance were calculated. The results were considered statistically significant if p was <0.01.

RESULTS AND DISCUSSION

From 2012 to 2018, in the Ophthalmology Clinic of Kirov Military Medical Academy, 1,196 patients underwent an electrophysiological examination, 59 of whom met our study inclusion criteria (59 eyes, 28 women and 31 men, average age 73.32 ± 7.54 years).

The distribution of patients by groups, gender, age, and type of vitreous chamber tamponade's agent is presented in Table 1. Figure 1 demonstrates changes in visual acuity indices throughout the follow-up period in the VE group and in the control group.

An analysis of changes with time of the kinetics of the optic nerve bioelectrical impulse revealed a significant increase ($p < 0.001$) in the temporal

Table 1 / Таблица 1

General characteristics of patients in main groups and in the control group
Общая характеристика пациентов в основных и контрольной группах

Indicator		Group I $n = 20$	Group II $n = 20$	Group III $n = 19$	Control group
Age		75.2 ± 7.3	77.3 ± 5.4	78.7 ± 6.2	72.7 ± 7.5
Gender	male	11	10	10	33
	female	9	10	9	37
Type of tamponing agent		Sterile air	Gas-air mixture	Balanced salt solution	–

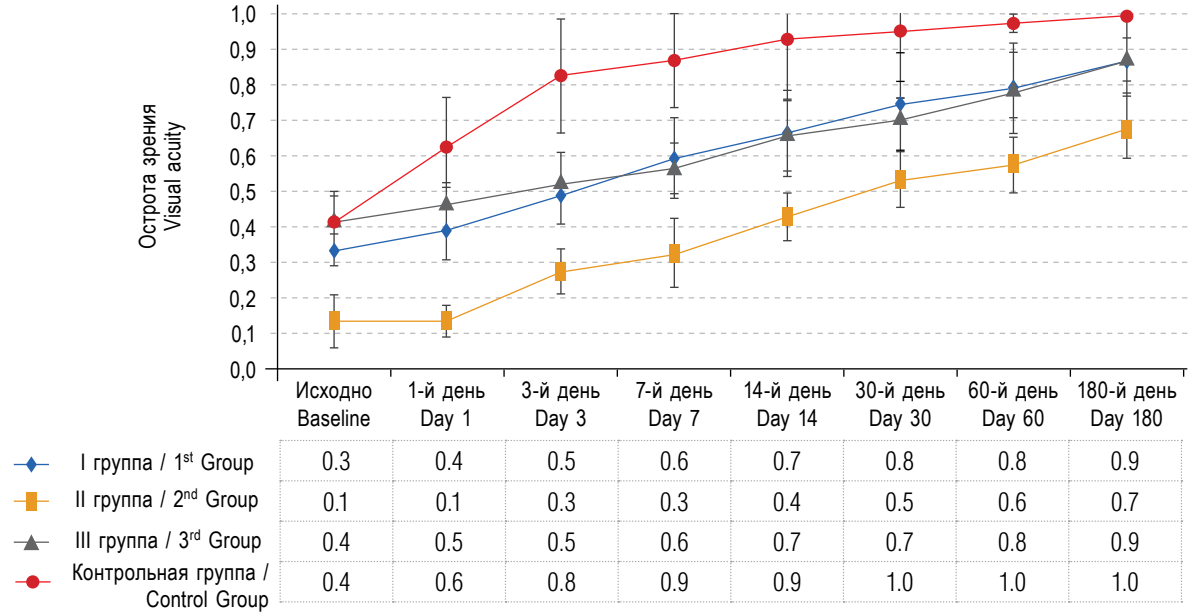
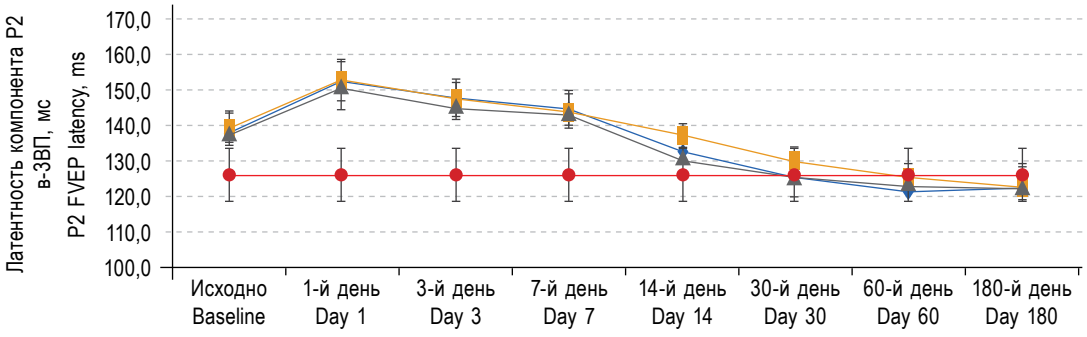


Fig. 1. Visual acuity dynamics

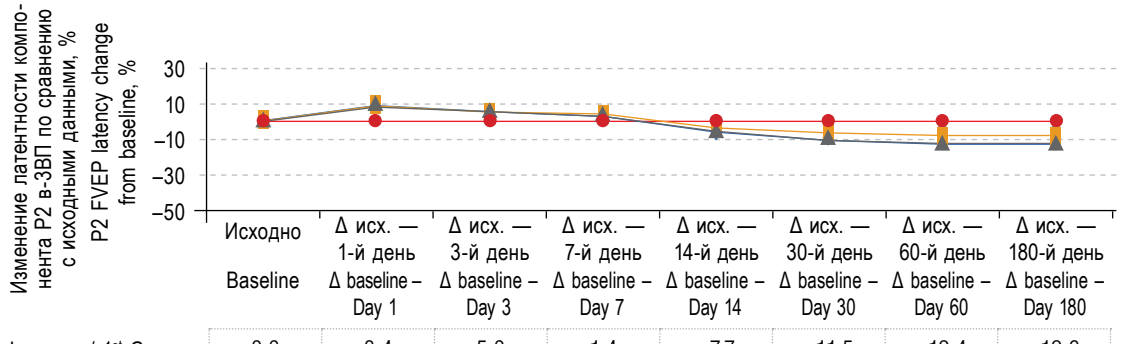
Рис. 1. Динамика остроты зрения



	Исходно Baseline	1-й день Day 1	3-й день Day 3	7-й день Day 7	14-й день Day 14	30-й день Day 30	60-й день Day 60	180-й день Day 180
I группа / 1st Group	137.3	153.2	148.4	144.3	131.5	125.1	120.9	121.6
II группа / 2nd Group	139.6	152.5	147.9	144.9	137.8	129.9	125.6	124.8
III группа / 3rd Group	138.3	151.2	146.4	143.3	129.5	124.1	122.9	122.6
Контрольная группа / Control Group	125.8	125.9	125.9	126.0	126.0	125.9	126.0	125.9

Fig. 2. Dynamics of the P2 Flash VEP latency

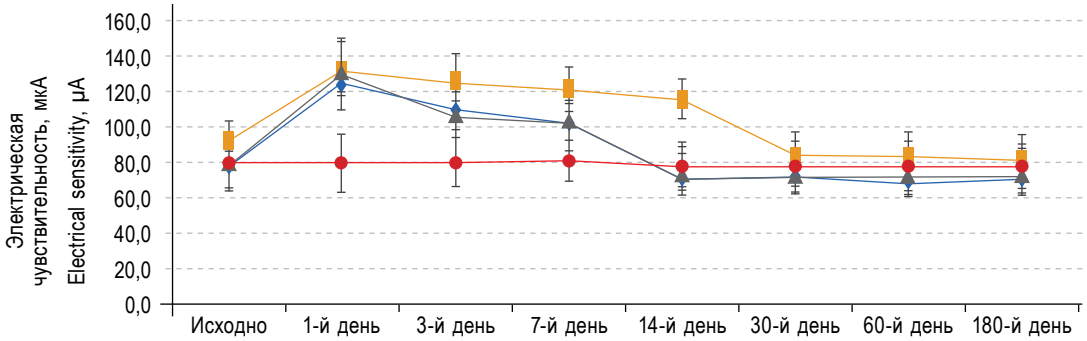
Рис. 2. Динамика латентности компонента P2 зрительных вызванных потенциалов на вспышку



	Исходно Baseline	Δ исх. — 1-й день Δ baseline – Day 1	Δ исх. — 3-й день Δ baseline – Day 3	Δ исх. — 7-й день Δ baseline – Day 7	Δ исх. — 14-й день Δ baseline – Day 14	Δ исх. — 30-й день Δ baseline – Day 30	Δ исх. — 60-й день Δ baseline – Day 60	Δ исх. — 180-й день Δ baseline – Day 180
I группа / 1st Group	0.0	8.4	5.0	1.4	–7.7	–11.5	–12.4	–12.6
II группа / 2nd Group	0.0	9.3	6.0	3.9	–1.2	–6.9	–9.9	–10.5
III группа / 3rd Group	0.0	9.4	4.0	2.0	–6.7	–10.5	–12.4	–12.6
Контрольная группа / Control Group	0.0	0.1	0.1	0.1	0.2	0.1	0.1	0.1

Fig. 3. Dynamics of the relative inhibition of the P2 Flash VEP latency

Рис. 3. Динамика относительного угнетения латентности компонента P2 зрительных вызванных потенциалов на вспышку



	Исходно Baseline	1-й день Day 1	3-й день Day 3	7-й день Day 7	14-й день Day 14	30-й день Day 30	60-й день Day 60	180-й день Day 180
I группа / 1st Group	78.0	123.0	111.0	103.0	74.0	75.0	73.0	74.0
II группа / 2nd Group	93.5	136.0	128.0	121.5	113.5	85.0	85.0	83.0
III группа / 3rd Group	80.0	133.0	107.0	101.0	77.0	76.0	76.0	76.0
Контрольная группа / Control Group	80.0	80.0	80.0	81.0	79.5	79.5	79.5	79.0

Fig. 4. Dynamics of the electrical sensitivity

Рис. 4. Динамика электрической чувствительности

parameters of the P2 component of FVEP on Day 1 after surgery in all three VE groups (Fig. 2, 3). From Day 3 after surgery, there was a tendency of the nerve impulse conduction velocity restoration along the optic nerve. The nerve impulse kinetics reached normal values on Day 14 after VE in groups I (air) and III (BSS), and on Day 30 after surgery in group II (gas + air).

According to the electrophosphene investigation results, a significant increase in the threshold of ES and CFPD was revealed on Day 1 after VE compared with the initial data in all three groups (Fig. 4–7). From Day 3 after surgery, the ES and CFPD indices gradually restored to normal values. Normalization of ES in VE groups I and III was detected on Day 7, while in VE group II, it was on Day 14 after surgery. CFPD indices normalized on Day 14 in VE groups I and III, and on Day 30 after surgery in VE group II.

Temporal parameters of the P2 component of FVEP, and electrophosphene indices in the control group were stable, and there were no significant differences at all terms of follow-up.

According to the results of the comparative analysis of the initial indices of the temporary parameters of FVEP in all groups, a statistically significant difference in the P2 component latencies of FVEP was revealed between group I and the control group, group II and the control group, and group III and the control group ($p < 0.001$).

According to the results of the comparative analysis of the initial CFPD indices in all groups, a statistically significant difference between the CFPD indices was found between group I and the control group, group II and the control group, and group III and the control group ($p < 0.001$).

The VE duration was 43.7 ± 4.4 min on average. According to the analysis of surgical procedure protocols, the average duration of VE was 42.7 ± 1.2 minutes (44.1 ± 3.8 min in group I, 42.2 ± 2.5 min in group II, and 41.9 ± 3.5 min in group III).

Table 2 presents the correlation analysis results. At all follow-up time points, no correlation was found between visual acuity indices and electrophysiological indices.

Table 2 / Таблица 2

Значение коэффициента корреляции между длительностью витрэктомии и электрофизиологическими показателями в основных группах
The value of the correlation coefficient between the vitrectomy duration and electrophysiology indices in main groups

Values under study	Correlation relationship		Correlation coefficient
	Type	Power	
t VE*/Δ P2 VFEP**	straight	strong	0.85
t VE*/Δ CFPD**			0.79
t VE*/Δ ES**		medium strength	0.65

Note: *vitrectomy time in minutes; **difference between the index on Day 1 after vitrectomy and the initial value, %.

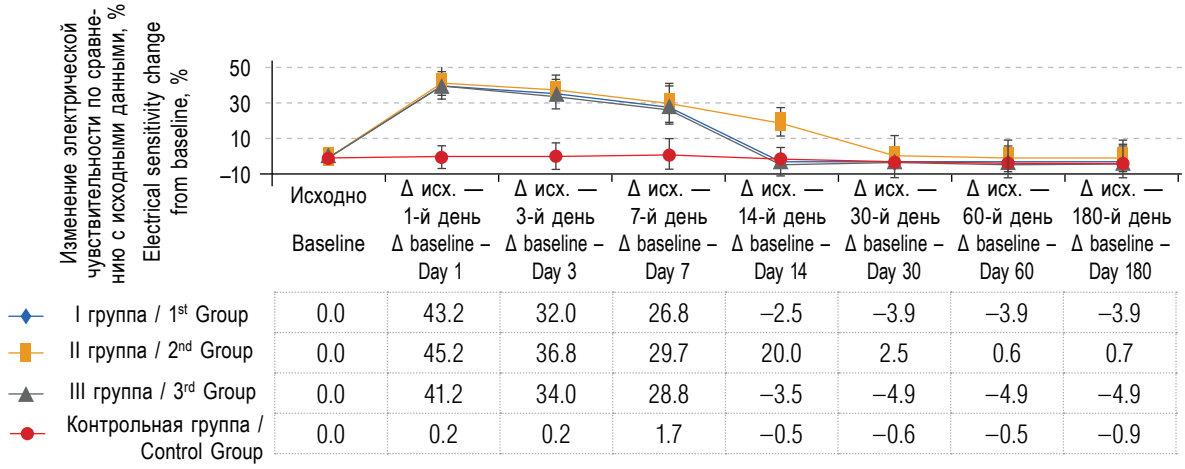


Fig. 5. Dynamics of the electrical sensitivity relative inhibition

Рис. 5. Динамика относительного угнетения электрической чувствительности

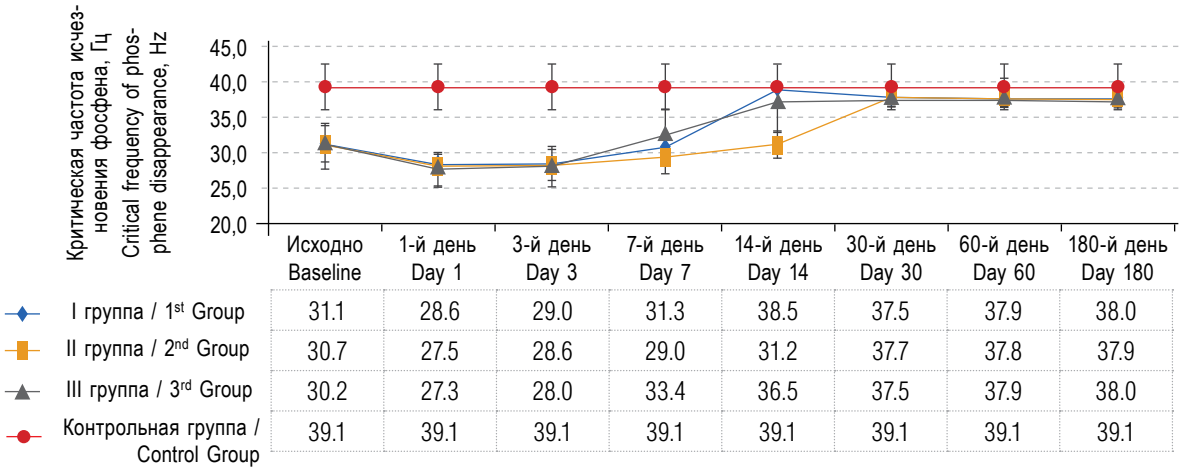


Fig. 6. Dynamics of the critical frequency of phosphene disappearance

Рис. 6. Динамика критической частоты исчезновения фосфена

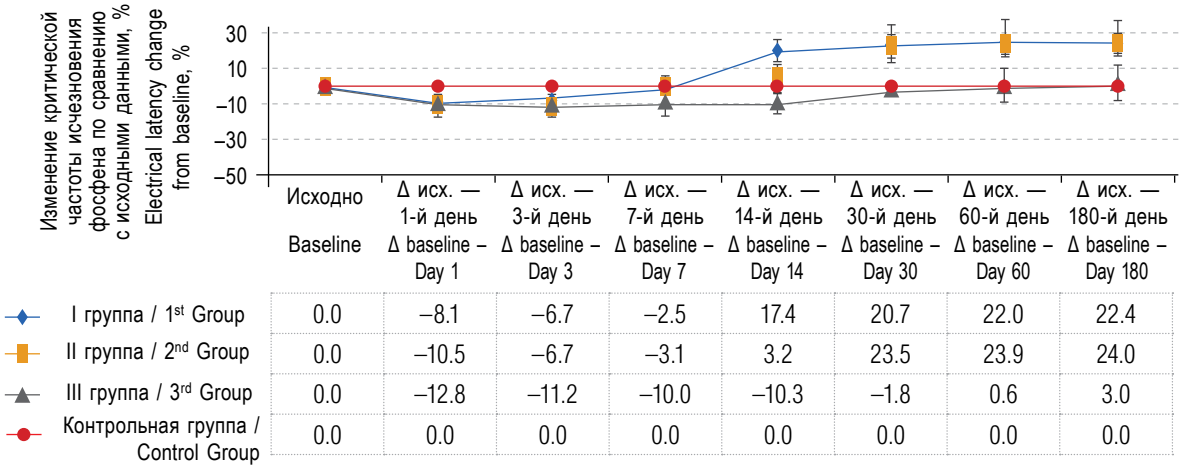


Fig. 7. Dynamics of the relative inhibition of the of the electrical lability

Рис. 7. Динамика относительного угнетения критической частоты исчезновения фосфена

On Day 1 of the follow-up in all the VE groups, a significant decrease in the functional activity of the optic nerve and retinal inner layers was noted. The decline in neuronal function could be explained by the VE depressive effect on the bioelectric response formation in neurons of internal retinal layers and the optic nerve. In our previous studies, a reversible significant decrease in electrogenesis in the early postoperative period was proven at the level of photoreceptors and bipolar cells after VE performed for macular hole and dislocation of nuclear lens fragments due to complicated phacoemulsification [7]. According to the Russian and international literature, the decrease in functional activity of retinal neurons, including those of inner layers, is explained by mechanical trauma to the retina during removal of pathological membranes [11]. Similar changes may be seen from chemical effects of artificial dyes that are used to enhance pathological membranes' contrast during surgery [12, 13].

Our results showed the time course of functional restoration of neurons in the inner layers of the retina and optic nerve after surgery. When comparing the changes in the latency of the P2 component to the initial level (%) on Day 1 after VE, there were no statistically significant differences between the three VE groups. The inhibition of the neuronal function of the inner retinal layers and optic nerve due to surgical procedure did not depend on the type of tamponade agent in the vitreous cavity. The change in the latency of the P2 component, starting from Day 3 after surgery, with air or BSS tamponade was significantly less than with gas-air tamponade and this remained so until Day 14.

Taking into account the same amount of surgical trauma, the absence of statistically significant differences in the VE duration between the three groups, the differences in the timing of restoration of the neuronal function in the inner retinal layers and optic nerve according to ES, CFPD, and FVEP between groups I, III, and II are probably associated with the implementation of pathological exposure to perfluoropropane in the gas-air mixture tamponing the vitreous cavity. Similar electrophysiological changes in the restoration of the retinal and optic nerve functional activity were noted in publications on electrophysiological assessment of the effect of various types of tamponade of the vitreous cavity (such as silicone oil, or various types of liquid perfluororganic compounds) on the restoration of neuronal activity of these structures [14–16].

CONCLUSIONS

1. Vitrectomy for VMTS causes significant reversible inhibition of the functional activity of the retina and optic nerve.

2. The VE duration determines the degree of inhibition of the functional activity of the retina and optic nerve in the postoperative period.

3. Tamponade of the vitreous chamber with a gas-air mixture (using perfluoropropane), in comparison with tamponade with sterile air and BSS, is a significant adverse factor affecting the rate of restoration of functional activity of the retina and optic nerve after surgery.

Additional information

The authors of this article declared no conflict of interest.

Contribution of authors

E.N. Nikolayenko created the concept and design of the study, collected and processed the material, performed statistical processing, wrote the text of the article, and prepared the illustrations.

A.N. Kulikov created the concept and design of the study, performed control over the implementation of all stages of the study, and wrote the final version of the article.

V.V. Volkov was involved in editing the text of the article.

V.F. Danilichev edited the text of the article.

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