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LIPID PEROXIDATION IN THE DEVELOPMENT OF SOME SYMPTOMS OF POST-COVID SYNDROME

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The relationship of lipid peroxidation with sleep disturbance, anxiety and depression in residents of Yakutsk who recovered from COVID-19 was studied. It has been established that oxidative stress in COVID-19 due to an increase in the level of reactive oxygen species (ROS) in the body can lead to hypoxia and psycho-emotional disorders, such as anxiety and depression.

Keywords: COVID-19, malondialdehyde, lipid peroxidation, post-COVID effects, hypoxia, sleep, anxiety, depression, oxidative stress.

Introduction. A novel coronavirus infection that causes severe acute respiratory syndrome COVID-19 has become a global pandemic with high morbidity and mortality [4,5].

The impact of the SARS-CoV-2 virus on the human body occurs primarily

in the lungs, which causes pneumonia. Penetrating into the lower parts of the respiratory tract (small bronchi and alveoli) and begins damage to lung cells, provoking a strong inflammatory reaction, due to which the lungs cannot provide all organs and systems with sufficient oxy-

gen, which leads to hypoxia. Studies by many authors indicate the existence of a directly proportional relationship between the severity of COVID-19 disease and hypoxia [3,8,11].

Hypoxia leads to excessive production and accumulation of ROS, therefore, to the initiation of lipid peroxidation (LPO) and the development of oxidative stress. Reactive oxygen species produced during cellular metabolism play an important role as signal transmitters [9]. The activation of cells that provide antimicrobial immunity, neutrophils and macrophages, and the production of pro-inflammatory cytokines largely depend on ROS [11]. The optimal level of ROS in the body is controlled by the antioxidant defense system (AOD) of cells, which includes enzymatic and non-enzymatic links. With insufficient activity of antioxidant protection, a phenomenon occurs as oxidative stress, where TBA-active products, including malondialdehyde (MDA), are a marker. In addition, hypoxia causes clinical signs, such as a change in the properties of hemoglobin, a decrease in the bioavailability of nitric oxide (NO), vasoconstriction, an increase in the synthesis of leukotrienes and prostaglandins, cytokines, etc. Prolonged hypoxic state during illness, in our opinion, may be the cause of the development of post-COVID symptoms, such as anxiety and depressive disorders, insomnia, etc.

The aim of the study is to evaluate the association of lipid peroxidation with sleep disorders, anxiety and depression in people who have recovered from COVID-19.

Material and methods. The study involved 164 residents of Yakutsk aged 20 to 72 who recovered from COVID-19. Of these, 96 women (58.18%), men 68 (41.46%). The mean age was 51.07 ± 0.97 years.

Informed consent for the study was obtained from all participants in the study (according to the protocol of the Ethical Committee of the YSC CMP No. 52 dated March 24, 2021). All the persons examined by us had extracts in which there were data from biochemical and morphological blood tests, computed tomography.

An oral survey was conducted with all the subjects, on the basis of which a questionnaire was filled out on the state of health, sleep, and a test was also performed on the HADS anxiety and depression scale. The material of the study was venous blood, which was taken on an empty stomach from the cubital vein. The initiation of free radical oxidation was assessed in blood plasma by the accumu-

lation of malondialdehyde concentration [1]. The measurements were performed using an Agilent Cary 100 UV-Vis spectrophotometer. Complete blood count was performed on a BC-3600 Mindray automatic hematology analyzer.

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 Kolmogorov-Smirnov criterion was used to test the normality of the distribution. The original quantitative variables are presented as a median with an interquartile range (25% - 75%). To compare two independent samples, the Mann-Whitney U-test was used. When comparing groups, differences were considered statistically significant at $p < 0.05$. When analyzing the relationship of features, the Spearman correlation method was used.

Results and discussion. All participants in the study had certain complaints about the state of health after the illness - COVID-19 [2]. Our data indicate that the parameters of the general and biochemical blood tests significantly change during the disease and after 8 months. In Table 1, we compared some indicators of the complete blood count during illness and 8 months after illness with control (persons who did not have COVID-19).

A comparative analysis (Table 1) of changes in the parameters of the general blood test at the time of the coronavirus disease and after 8 months, compared with the control group, indicates that in-

flammatory processes and lack of oxygen are observed in the body of patients during the disease. During the active struggle of the body with coronavirus, the content of leukocytes increases - 1.1 times, lymphocytes - 1.1 times, and the erythrocyte sedimentation rate (ESR) - 1.6 times in the blood. The level of erythrocytes decreases by 2.3 times from the norm ($4.3-6.2 \cdot 10^{12}/l$), the hemoglobin content also decreases by 1 times compared with the control group. 8 months after discharge from the hospital, the main indicators of the general blood test are normalized.

The results of our study show that in the body of residents of the city of Yakutsk, with a coronavirus infection, hypoxia develops. Intensive inflammatory processes were also going on in the body, as evidenced by an increase in the number of lymphocytes, leukocytes and sedimentation rate of erythrocytes.

It is known from the literature that COVID-19 causes diffuse damage to the endothelium of the alveolar capillaries, leading to a pathological process - hypoxia, which, in fact, is the cause of multiple organ dysfunction and death in patients with the SARS-CoV-2 virus [6]. The pathogenesis of COVID-19 has the following chain of flow in the body: 1-introduction of the pathogen into the alveolar cells of type II of the lungs, 2-development of diffuse alveolar damage, 3-reduction in the area of "breathing" alveoli, 4-diffuse lung compaction, 5-hypoperfusion in the capillaries of the lungs and the formation of

Table 1

Some indicators of the general blood test of those who recovered from COVID-19 (during the illness and after 8 months from the moment of discharge from the hospital) and the control group (persons who did not have COVID-19)

Blood cells	Control group	During COVID-19	After 8 month
	Me (Q1-Q3)		
Red blood cells	4.640 (4.270-4.990)	2.000 (2.000-4.430)	4.650 (4.360-4.975)
p		0.012	0.684
Hemoglobin	135.000 (120.000-151.000)	131.000 (118.000-142.000)	136.000 (128.000-146.000)
p		0.098	0.575
Leukocytes	5.600 (4.800-6.600)	5.810 (4.810-8.190)	5.600 (4.700-6.900)
p		0.160	0.758
Lymphocytes	33.400 (27.500-38.650)	33.650 (28.480-46.580)	30.000 (26.250-36.000)
p		0.464	0.001
Sedimentation rate of erythrocytes	10.000 (6.000-16.000)	18.500 (9.000-29.000)	16.000 (9.000-23.000)
p		0.000	0.000

Table 2

MDA scores on the HADS anxiety and depression scale in patients with coronavirus infection

Correlation coefficient	Levels of anxiety and depression	MDA indicators		
		1	2	3
$r=0.177$ $p=0.040$	Median anxiety	0.114 (0.068-0.256)	0.153 (0.100-0.229)	0.321 (0.153-0.500)
	p1-2	0.400		
	p1-3	0.017		
	p2-3	0.033		
$r=-0.021$ $p=0.805$	Median depression	0.140 (0.080-0.290)	0.137 (0.091-0.243)	0.168 (0.066-0.483)
	p1-2	0.881		
	p1-3	0.919		
	p2-3	0.665		

Note: 1 - normal, 2 - subclinically expressed anxiety and depression, 3 - clinically expressed anxiety and depression.

erythrocyte sludge, 6-intrabronchial and intraalveolar hemorrhages, 7-reduction of oxygen diffusion into the bloodstream, 8-hypoxemia and hypoxia of endothelial cells of the branches of the pulmonary arteries and veins, 9-hyperfibrinogenemia and thrombus formation, 10-inflammation [3]. From this chain of events, it can be seen that this pathogenetic chain has a hypoxic orientation, and most damage in the body is a consequence of hypoxia, and inflammation is naturally accompanied by oxygen starvation [8].

It is known that prolonged hypoxia affects the human central nervous system, and uncontrolled initiation of free radical processes can aggravate the effect of hypoxia, in this regard, we considered the concentration of MDA in the blood plasma (one of the end products of lipid peroxidation), in relation to the scale of anxiety and depression (HADS) developed by AS Zigmond R P. Snalth in 1983. The test is easy to use and process, which allows it to be used in general medical practice for the primary detection of anxiety and depression in patients. The data analyzed using this test is presented in table 2.

According to this scale, severe anxiety was observed in 6%, subclinically expressed anxiety - in 12%, and the norm was in 65% of people with post-COVID syndrome. The correlation coefficient showed a significant relationship between anxiety and the level of MDA in blood plasma. Significant differences in the concentration of MDA were found by us when comparing clinically expressed anxiety with the norm and subclinical anxiety.

Clinically expressed depression was noted in 4%, subclinically expressed depression in 15% and the norm was detected in 64% of the residents. Assessment

of depression on the HADS scale showed no dependence on the concentration of MDA in blood plasma (table 2).

When comparing the level of MDA in those who recovered from COVID-19 without sleep disturbance (0.158 (0.087-0.297)) with those who complained of disturbances in the rhythms of life (insomnia, sleep inversion, excessive sleepiness) (0.186 (0.115-0.296)) the level of MDA was higher by 15%.

Our data confirm that oxidative stress in COVID-19 due to increased levels of ROS in the body can lead to psycho-emotional disorders. This is evidenced by works that say that an increased level of oxidative stress exacerbates the severity of COVID-19 and can later cause neurological disorders, as one of the options for post-COVID consequences [7,10,12]. There is an opinion that patients with COVID-19 may experience delirium, depression, anxiety and insomnia [13]. Coronaviruses can cause psychopathological consequences through direct viral infection of the CNS or through an immune response [14].

We also considered such a concept as the odds ratio of those who recovered from COVID-19, who had sleep disorders, anxiety and depression, with indicators of erythrocyte sedimentation rate and hemoglobin in the blood. The data obtained are presented in table 3.

An analysis of the odds ratio showed that people who recovered from coronavirus infection COVID-19 with a high level of SRE in the blood have significantly more sleep disorders, and with a decrease in hemoglobin, the frequency of sleep disorders increases ($p = 0.030$). Changes in SRE and Hb did not reach the level of statistical significance in anxiety and depression.

Table 3

Of the odds ratio of the incidence of sleep disturbance, anxiety and depression with 95% confidence intervals in people who have had COVID-19 with SRE and Hb

Sedimentation rate of erythrocytes (SRE)		
Sleep	OR	2.000 (0.912-6.023)
	χ^2	3
	P	0.072
	F	0.054
Anxiety	OR	0.873 (0.397-1.920)
	χ^2	0.113
	P	0.736
	F	0.444
Depression	OR	1.710 (0.753-3.882)
	χ^2	1.668
	P	0.196
	F	0.137
Hemoglobin (Hb)		
Sleep	OR	0.307 (0.096-0.982)
	χ^2	4.253
	P	0.039
	F	0.030
Anxiety	OR	1.341 (0.502-3.583)
	χ^2	0.344
	P	0.557
	F	0.364
Depression	OR	0.604 (0.216-1.690)
	χ^2	0.930
	P	0.334
	F	0.239

Conclusion. The findings highlight the importance of oxidative stress in COVID-19, especially the role of lipid peroxidation. According to the data we received, residents of Yakutsk who recovered from coronavirus infection were found to have sleep disturbances and an increased sense of anxiety, which can later lead to more serious disorders. Thus, we recommend monitoring the state of health after suffering COVID-19 until the complete disappearance of post-COVID symptoms.

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S.A. Evseeva, V.V. Bogdashin, T.E. Burtseva, T.M. Klimova, A.M. Makarova, V.B. Egorova, V.P. Shadrin, G.A. Krichko FEATURES OF THE CLINICAL COURSE OF COVID-19 CORONAVIRUS INFECTION IN CHILDREN OF THE REPUBLIC OF SAKHA (YAKUTIA)

The article presents the results of retrospective analysis of the clinical histories of children hospitalized from March 23, 2020 to December 27, 2020 in the Republic of Sakha (Yakutia) "Children's Infectious Clinical Hospital" with the diagnosis of "Coronavirus infection caused by COVID-19" (ICD-10 code U07.1, U07.2). The features of the clinical course of a new coronavirus infection in 358 children were described. It was shown that during the first and second waves of COVID-19 in the Republic of Sakha (Yakutia) 56% of hospitalized children had respiratory tract infections. 36% were cases of pneumonia without respiratory failure. In 2 cases, a multisystem inflammatory syndrome with symptoms of incomplete Kawasaki syndrome was observed. In the remaining cases coronavirus infection caused by COVID-19 occurred against a background of intestinal infections of different etiology and concomitant diseases. Accumulation of epidemiological and clinical data will make it possible to find ways to prevent and treat the new infection, taking into account regional and population characteristics.

Keywords: coronavirus infection (COVID-19), pneumonia, children, North, Arctic, Yakutia.

Introduction. According to many authors, the clinical course of COVID-19 in children has its own peculiarities. The disease is often asymptomatic or has a subtle clinical picture [3,4,8]. The most common clinical manifestations are cough, febrile fever, and catarrhal manifestations [1]. According to the results of large-scale clinical and epidemiological studies, the main clinical manifestations of COVID-19 in children are upper airway lesions, pneumonia without or with respiratory failure, acute respiratory distress syndrome, sepsis, septic shock [6,7,8,9]. One of the most severe manifestations of

COVID-19 in children is considered to be the occurrence of multisystem inflammatory syndrome [5].

The lack of etiotropic treatment and prophylaxis for COVID-19 in children is of concern. Only symptomatic therapy and instrumental means for managing patients with severe manifestations of the disease are available. There is enough information about the peculiarities of the pathogenesis and clinical course of COVID-19 in children. However, there are few studies in the literature devoted to the peculiarities of the course of coronavirus infection in harsh conditions of