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EVALUATION OF MELATONIN LEVELS AFTER COVID-19 IN YAKUTSK RESIDENTS

The article presents the results of assessing the level of melatonin after Covid-19 in residents of Yakutsk. It was found that after the coronavirus infection, there is a decrease in the level of melatonin. Coronavirus infection affects the production of melatonin, which subsequently leads to disruption of vital rhythms.

Keywords: melatonin, Covid-19, anxiety, depression, insomnia.

Introduction. The COVID-19 pandemic has increased the number of patients suffering from insomnia. Sleep disturbance is an unfavorable prognostic factor in infections [9, 12]. The quality and duration of sleep play a key role in maintaining a person's physical and mental health. In turn, lack of sleep and psychoemotional disorders are risk factors and contribute to the emergence of serious diseases, including depression, stroke, chronic inflammation, cancer, as well as insufficient immune defense and individual predisposition to infectious diseases with an unfavorable outcome [13]. Sleep disturbance is directly related to a decrease in the production of melatonin (MT) in the human body.

Melatonin is a multifunctional hormone with diverse biological effects, such as immunomodulatory, antioxidant, geroprotective, anti-inflammatory, synchronization of circadian and seasonal rhythms [1].

Melatonin is a molecule that reduces overreaction of the innate immune response and excess inflammation, promoting adaptive immune activity. In addition, melatonin is an endogenous molecule produced in small amounts, the synthesis of which decreases with age. Anderson G., Reiter R.[4] and Zhang R. et al. [18] data from their studies confirm the positive use of melatonin preparations in patients with COVID-19.

Zambrelli E. et al. noted that melatonin at doses up to 10 mg is safe in patients in intensive care units, and it should be used for the prevention and treatment of sleep and psychoemotional disorders in COVID-19 [17]. It may also play a role in the treatment of "long-term COVID-19" pa-

tients experiencing similar conditions [11].

Some studies also mention the benefits of melatonin in the treatment of COVID-19. MT can reduce pulmonary fibrosis, which is a serious complication of COVID-19 [18, 15].

The aim of the study was to assess the level of melatonin in the urine of patients who recovered from COVID-19 in Yakutsk.

Material and research methods. The study involved 80 residents of Yakutsk aged 20 to 72 who had recovered from COVID-19. Of these, 40 women, 40 men. The mean age was 51.07 ± 0.97 years. To determine melatonin, a urine test was taken once.

Informed consent for the study was obtained from all study participants (pro-

tol of the local ethical committee of the Yakut Scientific Center for Complex Medical Problems No. 52 dated March 24, 2021). All examined persons had extracts with the data of biochemical, morphological blood analysis and computed tomography. An oral survey was conducted with all the examined, and a questionnaire was filled out on the state of health, sleep, and a test on the HADS anxiety and depression scale was also taken.

The determination of melatonin concentration in urine was carried out using the Melatonin-SulfateUrine ELISA kit (IBL international, Germany), by the method of three-phase enzyme immunoassay on a Uniplan photometer (Russia) at the Laboratory of Immunology and Biochemistry of the YSC KMP. Reference values

Table 1

Concentration of melatonin in urine depending on the statute of limitations of COVID-19 and computed tomography of the lungs

CT degree/term. months	Melatonin. average values	p
1/ 6	46.64± 8.86	<0.010
1/ 9	19.49± 3.17	
1 /6	46.64±8.86	<0.025
3 /6	22.95±4.15	

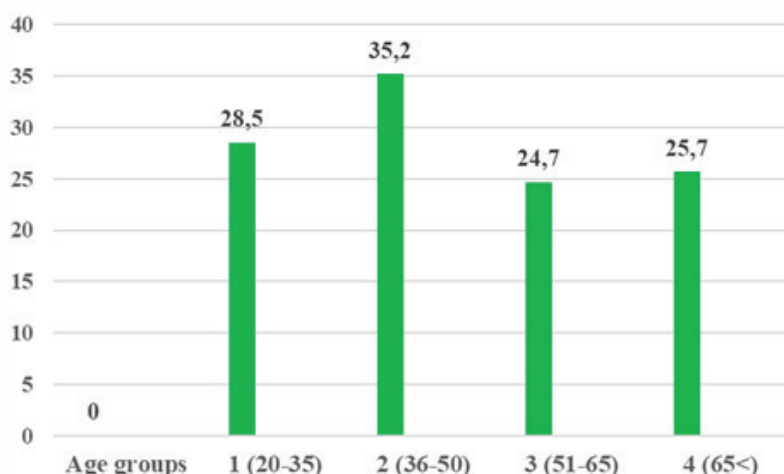


Fig. 1. Melatonin levels depending on age in recovered COVID-19 patients

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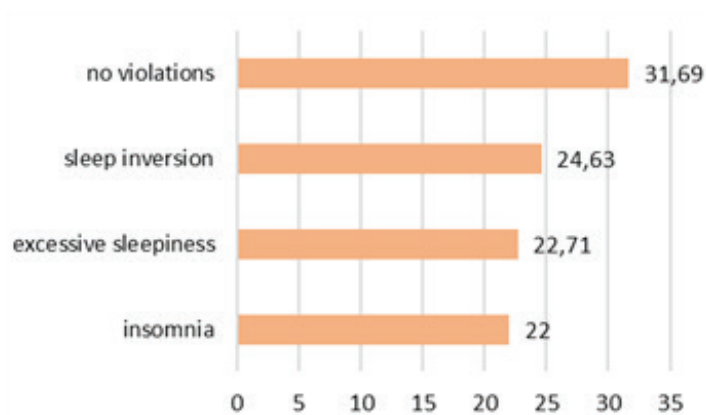


Fig. 2. Level of melatonin depending on the disturbance of vital activity rhythms, (ng/ml)

for melatonin in human urine are in the range of 7.5-58.1 ng/ml.

Statistical processing of our own research results was carried out using the Microsoft Excel application package and the IBM SPSS Statistics 24 statistical program. The initial quantitative variables are presented as a median with an inter-quartile range (25-75%). Statistical significance of differences determined by Student's t-test and ANOVA for independent groups. The critical value of the level of statistical significance of differences (p) was taken equal to 5%.

Results and discussion. In our study, we assessed the effect of the level of lung damage and recovery time on the concentration of melatonin in the urine of people who recovered from coronavirus infection. According to our data, the average value of melatonin in the urine, depending on the timing of computed tomography, shows that people who have recovered from coronavirus infection begin to experience a decrease in melatonin concentration after 9 months. from the beginning of the disease (Table 1). We also observe that the degree of lung damage significantly affects the production of melatonin in Covid-19: the higher the degree of lung damage (CT grade 3) ($p < 0.025$), the less melatonin is produced in the body. The data obtained can probably be explained by the duration of the effect of the virus on the body. There are studies that have shown that coronavirus infection has a long recovery period after recovery [11].

It is known that melatonin levels decrease with age, so older people are more likely to suffer from insufficient melatonin production [7]. According to our data, the level of melatonin in residents of Yakutsk, regardless of age, was within the normal range. The highest concentration of melatonin was in the age group of 36-50 years, the lowest in the

group of 51-65 years (Fig. 1). The trend of decreasing levels of melatonin in the body with age in older people continues.

We also examined the content of melatonin depending on gender. Table 2 shows that there is a tendency for an increase in the concentration of MT in the urine in men - 52.6% and a decrease in women - 42.3%. We can explain this fact by the fact that women are more sensitive at the psycho-emotional level than men.

Table 2		
Melatonin concentration depending on gender		
	Gender	
	Men	Woman
Normal (n/%)	20/52,6	19/46,3
Above normal (n/%)	10/26,3	9/22,0
Below normal (n/%)	8/21,1	13/31,7
χ^2 Pearson = 1,166, $p < 0,558$		

Note. CT - computed tomography, 2 - after 6 months, 3 - after 9 months. transferred COVID-19.

The relationship of rhythm disturbances with anxiety disorders is noted when the onset of an anxiety disorder precedes the onset of sleep disorders. From the data obtained, we found that in residents who had a coronavirus infection and noted in the questionnaire a complaint about a violation of the rhythms of life - insomnia, the concentration of melatonin decreased by 1.4 times, with excessive drowsiness and sleep inversion by 1.2

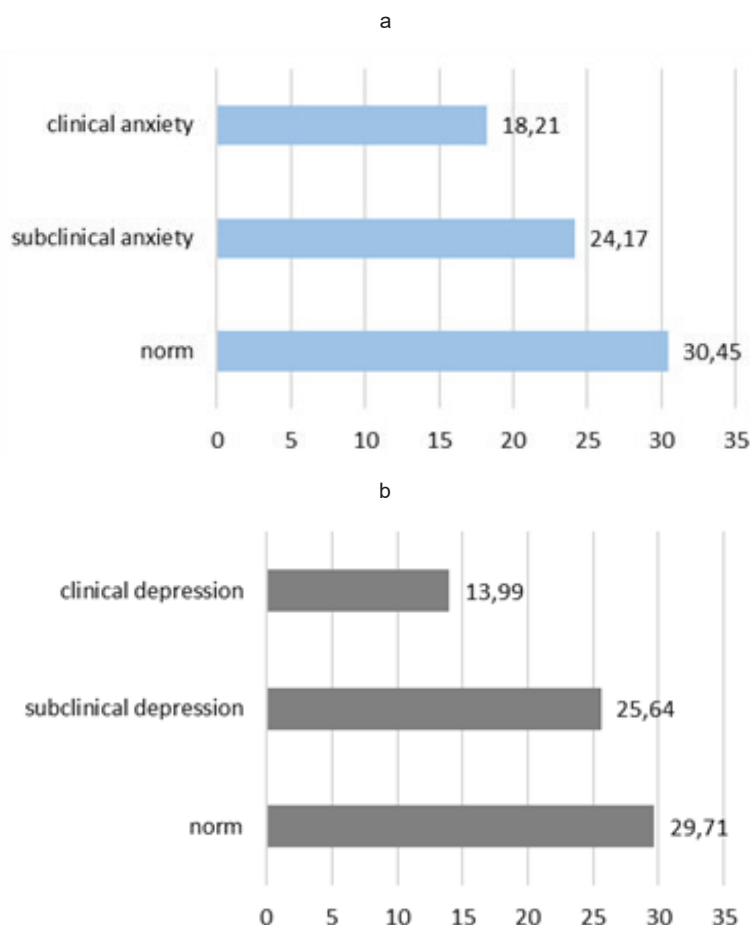


Fig. 3. Melatonin concentration on the HADS scale depending on: a - state of anxiety, b - state of depression, ng/ml

and 1.3 times, respectively, in comparison with the group - without sleep disturbance (Fig. 2). The results obtained showed that when the body is exposed to Covid-19, the level of melatonin decreases, which can lead to some changes in the functioning of the central nervous system (CNS) [11].

The main sleep disorders in people with coronavirus are insomnia (presomnic disorders) and restless legs syndrome. This may be directly related to infection, hypoxia and mental state [5]. According to E. Ibarra-Soronado et al., changes in sleep during illness are a component of the acute phase response that promotes recovery through mechanisms including cytokines and interleukins. The virus can reach the central nervous system through the nasal as well as hematogenous routes. The subsequent secretion of these immunological mediators is accompanied by reactions from the nervous and endocrine systems [6,10]. Also, the cytokine storm, which is an immune response in COVID-19, leads to inflammation and damage to the central nervous system. The SARS-CoV-2 virus mainly affects the prefrontal cortex, basal ganglia, and hypothalamus, i.e., those areas that are involved in sleep regulation [8].

Anxiety disorders are a predisposition to serious consequences in the human body. When interviewing the subjects, it was revealed that during the coronavirus infection, many experienced a sense of anxiety. From the responses to the test on the HADS scale, we obtained the following values: in the normal state, melatonin is 30.45 ng / ml, in patients with subclinical anxiety - 24.17 ng / ml and with clinically expressed anxiety - 18.21 ng / ml. From the data obtained, it can be revealed that there was a tendency for a decrease in the level of melatonin in anxiety disorders of the nervous system during coronavirus infection (Fig. 3).

A decrease in melatonin secretion may be involved in the mechanism of insomnia. Such serious disturbances in the psycho-emotional state of a person can lead to more serious consequences, such as high anxiety and depression. Anxiety spectrum disorders are among the most common consequences of coronavirus on the human psyche. People who are

not prone to excessive worries and worries notice that they have begun to take everything to heart, fear for themselves and their loved ones, as well as a second illness. All this leads to a general increase in the anxiety background among the population. Due to constant fear and anxiety, habitual life, a person's sleep are disturbed, which is already reflected in the physical condition [2].

On the HADS scale, the section associated with depression revealed that the level of melatonin was lower in patients with clinically severe and amounted to - 13.99 ng / ml, in subclinically expressed - 25.64 ng / ml, and was equal to 29.71 ng / ml in the norm. (Fig. 4). A number of studies have noted that decreased melatonin levels in patients have been associated with depressive disorders. Melatonin phasic changes are a major feature of most depressive disorders, and low melatonin levels have been described as a "characteristic" of depression [3, 14].

Conclusion. Melatonin is one of the important hormones for regulating the vital activity of the body. When exposed to coronavirus infection on the body, a significant decrease in the secretion of melatonin occurs. The content of melatonin in residents of the city of Yakutsk did not depend on age and was within the reference values. The concentration of melatonin in relation to sex showed that there is a tendency for men to have more MT in the urine than women. Insufficient synthesis of melatonin during Covid-19 leads to disturbances in the rhythms of human life.

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