Vascular disorders in the optic neuritis (ON) due to the inflammatory process lead to ischemia and persistent trophic changes in the inner layers of the retina with the loss of retinal ganglion cell neurons. The regulatory influence of the autonomic nervous system (ANS) on the vascular system and its active participation in the inflammatory reaction is known.

Purpose: to study the state of regional hemodynamics by the rheoophthalmography (ROG), the state of ANS by the heart rate variability (HRV) method and the level of adaptation potential (AP) of the cardiovascular system in patients with idiopathic ON and its complicated outcome.

27 women and 30 men (82 eyes) with idiopathic ON were examined in the Laboratory of Functional Methods Research of Vision. Control group - 27 healthy volunteers. ROG was performed on a computer rheoophthalmographic complex (Reocom, Ukraine, Kharkiv) for the eye pulse blood filling examination. The state of ANS was analyzed by HRV. AP was calculated by the R. Baevsky formula.

It was found out that the factor of ON course affected of the eye volumetric pulse blood filling (RQ‰) indicator: F=3.2, p=0.01. Intensity of AP was more common in the group of the partial atrophy of optic nerve (PAON). Parasympathetic activity was increased by 36.8% according to the HF (%) indicator in PAON group, which apparently characterizes the end of the inflammation productive phase.

Conclusions: the peculiarities of regional hemodynamics, the AP of the cardiovascular system and the regulation of the ANS in patients with ON and its outcome have been determined.

Key words: optic neuritis, eye hemodynamics, adaptation potential, autonomic nervous system.

The connection of the publication with planned research works.

The experimental study was performed within the framework of the research work “The effectiveness of immunocorrection in the treatment of ischemic neuropathy of the optic nerve”, state registration № 119U101224.

Introduction.

Optic neuritis (ON) is the inflammatory lesions of the optic nerve, which can lead to acute or subacute impairment of visual functions. Often ON affects people of a young age. It can be the first manifestation of the central nervous system disease [1, 2]. According to the data of modern literature, most of ON cases are idiopathic [3, 4]. Also, ON can be associated with recurrent demyelinating diseases. It is multiple sclerosis (MS), and less often is a spectrum of diseases associated with antibodies: optic myelitis and myelin-oligodendrocyte glycoprotein antibody disease [5]. In the modern studies, the fact of hemodynamic disturbances in the orbital vessels, ophthalmic artery, and vein is shown in patients with ON. The authors suggest hypotheses about hemodynamic and point to contradictions in the results [6,7]. The role of ischemia is also considered in pathophysiology of ON [8]. Inflammation of the vascular endothelium is also typically [9].

The prognosis for preserving the patient’s visual functions is important. The probable death of the nerve tissue and vascular disorders due to the inflammatory process lead to ischemia. It is lead to persistent trophic disorders, damage to the inner layers of the retina with the loss of retinal ganglion cell neurons due to retrograde degeneration of axons in the ON. The result is a reduction in the resolution of the visual analyzer and visual field defects. It is important to be able to correct the manifestations of the ischemic process and trophic disorder in time. The pathophysiology and natural course of idiopathic optic neuritis are insufficiently studied [10]. The chronic ischemia leads to diffuse death of axons [11]. After oxygen-glucose deprivation (OGD) within 60 minutes, mitochondrial fragmentation occurs sequentially in the axon and soma of neurons [12].

Regional hemodynamics is related to systemic hemodynamics, under of the influence of a complex hierarchical mechanism of regulation. The regulatory influence of the autonomic nervous system (ANS) on the vascular system, its active participation in the inflammatory reaction are the basis of the task of studying the adaptive response of the ANS in ON. In addition, autonomic dysfunction occurs in patients with ON and MS, but clinical studies disagree about the frequency and type of autonomic dysfunction [13]. Currently, the method of the ANS examinations based on heart rate variability (HRV) is available and widely used. There are few works about HRV in ophthalmopathology, which determined the type of autonomic dysfunction and its role in the pathogenesis of eye diseases [14-16]. There are few works in case of inflammatory ophthalmopathology [17].

The aim of the study.

To study the state of regional hemodynamics by the rheoophthalmography method, the autonomic nervous system by the heart rate variability method and the level of adaptation of the cardiovascular system in patients with idiopathic optic neuritis and its complicated outcome.

Object and research methods.

In the Laboratory of Functional Methods Research of the Organ of Vision of the SI “The Filatov Institute of Eye Diseases and Tissue Therapy of the National Academy of Medical Sciences of Ukraine” were performed...
examinations of 57 patients with ON of unknown etiology (idiopathic). ON was clinically defined as papillitis and its outcome. There were 27 women and 30 men (82 eyes), which consisted of 4 groups of patients. Group 1 – 25 patients (36 eyes) with acute primary ON. There were 14 patients with unilateral ON (14 eyes), 11 patients with bilateral ON (22 eyes). The duration of the disease in groups 1 (median and interquartile range): 12 (7-30) days. Group 2 – 9 patients (14 eyes) with primary ON, prolonged symptoms were more than 90 days. There were 4 patients with unilateral neuritis (4 eyes), 5 patients with bilateral neuritis (10 eyes). Group 3 were 10 patients (14 eyes) with partial atrophy of the optic nerve (PAON) as outcome of ON. There were 6 patients with unilateral neuritis (6 eyes), 4 patients with bilateral neuritis (8 eyes). In the groups 3 the duration of the disease was 1080 (180-1825) days. In the group 4 were 13 patients (18 eyes) with outcome of ON (macular edema, macular dystrophy, traction of the posterior hyaloid in the macula). There were 8 patients with unilateral neuritis (8 eyes), 5 patients with bilateral neuritis (10 eyes). The duration of the disease was 700 (150-1440) days. The age of the patients was 37.8±11.3 years. 5th group (control) consisted of 27 healthy volunteers of a similar age.

The examinations were performed according to the principles of safety, ethical attitude and application of the rules of working with patients in accordance with the "Bioethical Regulations of the Declaration of Helsinki on the ethical regulation of medical research", the Convention of the European Council on Human and Biomedical Rights and the relevant Laws of Ukraine. All participants provided written informed consent.

All patients underwent an ophthalmologic examination including refractionometry, tomometry, slit lamp biomicroscopy of the anterior segment and posterior segment of the eye. The macula of the retina, optic disc and peripapillary retina was assessed both ophthalmoscopically, biomicroscopically through a dilated pupil, and using OCT (Spectralis HRA+OCT (Heidelberg Engineering)). The threshold of electrical sensitivity and the critical frequency of flash fusion of the optic nerve were examined by phosphene. Fields of vision were performed by Humphrey perimetry (standard 24-2 SITA; Carl Zeiss Meditec). Patients were consulted by a neurologist, MRI and CT of the brain were performed. Cases with concomitant autoimmune and endocrine pathology were excluded from the examination. Rheoophthalmography (ROG) was performed on a computer rheographic complex (Reocom, Ukraine, Kharkiv). We used the parameters of volumetric pulse blood filling, which determines the rheographic coefficient Jantsch – RQ, % and the speed of volumetric blood filling of the eye according to the indicator V (Ω/s) of the reoophthalmogram.

The state of the ANS was determined by analyzing heart rate variability (HRV), which is a method of assessing the state of the mechanisms of physiological functions regulation, in particular, the general activity of regulatory mechanisms, neurohumoral regulation of the heart, the ratio between the sympathetic and parasympathetic divisions of the ANS. An ECG signal was recorded in the second standard lead in the supine position with calm breathing for 5 minutes by computer rheographic complex (Reocom, Ukraine, Kharkiv). We used the most informative statistical and spectral indicators recommended as international standards by the Working Group of the European Society of Cardiology and the North American Society of Cardiac Pacing and Electrophysiology [18].

<table>
<thead>
<tr>
<th>¥ (ms²)</th>
<th>total spectral power (reflects the total activity of regulatory mechanisms of the ANS).</th>
</tr>
</thead>
<tbody>
<tr>
<td>VLF (%)</td>
<td>the very low-frequency (0.003-0.04 Hz) component spectrum in the total power, probably reflects the central sympathetic energotropic contribution, the influence of higher autonomic centers on the cardiovascular subcortical center. VLF reflects the neuro-humoral state, hormonal and metabolic levels of regulation.</td>
</tr>
<tr>
<td>LF (%)</td>
<td>the low-frequency (0.04-0.15 Hz) component of the spectrum in the total power, mainly characterizes the influence of the sympathetic nervous system, the activity of the vasomotor center.</td>
</tr>
<tr>
<td>HF (%)</td>
<td>the high-frequency (0.15-0.40 Hz) component of the spectrum in the total power, which corresponds to the activity of parasympathetic regulation.</td>
</tr>
<tr>
<td>LF/NF</td>
<td>the ratio (balance) of sympathetic and parasympathetic influences.</td>
</tr>
</tbody>
</table>

The following calculation indices were also used for the assessment of the adequacy of regulation processes: 1) SI – stress index of regulatory systems (cond. unit); SI =AMO/(2dX*Mo). 2) Index of centralization (IC) (cond. unit) IC = (HF + LF) / VLF. These indicators reflect the degree of the heart rhythm centralization and characterize the level of sympathetic influences [19]. Adaptation potential (AP) was calculated according to the formula of R. Baevsky [20]: AP =0.011(HR)+0.014(SBP)+0.008(DBP)+0.009(W)-0.009(H)+0.014(Age)-0.27. HR is the number of heart contractions, SBP is systolic blood pressure, DBP is diastolic blood pressure, W is body weight, H is height, age.

The Kolmogorov-Smirnov test was used to assess the normality of distributions. The description of data was performed using the mean (M) and standard deviation (SD), as well as the median (Me) and the Lower-Upper Quartiles. Student’s T test for independent samples was performed for normally distributed data and Mann-Whitney U test was performed for non-normally distributed data in pairwise comparison. P value<0.05 was considered to be statistically significant. A dispersion univariate analysis was used (ANOVA), the results were presented in the effect of the influence according to the F-criterion, and correlations – according to the Spearman coefficients.

Research results.

The influence of the ON course factor on the eye volumetric blood filling according to the RQ indicator (%): F=3.2, p=0.01 was revealed by univariate analysis of variance. The factor of mono- or bilaterality of the ON did not affect RQ. The values of RQ were increased in patients of the 1st group in compared to the control by 15.5% (p<0.05) and were increased in patients of the 3rd and 4th groups by 35%-31 % (p<0.05). Also, the RQ in the 3-d group was decreased in compared to the control by 23.6% (p<0.05), which reflects the regional ischemic process (table 1).
The velocity of volumetric blood filling of the eye according to the indicator V (Ω/s) was also the highest in the 1-st group of acute ON by 33% (p=0.01) than the control and higher by 33% (p=0.05) than in the 4-d group (Table 2).

An inverse correlation between RQ and adaptation potential (AP) was found, r=-0.57 (p<0.05). When AP values was normal (when AP≥2.1 units), the RQ was 4.4±1.8‰. When the adaptation mechanisms were tensed (when AP=2.1-3.2 units), the RQ indicator decreased – 3.7±1.6‰. When adaptation was unsatisfactory (when AP<2.1 units), the RQ indicator was even lower (on average by 56%, as a manifestation of ischemia) – 1.8±0.6‰.

The cardiovascular system (CVS) reacts wonderfully to the changes of hematostasis constants and plays a significant role in the processes of adaptation from normal to pathological. In case of ON good adaptation (AP) was in 22.2% of cases, tensed adaptation was in 74% cases, poor adaptation was single.

It was shown that the tension of the adaptation mechanisms was common (p=0.04) in PAON, then in acute ON (Table 3). In the acute process, the CVS adapts to the pathology, but over time the functional reserves are depleted.

The total spectral power TP (total activity of the ANS regulatory mechanisms), as the HRV indicators, had no differences in the pathologies, but in PAON compared to the control. RQ was lower in PAON than in the acute ON, which is a vasoconstrictor [6]. This can lead to increased plasma levels of endothelin-1, which is a vasoconstrictor [6]. The intraocular pressure and systemic arterial circulation also plays a role. Oxygen saturation of optic nerve tissues is regulated by intraocular pressure and systemic arterial pressure, vascular resistance, and tissue oxygen consumption. If the intraocular pressure is increased above 40 mmHg or the ocular perfusion pressure decreased below 50 mmHg the autoregulation is overwhelmed and the optic nerve becomes hypoxic [22]. We have proven that the RQ in the acute ON was higher by 15.5% compared to the control. RQ was lower in PAON than the control by 23.6%, which reflects the regional ischemic process. There were similar response trends for the indicator of the volumetric blood filling velocity of the eye. The information about hemodynamic disturbances in the orbital vessels is somewhat diverse in ON, but in general it is directed according to our results [7, 23, 24].

The main system-forming factor for the organism as a dissipative system is adaptation – the speed to partial adaptation of the nervous system (SNS): VLF (%), which reflects the state of neuro-humoral, hormonal and metabolic levels of regulation and the LF (%), which determines the activity of the SNS and the activity of the vasomotor center, also did not differ by group (Table 4). This was confirmed by the analysis of calculated indicators. The stress index (SI), which reflects sympathetic activity, and the centralization index (CIC), which characterizes the level of central sympathetic influences, did not have significant differences between groups (Table 4). It should be noted that the HF (%) index, which reflects the activity of the parasympathetic nervous system (PNS), increased by 36.8% (p<0.05) in PAON in comparison with acute ON (Table 4).

### Discussion of research results.

The pathophysiology of vascular dysfunction is completely unknown in ON. There is thickening of the optic nerve in combination with demyelination, which can compress blood vessels inside the optic canal. This is enhanced by vasospasm due to increased plasma levels of endothelin-1, which is a vasoconstrictor [6]. This can lead to blood flow resistance in the artery and due to ischemia – to possible exoplasmatic stasis and loss of vision [21]. Systemic circulation also plays a role. Oxygen saturation of optic nerve tissues is regulated by intraocular pressure and systemic arterial pressure, vascular resistance, and tissue oxygen consumption. If the intraocular pressure is increased above 40 mmHg or the ocular perfusion pressure decreased below 50 mmHg the autoregulation is overwhelmed and the optic nerve becomes hypoxic [22]. We have proven that the RQ in the acute ON was higher by 15.5% compared to the control. RQ was lower in PAON than the control by 23.6%, which reflects the regional ischemic process. There were similar response trends for the indicator of the volumetric blood filling velocity of the eye. The information about hemodynamic disturbances in the orbital vessels is somewhat diverse in ON, but in general it is directed according to our results [7, 23, 24].

### Table 1 – The state of the eye volumetric pulse blood filling according to the RQ (‰) indicator of the reoophthalmogram in groups of patients with ON and its outcome

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Acute primary ON</th>
<th>Long-term primary ON</th>
<th>Partial atrophy of the optic nerve</th>
<th>Other outcomes of ON</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M±SD</td>
<td>M±SD</td>
<td>M±SD</td>
<td>M±SD</td>
<td>M±SD</td>
</tr>
<tr>
<td>N</td>
<td>36</td>
<td>11</td>
<td>13</td>
<td>9</td>
<td>30</td>
</tr>
<tr>
<td>RQ‰</td>
<td>4.5±1.7</td>
<td>3.7±1.6</td>
<td>2.9±1.3</td>
<td>3.1±1.3</td>
<td>3.8±1.7</td>
</tr>
</tbody>
</table>

**Notes:** M is the arithmetic mean, SD is the standard deviation, and N is the number of eyes.

### Table 2 – The velocity of volumetric blood filling of the eye according to the indicator V (Ω/s) of the reoophthalmogram in groups of patients with ON and its outcome

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Acute primary ON</th>
<th>Long-term primary ON</th>
<th>Partial atrophy of the optic nerve</th>
<th>Other outcomes of ON</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M±SD</td>
<td>M±SD</td>
<td>M±SD</td>
<td>M±SD</td>
<td>M±SD</td>
</tr>
<tr>
<td>N</td>
<td>35</td>
<td>11</td>
<td>13</td>
<td>9</td>
<td>30</td>
</tr>
<tr>
<td>V (Ω/s)</td>
<td>1.6±0.8</td>
<td>1.43±1.0</td>
<td>1.22±0.8</td>
<td>1.15±0.37</td>
<td>1.2±0.6</td>
</tr>
</tbody>
</table>

**Notes:** M is the arithmetic mean, SD is the standard deviation, and N is the number of eyes.

### Table 3 – The distribution of the adaptation potential (AP) of the CVS in groups of patients with ON and its outcome

<table>
<thead>
<tr>
<th>Course</th>
<th>AP&lt;2.1 (normal adaptation)</th>
<th>AP (2.1-3.2) (tensed adaptation)</th>
<th>AP (3.2-4.3) (poor adaptation)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N %</td>
<td>N %</td>
<td>N %</td>
</tr>
<tr>
<td>Acute primary ON</td>
<td>6</td>
<td>19</td>
<td>2</td>
</tr>
<tr>
<td>Prolonged course of the primary ON</td>
<td>0</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>Partial atrophy of the optic nerve</td>
<td>0</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td>Other outcomes of ON</td>
<td>2</td>
<td>10</td>
<td>0</td>
</tr>
</tbody>
</table>

**Notes:** N is the number of patients.
Table 4 – Peculiarities of the autonomic nervous system state according to indicators of heart rate variability (HRV) in groups of patients with ON and its outcome

<table>
<thead>
<tr>
<th>HRV</th>
<th>ON</th>
<th>Partial atrophy of the optic nerve</th>
<th>Other outcomes of ON</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=27</td>
<td>N=10</td>
<td>N=9</td>
</tr>
<tr>
<td>Median (Q-Q)</td>
<td>1+2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

Notes: Qi-Qup range – lower and upper quartile (25%-75%); N – number of patients; * - level of significant differences p<0.05 in comparison with group (1+2).

Conclusions.

The index RQ (%) (eye volume pulse blood filling) in the acute ON group was increased by 15.5% compared to the control group. In the PAON group RQ decreased by 23.6% compared to the control, which reflects the regional ischemic process. The velocity of the eye volume blood filling according to the indicator V (Ohm/s) was increased by 33% in the group of acute ON.

During the transition of the ON to the PAON, the parasympathetic activity of the autonomic nervous system was increased by 36.8% according to the HF (%) indicator.

In the PAON group tension of the adaptation vascular system mechanisms was more common. It seems to lead to the depletion of functional reserves of the vascular system.

Prospects for further research.

Based on the obtained results, develop anti-ischemic therapy for optic nerve atrophy.

References

OTHELLO Z. Lesko T. Vasilets S. Velichko M. Hyperbaric oxygen therapy in neurovascular ischemia.

Rezumе. Острі жовчний залів — це болючий, гострий період, що виникає при втраті відшкодування жовчного заліва.

Ключові слова: жовчний залів, гострий період, відшкодування, інфекція.

Висновки. Гострий період жовчного заліва є важливим етапом у їхньому розвитку, причому він визначає наступні стадії.

Відомо, що гострий період жовчного заліва характеризується наявністю відносно більш активного відшкодування жовчного заліва.

Мета: визначити стан регіонарної гемодинаміки методом реоофтальмографії на основі лабораторного дослідження.

Об’єкт і методи дослідження. Отримані дані про відшкодування жовчного заліва за результатами проведеного дослідження.

Результати. Неврит зорового нерва (НЗН) відноситься до запальних уражень зорового нерва.

Враховуючи регулюючий вплив вегетативної нервової системи (ВНС) на судинну систему, її активну участь в залівній реакції, важливо вивчити її адаптивні реакції при НЗН.

Мета: визначити стан регіонарної гемодинаміки методом реоофтальмографії, ВНС методом варіабельності серцево-судинної системи у хворих на НЗН недиференційованої форми.

Обстеження на основі лабораторніх методів дослідження органу зору ГУ «Інститут очних хвороб та тканинної терапії ім. В.П. Філатова НАМНУ» провели 57 пацієнтів з невритом зорового нерва (НЗН) нез’єднаною етологією (ідіопатичний НЗН).

Фактор перебігу хвороби НЗН впливає на об’єктивні параметри реоофтальмографії.

Резюме. Жовчний залів — це гострий інфекційний період, що включає відшкодування жовчного заліва.

Висновки. Була виявлена відповідь на вплив реоофтальмографії на вегетативну нервову систему.

Ключові слова: неврит зорового нерва, хвороба зорового нерва, регуляція, реоофтальмографія, вегетативна нервова система.
a reduction of the visual analyzer resolution and visual field defects. Prognosis is important for the preservation of the patient’s visual functions. Regional hemodynamics is closely related to systemic hemodynamics. It is under the influence of a complex hierarchical regulation mechanism.

Autonomic nervous system (ANS) influences on the vascular system, involves in the inflammatory response actively. It is important to study of ANS regulatory role in the adaptive response.

**Purpose:** to study the state of regional hemodynamics by the rheoophthalmography method, the autonomic nervous system by the heart rate variability method and the level of adaptation of the cardiovascular system in patients with idiopathic optic neuritis and its complicated outcome.

**Object and research methods.** In the Laboratory of Functional Methods of Research of the Organ of Vision of the SI “The Filatov Institute of Eye Diseases and Tissue Therapy of the National Academy of Medical Sciences of Ukraine” were performed examinations of 57 patients with ON of unknown etiology (idiopathic). ON was clinically defined as papillitis and its outcome. There were 27 women and 30 men (82 eyes). The age of the patients was 37.8±11.3 years. 5th group (control) consisted of 27 healthy volunteers of a similar age.

All patients underwent an ophthalmologic examination. Rheoophthalmography (ROG) was performed on a computer rheographic complex (Reocom, Ukraine, Kharkiv). Were used the parameters of volumetric pulse blood filling, which determines the rheographic coefficient Jantsch-RQ, ‰ and the speed of volumetric blood filling of the eye according to the indicator V (Ω/s) of the reoophthalmogram. The state of the autonomic nervous system (ANS) was determined by analyzing heart rate variability (HRV). Adaptation potential (AP) was calculated by the formula of R. Baevsky.

**Results.** The factor of the ON disease affected the eye volumetric blood filling according to the RQ indicator (%): F=3.2, p=0.01. RQ was increased by 15.5% in the ON acute period compared to the control group. RQ was reduced by 23.6% in the group with PAON compared to the control. It reflected the regional ischemic process. The velocity of the eye volumetric blood filling according to the V indicator (Ohm/s) in the group of acute ON was by 33% higher than the norm. The intension of the adaptation of vascular system was more common and the parasympathetic activity of the autonomic nervous system was increased by 36.8% according to the HF (%) indicator in the PAON group. It seems to lead to the depletion of functional reserves of the vascular system.

**Conclusions.** The peculiarities of regional hemodynamics, the adaptation potential of the cardiovascular system and the regulation of the autonomic nervous system in patients with ON and its outcome have been determined.

**Key words:** optic neuritis, eye hemodynamics, adaptation potential, autonomic nervous system

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A – Work concept and design, B – Data collection and analysis, C – Responsibility for statistical analysis, D – Writing the article, E – Critical review, F – Final approval of the article.

Received 12.11.2022
Accepted 02.05.2023