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INDICATORS OF ACTIVITY OF THE SYMPATO-ADRENAL SYSTEM IN PATIENTS WITH POST-COVID PNEUMONIA

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Abstract: Patients with long-term persistent symptoms after COVID-19 infection remain to this day the center of ongoing discussions regarding the choice of further treatment tactics. One of the most common manifestations of post-coronavirus syndrome is organizing pneumonia (OP). Determining additional biological markers of the severity of lung damage in AP has diagnostic value for timely correction of therapy in order to improve the prognosis of the disease. At the present stage, biological markers of severity are widely used in clinical practice, such as C-reactive protein, ferritin, D-dimer, lactate dehydrogenase, creatine kinase, procalcitonin, interleukin-6, NTproBNP/BNP (N-terminalpro B-typenatriureticpeptide, B-typenatriureticpeptide /B-typenatriureticpeptide) and troponin. The article will present the results of our own studies of post-Covid patients with AP to determine significant markers for diagnosing the severity of the condition.

Key words: coronavirus infection, COVID-19, post-Covid syndrome, organizing pneumonia, biological markers of severity.

In March 2019, the World Health Organization officially declared the emerging novel coronavirus disease 2019 (COVID-19) a pandemic (coronavirus disease 2019, COVID-19) caused by the SARS-CoV-2 (severe acute respiratory syndrome related coronavirus 2) virus, an RNA virus belonging to the Betacoronavirus genus[1]. Subsequently, in 2021, the World Health Organization defined the concept of coronary pneumonia, a condition that occurs in individuals with a history of confirmed or probable infection with the SARSCoV-2 virus within 3 months after the onset of the disease, which persists for 2 weeks or more. Characteristic symptoms of post-COVID pneumonia include weakness, shortness of breath, and cognitive impairment that affects daily activities. These complaints may either persist after the disease or occur after recovery. [2]. One of the pulmonary manifestations of post-COVID syndrome may be the development of post-COVID pneumonia (PP) or organizing pneumonia (OP) - a variant of interstitial pneumonia [3]. The development of which is described after SARS (Severe Acute Respiratory Syndrome) and MERS (Middle East Respiratory Syndrome), caused by coronaviruses related to SARS-CoV-2 [4].

Post-COVID pneumonia is most often characterized by a subacute onset; typical symptoms of the disease are fever, chest pain, unproductive cough, shortness of breath at rest and during physical exertion. Signs of respiratory failure develop as the patient's condition worsens, requiring further respiratory support.

Impaired activity of the SAS is important in the pathogenesis of autoimmune processes. As is known, the state of tone and reactivity of the SAS can be assessed by studying the excretion of catecholamines (CA), products of biogenic amine metabolism and enzymes involved in their metabolism [5]. A more informative and adequate approach to the study of the SAS for clinical trials is a systematic approach that includes simultaneous determination of the excretion of the precursor of CA synthesis - dioxyphylamine (DOPA) and its

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spectrum: dopamine (DA), norepinephrine (NA) and adrenaline (A). Neurotransmitters of the autonomic nervous system have a significant effect on immune processes. Receptors to catecholamines have been found on lymphocytes [Bourne H. et al., 1974], through which they affect the processes of proliferation and transformation of lymphocytes, rosette formation, antibody synthesis, cytotoxicity and intercellular cAMP levels [6]. It has been established that neuroendocrine structures not only influence the immune system, but also receive information about the implementation of the immune response via feedback. The state of the SAS has been studied in various diseases of the cardiovascular system (Khuzhamberdiev M.A., 1985-1999, Boymirzaev M.I., 2000, Uzbekova N.R. 2017) [7]. Thus, in the works of N.A. Gratsiansky et al. (2000) it was shown that as a result of increased lipolysis, an excess of lipoproteins (LP) is created and sympathetic-adrenal reactions in patients predominate for a long time. According to Shitov V.N. et al. (2005), there is a significant increase in the excretion of adrenaline (A) in the urine with a reduced or unchanged quantitative content of norepinephrine (NA).

The aim of this study was to study the state of the sympathetic-adrenal system in post-COVID pneumonia.

Materials and methods of the study. The study material was patients with pneumonia of various etiologies. Groups of pneumonia of COVID etiology and pneumonia of bacterial etiology were identified. The 1st group consisted of 20 patients with pneumonia of bacterial etiology, the average age of which was 35.7 ± 2.5 years, the 2nd group consisted of 20 patients with AP COVID etiology, the average age of which was 47.1 ± 5.4 years, females prevailed and made up 68% of all those examined.

For a comprehensive assessment of the state of the sympathetic-adrenal system, the level of catecholamines CA in daily urine was determined using the trioxyindole fluorometric method modified by E.Sh. Matlina, Z.M. Kiselevva, I.E. Sofieva (1965), the level of monoamine oxidase in the blood serum according to the method of Balakleyevsky A.I. 1976.

The obtained results of clinical studies were processed using Student's tables. The critical level of reliability of the null statistical hypothesis was taken to be 0.05.

Results and discussion of the study. It was found that CA in urine is one of the adequate methods for assessing the tone and reactivity of the SAS. Studying the daily excretion of CA in urine in those examined by us, it was found that patients with pneumonia had a significant increase in the excretion of free, conjugated, total A and NA in urine. Observations showed that patients with post-COVID pneumonia have more pronounced disorders in the functional activity of the SAS.

In patients with post-COVID pneumonia, a statistically significant increase in A excretion by 59.7% ($P < 0.001$) was observed, which is 2.5 times higher than the values of the control group ($P < 0.001$). In patients with bacterial pneumonia, a significant increase in daily A excretion by 54.3% was also observed, which is 2.2 times higher than the values of the control group ($P < 0.001$) and 12.6% lower than the values of patients with post-COVID pneumonia. (Table 1).

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The daily excretion of norepinephrine (NA) was also significantly increased and was the highest in relation to A, DA and DOPA. Thus, the NA content in patients with post-COVID pneumonia was 46.2±0.8 μg/day, which is 66.6%, or 2.99 times higher than the values of the control group ($P < 0.001$). In patients with bacterial pneumonia, a significant increase in the daily excretion of NA was also noted by 64.3%, which is 2.3 times higher than the values of the control group ($P < 0.001$) and 6.3% (1.1 times) less than the values of patients with post-COVID pneumonia. ($P < 0.001$).

The excretion of dopamine (DA) in the examined patients did not change significantly. Thus, the daily excretion of DA in patients with post-COVID pneumonia was slightly increased by 2.2%, lower than the values of the control group ($P < 0.05$). In patients with pneumonia of bacterial etiology, the daily excretion of DA was 0.64% higher than the values of the control group ($P < 0.05$) and 2.8% lower relative to the values of patients with post-COVID pneumonia (Table 1).

The DOPA level was moderately elevated relative to the control group. Thus, in patients with post-COVID pneumonia, it was 47.1±1.9 μg/day, which is 11.1% higher than the control group and 7.9% higher than the patients with bacterial pneumonia (Table 1).

Table 1. Indicators of daily excretion of catecholamines (CA) in patients with pneumonia of various etiologies (mcg/day).

Indicators \ Groups		Healthy (n =15)	Patients with post-COVID pneumonia (n=20)	Patients with pneumonia of bacterial etiology (n=20)	P_{1-2}	P_{1-3}	P_{2-3}
Adrenalin	своб	4,29±0,33	10,9±0,4	9,1±0,21	p<0,001	p<0,001	p<0,001
	конъюг	3,9±0,35	9,7±0,33	8,9±0,21	p<0,001	p<0,001	p<0,001
	сумм	8,23±0,326	20,6±0,5	18,0±0,4	p<0,001	p<0,001	p<0,001
Norepinephrine	своб	8,1±0,31	24,1±0,71	22,1±0,59	p<0,001	p<0,001	p<0,01
	конъюг	7,15±0,36	23,1±0,79	21,2±0,6	p<0,001	p<0,001	p<0,05
	сумм	15,45±0,5	46,2±0, 8	43,3±0,71	p<0,001	p<0,001	p<0,05
Dopamine	своб	176,0±9,07	180,6±8,1	178,2±8,1	p<0,001	p<,001	p<0,005
	конъюг	187,0±7,3	191,1±7,4	183,2±8, 1	p<0,001	p<0,001	p<0,05

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	сумм	363,7±13,8	371,7±10,8	361,4 ±9,9	p<0,001	p<0,001	p<0,05
DOPA		41,83±2,17	47,1±1,9	45,4±1,81	p<0,01	p<0,001	p<0,01

Studies of the activity of MAO on the first day of stay in the hospital revealed a moderate decrease in its activity in patients with pneumonia post -shocks and in patients with pneumonia of bacterial etiology. In healthy ones, this indicator was 0.07 ± 0.001 units/EXT. So in patients with post -shutches with pneumonia, its level was 0.03 ± 0.002 units/EXTA, in patients with pneumonia of bacterial etiology 0.04 ± 0.001 d/EXT (Table 2.).

Table 2. The activity of monoaminexidase (MAO) in healthy and patients with pneumonia (unit/ext.)

№	**Group**	**MAO** (unit/ext.)
I	**Healthy (n=15)**	0,07±0,001
II	**Patients with post-COVID pneumonia (n=20)**	0,03±0,002
III	**Patients with pneumonia of bacterial etiology (n=20)**	0,04±0,001
	P_{1-2}	P<0,001
	P_{1-3}	P<0,001
	P_{2-3}	P<0,001

Conclusion.

The obtained data indicate that patients with post-COVID pneumonia had high activity of the sympathetic-adrenal system, which plays an important role in the pathogenesis of disease progression. This necessitates the development of special tactics of pathogenetic drug treatment.

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