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ELECTROENCEPHALOGRAPHIC INDICATORS IN PEOPLE WITH PANIC DECODERS

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Panic disorders are characterized by spontaneous and non-standard occurrence. In a state of panic attacks, a person experiences overwhelming fear, becomes defenseless. Situations with the 2019 coronavirus pandemic contribute to the spread of these disorders.

The main scientific method of studying neurobiological changes in panic attacks is the electroencephalographic (EEG) method. The purpose of this work is to analyze and summarize the literature data on the state of bioelectrical activity of the brain in people with panic disorders.

It is almost impossible to study the bioelectrical activity of the brain during a panic attack. Therefore, examinations are performed in the periods between attacks. There are some laboratory researches, where certain stimuli caused fear and anxiety, and against this background, studied the electrical state of the brain.

The researchers found a change in the electrical activity of the brain during panic attacks, the activation of different rhythms in different parts of the hemispheres during typical and atypical panic attacks, as well as an increase in interhemispheric functional disintegration. Increased arousal is associated with the dominance of the sympathetic nervous system. Excitement covers the amygdale, brain stem, insular cortex. Analysis of the scientific literature on the bioelectrical activity of the brain in people with panic disorders has shown ambiguity. There is also a link between the state of the neurons of the respiratory center and the experience of panic. A more thorough study of this issue may underlie non-pharmacological treatment, in particular, the use of respiratory practices and others.

Key words: panic disorders, electroencephalogram.

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Introduction. Panic attacks are episodic experiences of severe fear or apprehension. This condition usually begins suddenly, reaches its peak in 10 minutes and ends within half an hour. Often in this situation a person suffocates, thinks that one has a heart attack, or that one is dying or losing one's mind.

The prevalence of panic disorders in the world's population is 7-9%. Such disorders are more common in adulthood, in women than in men, in single people, in people who have experienced severe stress, in people who had a problematic family environment in childhood, in urban residents, compared to rural ones. Panic

disorders are often comorbid with other mental health problems, including depression. Panic attacks can develop against the background of suicide attempts.

The presence of panic attacks significantly complicates life, disrupts adaptation in society and qualitatively changes the adequacy of human behavior, often makes it antisocial.

Recently, due to the increasing pressure on the human psyche, the percentage of people with panic disorders is growing.

Today, the world is facing the 2019 coronavirus pandemic (COVID-19), which is actively encouraging scientists to rethink mental health issues. There is evidence of a link between coronavirus infection, quarantine and increased panic attacks. Experts claim that the symptoms of depression, anxiety, apathy, panic attacks can occur even within a few months after infection with COVID-19 [1, 2].

Panic attacks accompany the activities of a certain number of athletes, servicemen, workers in high-risk professions.

Due to the fact that panic attacks are associated with changes in the human psyche, it is important to understand the physiological processes that take place in the brain.

To date, there is very little scientific data on the neurobiology of panic disorders. There are some scientific studies that show disorders of certain brain structures in various anxiety disorders, including limbic-reticular complex, brainstem, and some parts of the cerebral hemispheres [3, 4]. Few studies of brain biochemistry in panic disorders, in particular, neurotransmitters [5, 6, 7, 8, 9].

Purpose of research – analysis and generalization of literature sources on the state of bioelectrical activity of the brain in people with panic disorders.

Object and methods of research. Systematic review and analysis of literature sources in PubMed, EMBASE, SPORTDiscus, PsycINFO, Cochrane and Google Scholar databases.

Research results and their discussion. A full human life is impossible without the normal functioning of the nervous system, especially the brain. The consequences of disturbances in the brain are a variety of pathological conditions that complicate human life and significantly impair quality of life.

Electroencephalography (EEG) is a modern effective method for studying the electrical activity of neurons in various brain structures. Electroencephalographic method of research is used, in particular, to determine the nature of neurological symptoms, such as depression, panic attacks, fainting, etc. EEG indicators, especially in dynamics, are appropriate for the choice of adequate therapeutic tactics.

Experts note that the response to treatment in clinical practice is much less effective than it seems. There is much evidence to suggest the presence of a chronic or recurrent clinical course in panic disorder. Potential physiological pathologies such as genetic susceptibility, altered brain function, brain-derived neurotrophic factor, and prolonged inflammation should be considered to explain treatment resistance.

The authors conclude:

- 1) panic disorder is often a chronic or recurrent disorder;
- 2) one third of patients with panic disorder will be resistant to treatment;
- 3) the biopsychosocial risk model may explain resistance to treatment;
- 4) with resistant to treatment panic disorder, a combination of antidepressants and cognitive-behavioral therapy should be considered.

Scientists advise to include the detection and concomitant treatment of psychiatric comorbidities, medical comorbidities, and the detection of parental psychopathology and psychosocial disorders to develop strategies for treating disorders in people with resistance to treatment. Optimal drug correction or a combination of medication and psychotherapy may be an adequate therapeutic strategy for treatment-resistant binary disorder. Further studies of the bioelectrical activity of the brain of people with panic disorders may help to understand the mechanisms of resistance to the treatment of binary disorders and identify new strategies for treating this pathology [10].

Scientists have found that panic paroxysms may be part of the manifestations of epilepsy. Therefore, the activity of various brain structures in panic attacks should be studied quite carefully, because in parallel, signs of epilepsy can be detected at an early stage.

Jennifer J Newson et al. (2019) studied electroencephalograms of persons suffering from various mental disorders: depression, attention-deficit hyperactivity disorder (ADHD), autism, drug addiction, bipolar disorder, anxiety, panic disorder, post-traumatic stress disorder, obsessive-compulsive disorder and schizophrenia. The researchers set a goal to determine whether there are patterns between such disorders in certain alpha, beta, gamma, theta and delta waves. The most dominant pattern of change among several types of disorders, such as schizophrenia, hyperactivity, obsessive-compulsive disorder, is the activation of delta and theta waves and the suppression of alpha, beta and gamma waves. But the authors do not state unequivocally that such different disorders have the same picture of the electrical activity of brain neurons [11]. The data obtained by these scientists resonate with research [12].

The results of the study of the electrical activity of N.N. Lebedeva et al. (2019) note a decrease in the frequency range of beta-1 in the EEG after a cognitive test in patients with mixed anxiety and depressive disorder. Patients with hypochondriac disorder had a reduced duration of RR intervals; increased frequency range of beta-1 at rest; increase in the dominant frequency of beta-2 during the cognitive test and the standard deviation of the frequencies of theta waves after the cognitive test [13].

It is important that Kristie L Poole & Louis A Schmidt (2019) detected the frontal correlation of delta-beta

brain waves, salivary cortisol and social anxiety from childhood [14].

In the case of violation of protective mechanisms, the individual exaggerates the threat, experiences increased anxiety [15].

Johannes Rentzsch et al. (2016) conducted a neurobiological study in people with panic disorders to identify differences in healthy individuals, when treating sudden sound stimuli unrelated to fear. The results of their research confirm the idea of weak (reduced) processing of such stimuli, especially the duration of sound [16].

To determine the involvement of the hippocampus in anxious states, studies were performed on laboratory rats, but it did not give pronounced results [17]. The question remains open. Although there is a claim about the prognosis of theta activity of the hippocampus as an indicator of anxiety, in particular in rodents.

Neuroanatomical changes were observed in studies by Elizabeth I. Martin & Kerry J. Ressler. Single-photon emission computed tomography showed a decrease in metabolism in the left lower parietal lobe and an overall decrease in bilateral cerebral blood flow in patients with panic disorder compared to control subjects. Such patients also showed a bilateral decrease in frontal activity, but an increase in activity in the right medial and upper frontal lobes. The shift to the right hemisphere correlated with the severity of the disorder in some patients.

A spontaneous panic attack showed a significant increase in the activity of the right amygdala. Other studies have shown that when pronouncing words that evoke negative emotions, patients with panic disorders show activation of neurons in the right amygdala and right hippocampus. With the appearance of visual stimuli that provoke anxiety, such patients have increased activity in the cortex of the lower frontal lobe and in the hippocampus.

When implanting EEG electrodes in patients diagnosed with panic attacks, it was found: excessive theta activity on the EEG, increasing the amplitude of evoked potentials and increasing the frequency of extracellular neuronal activity in cortico-subcortical structures in the period between panic attacks [3].

Attention is paid to such issues as the study of inter-hemispheric asymmetry of EEG activity in patients with panic disorders [18]. Thus, patients with panic attacks in the right hemisphere showed a significant decrease in the total absolute power density of the alpha rhythm, as well as an increase in the total absolute power density of the rhythms in the beta-1 range and theta range compared with control subjects. Such changes took place mainly in the temporal and frontal leads.

In the left hemisphere, the decrease in the total absolute power density of the alpha rhythm and the increase in the total absolute power density of the rhythms in the beta-1 range was less pronounced. Regarding changes in theta rhythm, no significant changes were observed in comparison with the control group [18].

Gordeev also conducted research and comparative analysis of the specifics of changes in the background electrical activity of the brain of patients with typical and atypical panic attacks. In both cases, there was a decrease in the spectral power of the alpha rhythm on the EEG of the right hemisphere compared with a group of healthy people. The following differences were found: in

typical panic attacks, an increase in the spectral power of beta-1 rhythm in the frontal, temporal, central and parietal parts of the right hemisphere, and in atypical – theta rhythm power in the temporal regions of this hemisphere. It has been suggested that in patients with typical panic attacks the activity of nonspecific systems of the mesencephalic reticular formation increases, and in patients with an atypical form of attacks – increased activity of the temporomandibular structures of the brain [3].

Thus, based on the obtained results, the authors conclude that the strengthening of functional disintegration of interhemispheric asymmetry is due to increased activation of the hypothalamic-septo-hippocampal system, resulting in a violation of psychological adaptation. Such persons have a high level of depression, reactive and personal anxiety, which eventually leads to the development of autonomic crises and panic disorders [18]. Thus, autonomic crises are directly related to panic attacks [6].

The results of scientific studies show that autonomic disorders reach their maximum values in “panic migraine”, when at the height of the typical form of migraine there are signs of panic attacks [6].

It is known that when experiencing stress, the sympathetic nervous system is activated, and later it is inhibited, while the parasympathetic nervous system helps the body to move to a calmer state. For a panic attack, for some reason, the parasympathetic nervous system is not able to get involved in time. As a result, the person remains in a state of heightened arousal.

Research shows that during a panic attack, arousal affects the amygdala as well as the central gray matter (around the cerebral aqueduct) of the midbrain, which provides certain protective responses to the body and is associated with adaptive behavior. At the same time, stimulation of the periaqueductal gray matter and the hypothalamus causes symptoms of fear similar to panic attacks.

The smallest part of the brain – the insula – is critical for interoceptive awareness. It has been suggested that the insular cortex may be directly related to the occurrence of panic disorders [19].

Electroencephalographic studies alone are not enough to understand changes in brain function in panic disorders. Thus, in particular, magnetic resonance imaging (MRI) studies reveal pathological changes in the brain (eg. cysts in the insula, hidden angiomas in the temporal and parietal areas, destruction after cerebrovascular lesions in the parietal region) [3].

Biochemical studies of the brain complement the picture of the brain. Particular attention is paid to biochemical systems that have the functions of excitation and inhibition – glutamatergic and gamma-aminobutyric. It should be noted that these systems are directly related to anxiety states [6].

Decreased concentrations of gamma-aminobutyric acid in the occipital cortex have also been reported in people with panic disorders.

In panic disorders, changes in the autonomic nervous system lead to a violation of humoral regulation. In particular, there are changes in the content of neurotransmitters, such as: gamma-aminobutyric acid, norepinephrine, dopamine, serotonin, neuropeptides, etc. Gamma-aminobutyric acid (GABA) is a major inhibitory

neurotransmitter that controls and regulates the excitability of neurons, especially the central nervous system. There is a direct relationship between the suppression of the GABAergic system and increased anxiety. In panic disorders, there is a decrease in the sensitivity of GABA receptors in the benzodiazepine region. It is known, benzodiazepines in interaction with GABA receptors increase its affinity for these receptors, which increases the flow of chlorine ions into the cytoplasm of neurons. This, in turn, increases the inhibitory postsynaptic potential. The excitability of neurons is reduced [5].

A number of current studies have focused on the correlation between neurophysiological and biochemical parameters in anxiety disorders. Thus, in patients with depression with increasing serotonin levels, there was the predominance of the pattern of synchronization on the EEG with an increase in the representation of theta rhythm and a decrease in the index of beta activity in the anterior right hemisphere. In patients with anxiety disorders, on the contrary, with increasing serotonin levels a pattern of desynchronization was recorded in the anterior leads and in the right posterior temporal areas [20].

Breathing is the most important function of the body, in violation of which emotions of fear and panic appear. Usually, panic attacks occur unexpectedly, but a number of scientists have conducted experiments in the laboratory in order to provoke this condition for a scientific understanding of the neurobiology of panic. Research shows a link between the state of the neurons in the respiratory center and the experience of panic. The respiratory center is directly connected to chemosensitive neurons, which receive information about the content of carbon dioxide in the blood. Inhalation of carbon dioxide, lactate infusion, and pulmonary hyperventilation cause changes in blood pH and can cause brain acidosis, which can affect neuronal function by increasing the activity of pH-sensitive receptors. These studies suggest that a better understanding of panic disorder is possible with in-depth knowledge of the regulation of brain pH and pH-sensitive receptors [7, 9]. In patients with panic disorder, fear of respiratory symptoms has been associated with brainstem hyperactivation. Panic attacks also affect the cardiovascular system. According to Katharina Feldker et al. fear of cardiovascular symptoms is associated with insula activation [8].

A detailed understanding of the correlation between the electrical activity of brainstem respiratory neurons and panic disorders has become quite relevant in the last two years, when there was an urgent need to study the incidence of a new virus – coronavirus (COVID-19) and its consequences. Scientists have already claimed that COVID-19 will lead to new diseases and may cause or exacerbate existing mental illnesses. The stress caused by the pandemic causes widespread fear and concern for one's own health and the health of relatives. This has an impact on sleep, nutrition, difficulty concentrating, worsening chronic diseases. People with a weak will tend to increase the use of alcohol, tobacco and other drugs. Mass measures are poorly tolerated: blocking, isolation and quarantine, which can also lead to an increase in mental illness, especially depression, anxiety and suicidal tendencies. Scientists believe that new mental health problems should be expected after the end of the pandemic [1].

There is very little research in the scientific literature on whether a new epidemic could cause disease onset or exacerbate panic attacks. Scientists are mainly focused on the risks of an increase and exacerbation of other mental disorders as a result of the COVID-19 epidemic. There are studies of obsessive-compulsive disorder, post-traumatic stress disorder, and generalized anxiety disorder. However, experts emphasize the high probability of increased risk of occurrence or exacerbation of panic disorders. In patients with pronounced respiratory symptoms there is a reaction of fear to interoceptive sensations.

At the same time, doctors warn that people who have already had panic disorders before this viral disease should be treated very carefully. For patients with comorbid conditions (panic disorder/panic attacks and COVID-19), it is particularly important to be aware of the risk of hypokalemia during treatment. Caution is required when prescribing certain psychotropic drugs, such as the antidepressants citalopram and escitalopram, which are the primary treatment for panic disorder, and hydroxyzine, which is aimed at relieving anxiety. Further study of the impact of the current pandemic on the diagnosis and treatment of panic disorder (separately or concomitantly with COVID-19) is relevant and important [2].

Conclusions.

1. A certain amount of scientific material (not always unambiguous) on the bioelectrical activity of CNS neurons in persons with panic disorders using EEG methods

has been accumulated. The recorded changes occur in the cortex of different parts of the hemispheres and in different structures of the subcortical nuclei, the brainstem. There are differences in the state of the brain in people with typical and atypical panic disorders, as well as increased functional disintegration of interhemispheric asymmetry in people with panic attacks.

2. Panic disorders usually occur unpredictably in the patient, so it is almost impossible to conduct a neurobiological study at the time of a panic attack. Almost all scientific results were obtained in the period between panic attacks. Therefore, the state of brain neurons during the panic attack itself is still unknown.

3. The described changes in the rhythms of neurons in panic attacks may coincide with those in other psychopathologies. To understand the changes in the brain in panic disorders, EEG studies should be supplemented by other methods, in particular, magnetic resonance imaging, biochemical studies of the brain and others.

4. The variability of brain electrical activity is interesting in the context of the covid pandemic and its consequences due to the increase in the state of anxiety and panic disorders.

Prospects for further research in this direction. Further research should focus on understanding the electrical activity of the brain in people with panic disorders in non-pharmacological treatment, in particular, in the use of respiratory practices.

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ПОКАЗНИКИ ЕЛЕКТРОЕНЦЕФАЛОГРАМИ У ОСІБ ІЗ ПАНІЧНИМИ РОЗЛАДАМИ

Бабак С. В.

Резюме. Панічні розлади досить поширені серед населення світу. Симптоми панічних атак виникають непередбачувано та спонтанно. Особи, що підлягають таким нападам у більшості випадків неспроможні швидко та адекватно включитись в поточний момент життя. Це викликає страх, підвищену тривожність, і, навіть, асоціальність.

Вчені зайняті пошуками вирішення проблем панічних атак через розуміння нейробиологічних змін у мозку. Зокрема, використовується електроенцефалографічний (ЕЕГ) метод дослідження. Складність вивчення біоелектричної активності мозку полягає у тому, що практично неможливим є проведення такого дослідження під час панічної атаки. Всі обстеження осіб із панічними розладами проводились в періодах між нападами. Є лише окремі дані стосовно дослідження ЕЕГ в лабораторії, де певними подразниками викликали емоції страху, тривоги, і на цьому тлі, досліджували електричний стан мозку.

Вченими виявлено відмінності у електричній активності мозку у пацієнтів із типовими та атипичними панічними атаками: при типових панічних атаках – зареєстровано збільшення спектральної потужності бета-1-ритму в лобних, скроневих та тім'яних частках правої півкулі, а при атипичних – потужності тета-ритму у скроневих областях цієї півкулі.

Також відмічено посилення функціональної дезінтеграції міжпівкульної асиметрії, яке зумовлено підвищенням активації гіпоталамо-септо-гіпокампулярної системи. В правій півкулі, переважно у скроневих і лобових відведеннях, зареєстровано достовірне зменшення загальної абсолютної щільності потужності альфа-ритму, а також збільшення загальної абсолютної щільності потужності ритмів в бета-1-діапазоні і тета-діапазоні.

При панічних атаках людина залишається в стані підвищеного збудження з причини домінування симпатичної нервової системи, активність якої поступово знижується. В такому стані збудження охоплює мигдалину, стовбур мозку. Можливо, і кора острівця може мати безпосереднє відношення до виникнення панічних розладів.

Для розуміння особливостей змін у функціонуванні мозку при панічних розладах показники електроенцефалографічних досліджень мають доповнюватись результатами інших методів досліджень. Потрібно активно залучати біохімічні дослідження, дані магніто-резонансної томографії. У певних осіб панічні розлади виникають на тлі інших психопатій. Іноді дані енцефалографії подібні до стану, наприклад, епілепсії.

Використання однофотонної емісійної комп'ютерної томографії показало зміну метаболізму та загальне зниження двобічного мозкового кровотоку у певних структурах мозку у пацієнтів із панічними розладами.

Біохімічні дослідження, при наявності панічних розладів, спрямовані в основному на глутаматергічні та гамма-аміномасляноергічні системи, які мають функції збудження та гальмування.

Наукові дослідження показують зв'язок між станом нейронів центру дихання та переживанням паніки.

Аналіз наукової літератури стосовно біоелектричної активності мозку у осіб із панічними розладами показав неоднозначність, що потребує подальших досліджень.

Ще однією дуже вагомою причиною для активації досліджень панічних розладів за останні два роки стала пандемія коронавірусу.

Ключові слова: панічні розлади, електроенцефалограма.

ELECTROENCEPHALOGRAPHIC INDICATORS IN PEOPLE WITH PANIC DISORDERS

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Abstract. Panic disorders are quite common among the world's population. Symptoms of panic attacks occur unpredictably and spontaneously. Persons who are experiencing such attacks are in most cases unable to engage quickly and adequately in the current moment of life. This causes fear, increased anxiety, and even antisocial inclinations.

Scientists are busy looking for solutions to panic attacks through an understanding of neurobiological changes in the brain. In particular, the electroencephalographic (EEG) method of research is used. The difficulty of studying the bioelectrical activity of the brain is that it is almost impossible to conduct such a study during a panic attack. All examinations of persons with panic disorders were conducted in the periods between attacks. There are only some data on the study of EEG in the laboratory, where certain stimuli caused emotions of fear, anxiety, and against this background, studied the electrical state of the brain.

The researchers found differences in the electrical activity of the brain in patients with typical and atypical panic attacks: in typical panic attacks – an increase in the spectral power of beta-1-rhythm in the frontal, temporal and parietal lobes of the right hemisphere is registered, and in atypical – theta-rhythm power in the temporal areas of this hemisphere is registered.

There is also an increase in the functional disintegration of interhemispheric asymmetry, which is due to increased activation of the hypothalamic-septo-hippocampal system. In the right hemisphere, mainly in the temporal and frontal leads, a significant decrease in the total absolute power density of the alpha rhythm, as well as an increase in the total absolute power density of the rhythms in the beta-1 range and theta range.

During panic attacks, a person remains in a state of heightened arousal due to the dominance of the sympathetic nervous system, the activity of which gradually decreases. In this state, the excitement covers the amygdala, the brain stem. It is possible that the insular cortex may be directly related to the occurrence of panic disorders.

To understand the peculiarities of changes in the functioning of the brain in panic disorders, the indicators of electroencephalographic studies should be supplemented by the results of other research methods. It is necessary to actively involve biochemical studies, magnetic resonance imaging data. In some people, panic disorders occur

against the background of other psychopathy. Sometimes encephalography data are similar to a condition such as epilepsy.

The use of single-photon emission computed tomography has shown changes in metabolism and a general decrease in bilateral cerebral blood flow in certain brain structures in patients with panic disorders.

Biochemical studies, in the presence of panic disorders, focus mainly on glutamatergic and gamma-aminobutyric systems, which have the functions of excitation and inhibition.

Research shows a link between the state of the neurons in the respiratory center and the experience of panic.

Analysis of the scientific literature on the bioelectrical activity of the brain in people with panic disorders has shown ambiguity that requires further research.

Another very important reason for activating research on panic disorders in the last two years was the coronavirus pandemic.

Key words: panic disorders, electroencephalogram.

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ОСОБЛИВОСТІ ЗАСТОСУВАННЯ ПРОТИВІРУСНИХ ЛІКАРСЬКИХ ЗАСОБІВ ДЛЯ ЛІКУВАННЯ І ПРОФІЛАКТИКИ ЗАХВОРЮВАНЬ, ЩО СПРИЧИНЕНІ ВІРУСНОЮ ІНФЕКЦІЄЮ COVID-19

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Звичайно ефективність терапії фармакологічними і лікарськими засобами для терапії інфекцій, що вперше з'явилися нещодавно, вивчається упродовж багатьох років. Однак, для лікування захворювань, що зумовлені такою небезпечною інфекцією як COVID-19, необхідно знайти препарати для ерадикації коронавірусу за набагато коротший період. Метою дослідження був аналіз ефективності терапії різними противірусними препаратами коронавірусної хвороби.

Противірусні препарати рибавірин та ремдесевір мають провідне місце при терапії різних форм коронавірусної хвороби, в тому числі для лікування хворих з тяжкою формою, коли для них є необхідною киснева підтримка. Противірусні лікарські засоби фавіпіравір та його аналоги авіфавір, ареплівір та коронавір, а також ергоферол, доцільно використовувати лише для лікування хворих, інфікованих вірусом SARS-CoV-2, із легким та середнім за тяжкістю перебігом. Препарат, що використовується для терапії СНІДу лопінавір/ритонавір полегшує перебіг навіть тяжкої форми коронавірусної хвороби. Для профілактики і лікування коронавірусної хвороби слід використовувати інтерферони та індуктори інтерферону. Найбільш доцільним є застосування інтерферону

альфа-2b та індуктору інтерферону циклоферону. Для лікування пацієнтів з COVID-інфекцією різного ступеню тяжкості для її профілактики доцільно призначати препарати, що містять реліз-активні атитіла до інтерферону гамма – ергоферон та анаферон. До заповіжних заходів при інфікуванні вірусом SARS-CoV-2 належить використання інтерферонів та індукторів інтерферону, зокрема циклоферону.

Ключові слова: коронавірусна хвороба, противірусні засоби, інтерферони, індуктори інтерферону.

Зв'язок публікації з плановими науково-дослідними роботами. Дана робота є фрагментом НДР “Вивчення ролі умовнопатогенних та патогенних інфекційних агентів з різною чутливістю до антимікробних і противірусних препаратів у патології людини” (№ ДР 0118u4456).

Вступ. Звичайно ефективність терапії фармакологічними і лікарськими засобами для терапії інфекцій, що вперше з'явилися нещодавно, вивчається упродовж багатьох років. Однак для лікування захворювань, що зумовлені інфекцією COVID-19, необхідно знайти препарати для ерадикації коронавірусу за набагато коротший період. Це зумовлено дуже швидким її розповсюдженням та великою смертністю пацієнтів, що хворіють на COVID-полісегментарну