DYNAMICS OF MAIN MARKERS OF PROTEIN METABOLISM AND MICROELEMENTS IN PATIENTS WITH NEW CORONAVIRUS INFECTION

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ДИНАМИКА ОСНОВНЫХ МАРКЕРОВ БЕЛКОВОГО ОБМЕНА И МИКРОЭЛЕМЕНТОВ У ПАЦИЕНТОВ С НОВОЙ КОРОНАВИРУСНОЙ ИНФЕКЦИЕЙ

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Objective. To study the dynamics of the main markers of protein metabolism and microelements in patients with a new coronavirus infection.

Materials and methods. A prospective clinical and laboratory study of the dynamics of the main markers of protein metabolism and microelements was carried out in 62 patients with a new coronavirus infection complicated by the development of pneumonia with a moderate course on the basis of Perm regional clinical hospital of infectious diseases in 2021–2022. On the 1st and 14th days of hospitalization all patients underwent general clinical and biochemical studies. The concentrations of total protein, albumin, transferrin, Fe, Zn and Cu was also determined. Statistic processing of the results was carried out using Microsoft Excel 2000 and "Statistica 10".

Results. A decrease in visceral pool proteins was revealed. It indicated their active consumption and formation of hypermetabolism – hypercatabolism syndrome in a moderate course of the infection. A progressive deficiency of Fe and Zn, correlating with life-threatening complications and deaths was revealed.

Conclusions. The course of a new coronavirus infection contributes to the development of metabolic disorders, and the identified deficiency of macro- and microelements is a predictor of a severe course of the infection.

Keywords. New coronavirus infection, markers of protein metabolism, microelements.

Цель. Исследование динамики основных маркеров белкового обмена и микроэлементов у пациентов при новой коронавирусной инфекции.

Материалы и методы. На базе Краевой клинической инфекционной больницы г. Перми в 2021–2022 гг. проведено проспективное клинико-лабораторное исследование динамики основных маркеров белкового обмена и микроэлементов у 62 пациентов при новой коронавирусной инфекции, осложненной развитием пневмоний со среднетяжелым течением. На 1-й и 14-й дни госпитализации у всех пациентов выполнялись общие клинико-биохимические исследования, а также определение концентрации общего белка, альбумина, трансферрина, Fe, Zn и Cu. Статистическую обработку результатов проводили с использованием Microsoft Excel 2000 и Statistica 10.

Результаты. Зафиксировано снижение белков висцерального пула, указывающее на их активное потребление и формирование синдрома гиперметаболизма – гиперкатаболизма при среднетяжелом течении инфекции. Выявлен прогрессирующий дефицит Fe и Zn, коррелирующий с наличием жизнеугрожающих осложнений и летальными исходами.

Выводы. Таким образом, течение новой коронавирусной инфекции способствует развитию нарушений обмена веществ, а выявленный дефицит макро- и микроэлементов является предиктором тяжелого течения инфекции.

Ключевые слова. Новая коронавирусная инфекция, маркеры белкового обмена, микроэлементы.

INTRODUCTION

Since the beginning of the Autumn season of this year, the incidence of new coronavirus infection (NCVI, COVID-19) has increased in Russia, which has been associated with the continuation of the pandemic that has affected more than 110 countries worldwide[1]. According to official statistics, in Autumn of 2023, more than 600 million individuals suffered this pathology, and lethal outcomes have been reported in 6 million patients. In the Perm region, a seasonal increase in the incidence of NCVI[2] has been recorded. According to the literature, various infectious lesions, changes in the metabolism of macro and microelements, and malnutrition contrib-

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[1] Federal Service for Supervision of Consumer Rights Protection and Human Welfare, available at: https://www.rospotrebnadzor.ru/activities/recommendations.

[2] Federal Service for Supervision of Consumer Rights Protection and Human Welfare in the Perm Territory, available at: https://59.ru/text/health/2023/07/28/72544472.

ute to the formation of multiple-organ failure, leading to the most severe form of systemic inflammatory reaction[3] [1–3]. Additionally, several scientific studies noted the significant role of specific pathogens (viruses, bacteria, protozoa) in changes in the concentrations of microelements and vitamins in the dynamics of the disease courses, which contributes to disruption of the immune system and leads to irreversible outcomes [4–6]. Currently, the issues of the COVID-19 pathogenesis and the dynamics of changes in the main markers of protein metabolism and microelements remain insufficiently transparent. Moreover, there are assumptions that studying the concentration of basic proteins and microelements is beneficial in performing qualitative adjustments to changes in metabolic processes, and timely replenishment of energy deficiency will improve the results of therapy of the respiratory system in case of COVID-19[4] [7].

The study aimed to analyze the dynamics of the main markers of protein metabolism and trace elements in patients with a NCVI.

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[3] Metabolic monitoring and nutritional support during long-term mechanical ventilation, Clinical guidelines. approved by the Presidium of the FAR on September 8, 2018. available at: http://far.org.ru/recomendationdownload.

[4] Rocco Barazzoni, Stephan CBischoff, Zeljko Krznaric, Matthias Pirlich, and Pierre Singer, Practical Guidance on Nutrition for Persons with SARS-CoV-2 Infection and Other Statements from Experts of the European Association of Clinical Nutrition and Metabolism; approved by the ESPEN Council, available at: https://cardio-web.ru/files/covid19/en/guide_to_nutrition_for_patients_COVID_19.pdf

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MATERIALS AND METHODS

A prospective clinical and laboratory examination of 492 patients with NCVI, complicated by the development of moderately severe pneumonia, was conducted at a regional clinical infectious diseases hospital in Perm in 2021–2022. The examined group included patients aged 20–75 years with viral pneumonia confirmed by X-ray or CT examination, with laboratory verification of the RNA of the SARS-CoV-2 virus by the molecular biological method (PCR) using the nucleic acid amplification test, and meeting the criteria for moderate NCVI according to the current versions of methodological recommendations of the Russian Ministry of Health. The study excluded patients aged < 20 years, persons hospitalized with decompensation of concomitant chronic diseases, those who received the vaccine, and pregnant women. Subsequently, using a mechanical selection method, a group of 62 people was formed, for whom, in addition to the recommended examination methods[5], the concentrations of total protein, albumin, transferrin, and Fe, Zn, and Cu were determined on hospitalization days 1 and 14.

Statistical processing of the results was performed using Microsoft Excel 2000 and Statistica 10. The values of indicators for qualitative characteristics were presented as $\% \pm m$ and those for quantitative characteristics as $Me\ (Q_1;\ Q_3)$. Significant differences

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[5] Ministry of Health of the Russian Federation. Temporary guidelines. Prevention, diagnosis and treatment of new coronavirus infection. Version 17. (12/14/2022). 259.

were assessed using the Mann–Whitney and Chi-square tests; the differences were considered significant at $p < 0.05$. The relationship between the quantities was studied using the pair correlation coefficient r.

RESULTS AND DISCUSSION

Patients aged 20–73 years (average: 58.6 years [54.7; 61.4]) were examined; there were 63.0 % ± 6.1 % men (39 individuals) and 37.0 % ± 6.1 % women (23 individuals). Hospitalization was performed on days 1–3 of the disease in 19 patients (30.6 % ± 5.9 %), days 4–5 in 35 patients (56.4 % ± 6.3 %), and later than day 6 in 8 patients (13.0 % ± 4.3 %). There were on average 22 (19.5; 24.5) bed days. At the time of hospitalization, 45 patients (72.5 % ± 5.7 %) had concomitant pathology, and 16 patients (25.8 % ± 5.6 %) had combined lesions of various systems. Most chronic lesions were registered in the cardiovascular system (hypertension, coronary heart disease, angina pectoris, varicose veins, $p < 0.05$), as well as chronic pathology of the endocrine, respiratory, urinary, and digestive systems (Fig. 1). The C-reactive protein level expectedly increased from 55.1 (15.3; 85.6) mg/l at the time of hospitalization to 68.9 (52.3; 126.1) mg/l by hospitalization day 14. As a result, the relationship between high concentrations of this protein and disease severity was confirmed ($r = 0.641; p < 0.001$), which was characterized by the volume of pulmonary damage and prevalence of inflammatory infiltration. The number of leukocytes, which initially had low levels in week 2 of the disease, increased from $3.5 \bullet 10^9/l$ (3.1; 4.3) to $5.0 \bullet 10^9/l$ (3.9; 6.4). When assessing body mass index, normal indicators were recorded in 27 patients (43.5 % ± 6.3 %), increased nutrition in 22 cases (35.4 ± 6.1 %), obesity at degrees 1 and 2 in 9 cases (14.6 % ± 4.5 %), and malnutrition in 4 patients (6.5 % ± 3.1 %). Thus, the identified laboratory data met the criteria for moderate severity of COVID-19 at the time of hospitalization. Considering the opinion of Russian authors that risk factors for an unfavorable outcome of NCVI include age over 35 years, a history of chronic diseases, lack of specific prevention, and correction of macronutrient metabolic disorders that does not meet the body's needs [8–10], the next stage of our study was investigating the main indicators of protein metabolism.

In the examined patients, the concentration of total protein at the time of hospitalization was determined below the reference values, whereas albumin and transferrin were recorded within normal limits (Fig. 2). However, by hospitalization day 14, a decrease was noted in the indicators of the high-molecular organic substances we studied, indicating their high consumption by the macroorganism during NCVI and the lack of rapid replenishment, despite the fact that in the hospital, all patients received traditional hospital nutrition. Negative dynamics revealed by hospitalization day 14 indicated the development of hypermetabolism–hypercatabolism syndrome with

the breakdown of tissue proteins and worsening of the course of COVID-19. In week 2 of hospitalization, chronic disease exacerbations were noted, and a relationship was observed between a decrease in the main markers of the protein pool and the complications that occurred ($r = 0.512$; $p = 0.013$). At the end of week 2 and beginning of week 3, due to the progression of multiple-organ dysfunction syndrome against NCVI with a significant decrease in macroelements, lethal outcomes were recorded in four patients (3.9 % ± 2.5 %).
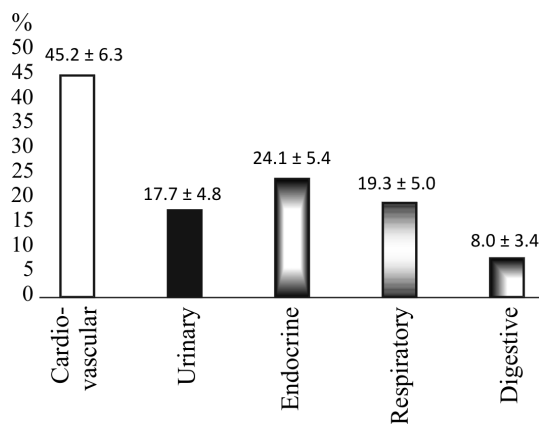
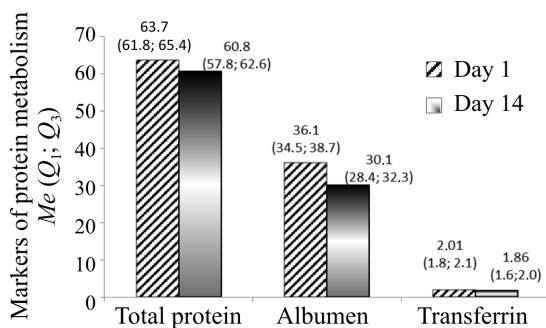*Fig. 1. Concomitant system lesions in patients with COVID-19, %*

Fig. 2. Dynamics of levels of protein metabolism markers on the days 1 and 14 of hospitalization Me (Q_1; Q_3)

In the Russian literature, studies on the developing deficiency of visceral pool proteins in HIV-positive patients and those in intensive care units were found [2, 10]. Notably, a recognized risk group for a decrease in muscle mass and an increase in a systemic inflammatory response with a predominance of macronutrient breakdown are patients in intensive care units with respiratory failure of various etiologies [11, 12] and in patients hospitalized with moderate NCVI; such studies have not been previously conducted.

The next stage of our study was evaluating the dynamics of the content of microelements during NCVI. On hospitalization day 1, Fe indicators, according to WHO[6], were determined within acceptable limits (Fig. 3); erythrocytes at this time were $3.6 \cdot 10^{12}/1$ (3.4; 3.6) and hemoglobin was 113 (110; 116) g/l, which corresponded to a deficiency of these indicators in males and lower limits of acceptable values in females. By day 14 of the disease, iron deficiency increased ($p < 0.05$), and its relationship with the negative dynamics of transferrin was revealed ($r = 0.801$; $p = 0.000$).

A crucial microelement in our body is zinc, which is used in various biological cycles of macroorganisms. Its deficiency can

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[6] World Health Organization. Maternal Health and Safe Motherhood Program World Health Organization. Nutrition Program (1992). The prevalence of anemia in women: a tabulation of available information, 2nd ed. World Health Organization, available at: https://iris.who.int/bitstream/handle/10665/59705/WHO_MSM_92.5.pdf?sequence=1

lead to increased production of interleukin-6 proteins, decreased local immunity in the lung tissue, and a "cytokine storm" [13, 14]. In the examined patients, already on hospitalization day 1, a reduced concentration of this microelement was determined with <10.4 µmol/l (Fig. 3); by day 14, a progressive decrease in its values was revealed ($p < 0.05$). In patients with zinc levels < 9.9 µmol/l, the course of COVID-19 was aggravated by the development of multiple-organ failure and decompensation of co-morbid diseases, and therefore, a relationship was registered between Zn deficiency and infection severity ($r = 0.603; p = 0.008$). In the group of patients examined, lethal outcomes were registered in seven patients (11.2 % ± 4.0 %), with Zn values of 8.0 (7.5; 8.1) µmol/l and Fe values of 7.4 (7.0; 7.6) µmol/l, which enabled to identify a relationship between low levels of microelements and lethal outcomes in NCVI patients ($r = 0.596; p = 0.004$).

When studying the concentration of copper during NCVI, we did not obtain significant differences on hospitalization days 1 and 14 ($p > 0.05$); its values remained within the reference range (Fig. 3). Several authors indicated that with an unfavorable course of COVID-19, the occurrence of complications and *exitus letalis* and Cu levels above normal were recorded, and this should be regarded as an independent parameter of the severity of NCVI [15]. However, in this study, the above statement could not be confirmed.
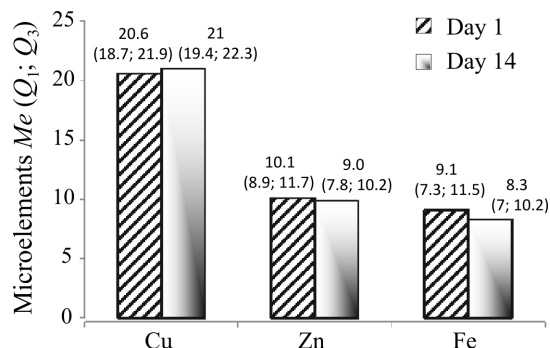

Fig. 3. Dynamics of microelements concentration on hospitalization days 1 and 14, Me ($Q_1; Q_3$)

Thus, in the dynamics of the disease, decreased Fe and Zn concentrations and macroelements were noted, which indicated the influence of the infectious agent on the development of metabolic disorders in patients with moderate NCVI.

CONCLUSIONS

1. In patients with moderate COVID-19, the progression of the deficiency of the main markers of the protein pool and vital microelements is determined over time.

2. Macro and microelement deficiency is a predictor of severe COVID-19.

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