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ЗДРАВООХРАНЕНИЯ
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САМАРКАНДСКИЙ
ГОСУДАРСТВЕННЫЙ
МЕДИЦИНСКИЙ УНИВЕРСИТЕТ

ИННОВАЦИОННЫЕ ТЕХНОЛОГИИ В ЗДРАВООХРАНЕНИИ: НОВЫЕ ВОЗМОЖНОСТИ ДЛЯ ВНУТРЕННЕЙ МЕДИЦИНЫ

МАТЕРИАЛЫ

международной научно-практической конференции
(Самарканд, 22 апрель 2022 г.)

Под редакцией
Ж.А. РИЗАЕВА

ТОМ I

Самарканд-2022

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Инновационные технологии в здравоохранении: новые возможности для внутренней медицины: Материалы международной научно-практической конференции (г. Самарканд, 22 апрель 2022 г.) / отв. ред. РИЗАЕВ Ж.А. - Самарканд: СамГМУ, 2022. – 736 с.

В сборнике собраны материалы, которые содержат статьи и тезисы докладов, представленных на международной научно-практической конференции «Инновационные технологии в здравоохранении: новые возможности для внутренней медицины», проведенной в СамГМУ 22 апрель 2022 г. Значительная часть материалов отражает современные проблемы внутренней медицины, посвященные поиску эффективных методов диагностики, лечения и профилактики заболеваний внутренних органов.

Представленные материалы будут интересны специалистам всех направлений внутренней медицины и широкому кругу читателей, интересующихся вопросами возникновения и профилактики основных заболеваний терапевтического профиля.

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РОЛЬ И ВЛИЯНИЕ НЕДОСТАТКА ГЛУТАТИОНА В ПОСТКОВИДНОМ ПЕРИОДЕ

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АННОТАЦИЯ

Многие люди, переболевшие коронавирусом даже в легкой форме, отмечают, что испытывают различные негативные ощущения в организме даже спустя месяцы после выздоровления. В настоящее время появился специализированный термин для определения этого состояния — постковидный синдром. Цель изучения особенностей клинического течения постковидного периода и влияния комплексного применения глутатиона на восстановительный период больных, перенесших COVID-19.

Материал и методы. Проанализировано клиническое состояние 58 больных COVID-19, поступивших на стационарное лечение в кардиологическое отделение многопрофильной клиники ТМА через 20-30 дней после исчезновения симптомов коронавирусной инфекции. Несколько доказательств, представленных в нашем биохимическом анализе, позволяют предположить, что низкие уровни GSH могут быть одной из основных причин чрезмерной воспалительной реакции, связанной с тяжелыми симптомами COVID-19, и указывают на то, что увеличение GSH в организме может уменьшить количество пациентов с симптомами. Будущие клинические исследования уровней GSH у пациентов с COVID-19 могут стать отправной точкой для изучения этой возможности.

Ключевые слова: постковидный синдром, глутатион, коронавирус, COVID-19.

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ROLE AND EFFECT OF GLUTATHIONE DEFICIENCY IN THE POST-COVID PERIOD

ANNOTATION

Many people who have been ill with coronavirus, even in a mild form, note that they experience various negative sensations in the body even months after recovery. Currently, a specialized term has appeared to define this condition - post-covid syndrome. Purpose study of the features of the clinical course of the post-COVID period and the effect of the complex use of glutathione on the recovery period of patients who underwent COVID-19.



Material and methods. The clinical condition of 58 patients with COVID - 19 who arrived for inpatient treatment at the cardiology department of the TMA multidisciplinary clinic, 20-30 days after the disappearance of symptoms of coronavirus infection, was analyzed. Several pieces of evidence presented in our biochemical analysis suggest that low GSH levels may be one of the main causes of the excessive inflammatory response associated with severe COVID-19 symptoms and indicate that an increase in GSH in the body may reduce the number of symptomatic patients. Future clinical studies of GSH levels in patients with COVID-19 may be a starting point to explore this possibility.

Keywords: post-COVID syndrome, glutathione, coronavirus, COVID-19.

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KOVIDDAN KEYINGI DAVRANDA GLUTATYON ETISHMASLIGINING ROLI VA TA'SIRI

ANNOTATSIYA

Koronavirus bilan og'rigan, hatto yengil shaklda bo'lgan ko'plab odamlar tuzalganidan keyin ham bir necha oy o'tgach, tanada turli xil salbiy his-tuyg'ularni boshdan kechirishlarini ta'kidlashadi. Hozirgi vaqtda ushbu holatni aniqlash uchun maxsus atama paydo bo'ldi - post-covid sindromi. COVID-19 dan keyingi davrning klinik kechish xususiyatlarini va glutationdan kompleks foydalanishning COVID-19 dan o'tgan bemorlarning tiklanish davriga ta'sirini o'rganishdan maqsad.

Materiallar va usullar. TMA ko'p tarmoqli klinikasining kardiologiya bo'limiga statsionar davolanishga yotqizilgan COVID-19 bilan kasallangan 58 nafar bemorning koronavirus infeksiyasi belgilari yo'qolganidan 20-30 kun o'tib klinik holati tahlil qilindi. Bizning biokimyoviy tahlilimizda taqdim etilgan bir nechta dalillar GSH darajasining pastligi og'ir COVID-19 belgilari bilan bog'liq bo'lgan haddan tashqari yallig'lanish reaksiyasining asosiy sabablaridan biri bo'lishi mumkinligini ko'rsatadi va organizmdagi GSH ning ko'payishi simptomatik bemorlar sonini kamaytirishi mumkinligini ko'rsatadi. COVID-19 bilan og'rigan bemorlarda GSH darajasining kelajakdagi klinik tadqiqotlari bu imkoniyatni o'rganish uchun boshlang'ich nuqta bo'lishi mumkin.

Kalit so'zlar: post-COVID sindromi, glutation, koronavirus, COVID-19.

Introduction

Many people who have been ill with coronavirus, even in a mild form, note that they experience various negative sensations in the body even months after recovery. Currently, a specialized term has appeared to define this condition - post-covid syndrome.

Post-COVID-19 syndrome, also known as Long Covid, is a consequence of coronavirus infection (COVID-19), in which up to 20% of people who have had a coronavirus infection suffer from long-term symptoms lasting up to 12 weeks and in 2.3% of cases longer. But there is no exact timeline for when the post-COVID syndrome will manifest itself. This can happen soon after discharge and after three months. Moreover, a mild form of covid is not a guarantee of the absence of post-covid syndrome.[1]. In December, the UK Office for National Statistics estimated that one in ten people who contracted the coronavirus continued to suffer from long-term symptoms that lasted three months or more.[7].

Post-COVID symptoms include problems that come on in waves or on an ongoing basis, such as:

- weakness, paralyzing weakness - in many patients who have had a covid infection, weakness remains so pronounced that it does not allow them to perform their usual activities, up to a decrease in the possibilities of ordinary self-service, the inability to visit the store and other essential places.



- shortness of breath, a feeling of lack of air, incomplete inspiration, apnea, heaviness behind the sternum, discomfort in the chest, and all this can be without pronounced lung damage, normal indicators of control X-rays and CT studies.

- varying degrees of severity, mental disorders: tearfulness, bad mood, depressive mood, sleep disturbance, suicidal thoughts; cognitive impairments (memory loss, brain fog, spatial disorientation, anxiety and panic attacks) are often noted.

- violation of thermoregulation of the body: not only an increase of 37.0 - 37.4 C, but also a decrease in body temperature: 35.5 C or 36.0 C, such a temperature in post-covid syndrome, as a rule, is not regulated by anything.

- loss of smell, distortion of smell / taste can remain the same for quite a long time, but is much less common than other symptoms.

- severe headaches, not related to temperature or increased blood pressure, myalgic muscle pain, joint pain; paresthesias are noted - a feeling of "needles", "goosebumps", burning sensations and other unpleasant symptoms that everyone has experienced in life, for example, after serving a leg or lying down an arm.

- skin lesions, various rashes: vascular and vasculitic manifestations on the skin.

- disorder of the gastrointestinal tract, diarrhea that occurs in waves and does not depend on diet or medication is more common in patients who previously suffered from gastrointestinal pathology and (or) received massive antibiotic therapy during the acute period of the disease [8].

Numerous literature data convincingly indicate that oxidative stress (OS) and the inflammation potentiated by it form the basis of the pathogenesis of various chronic diseases, including diseases that aggravate the course of the new coronavirus infection COVID-19 (diabetes mellitus, severe obesity, bronchopulmonary diseases, cardiovascular disease, cancer, and liver disease).

The cause of OS is an imbalance in the redox homeostasis system, characterized by excessive production of reactive oxygen species and/or insufficient activity of the antioxidant defense system. A comprehensive and in-depth analysis of the literature data led to the conclusion that among all the potential antioxidants in the body, it is glutathione that provides a stable foundation for the normal functioning of the antioxidant system, and its deficiency can cause serious disorders of various organs and systems.

Deficiency of endogenous glutathione accompanies many chronic diseases that worsen the prognosis of COVID-19. A decrease in glutathione levels in these patients already shifts redox homeostasis towards oxidative stress, thereby potentiating inflammatory changes in the lungs.[9].

By T.M. Hagen (1990) Glutathione is a natural food component found in fruits, vegetables and meats. A person consumes about 150 mg of GSH per day with food. As research has shown D.P. Jones (1992) with the participation of healthy volunteers, after oral administration of synthetic GSH at a dose of 15 mg/kg of body weight, the level of glutathione in the blood plasma increases by 1.5-10 times relative to the original; peak concentration is observed 1 hour after ingestion. It has been proven that exogenous glutathione can compensate for the deficiency of internal glutathione during intoxication and other pathological conditions that are accompanied by oxidative stress (T.Y. Aw, 1991). These data create prerequisites for the use of glutathione in diseases of the relevant organs that are actively involved in the processes of detoxification and removal of harmful substances from the body: kidneys, liver, lungs, as well as in systemic diseases accompanied by endothelial dysfunction and oxidative stress - diabetes mellitus, atherosclerosis and etc.

In the United States, at the end of April, the 1st confirmation of the proposed concept appeared: New York doctors observed 2 patients with COVID-19, who recorded a rapid improvement in their general condition after a single intravenous injection of reduced glutathione (shortness of breath practically disappeared 1 hour after the injection)[10] Clinical trials of the efficacy of N-acetylcysteine (a precursor and modulator of endogenous glutathione synthesis) in the treatment of severe patients with COVID-19 have already been initiated in the USA [11].

In connection with these scientific facts, it is of interest to study the role of glutathione in the recovery period after a coronavirus infection.

Purpose study of the features of the clinical course of the post-COVID period and the effect of the complex use of glutathione on the recovery period of patients who underwent COVID-19.



Material and methods. The clinical condition of 58 patients with COVID - 19 who arrived for inpatient treatment at the cardiology department of the TMA multidisciplinary clinic, 20-30 days after the disappearance of symptoms of coronavirus infection, was analyzed. The absence of an active phase of the disease was laboratory confirmed by several studies: a negative test for COVID-19 and the absence of IgM or the presence of an IgG titer. Of the examined persons, there were 37 men and 21 women with a confirmed diagnosis of coronary artery disease and hypertension. All patients underwent clinical (verbal assessment of pain in the heart), laboratory (lipid spectrum, coagulogram and other biochemical tests) and instrumental methods of research (ECG, echocardiography). All patients were assessed risk factors (FR) major diseases of coronary heart disease (CHD) and arterial hypertension (AH). The average age of men and women in the study was 62.7 ± 0.76 years.

The exclusion criteria were complications of IHD (unstable angina pectoris, acute myocardial infarction, acute and 3-4 functional classes of chronic heart failure (CHF), arrhythmias and conduction disturbances of moderate and severe gradations) and hypertension (hypertensive crises, acute and chronic cerebrovascular accident, severe encephalopathy).

Results. When collecting anamnestic and clinical data, the following risk factors were identified in 58 patients: obesity - 11 (18.9%), smoking - 8 (13.8%), anxiety-depressive syndrome - 32 (55.2%), increased sugar in the blood - 12 (20.7%), hypercholesterolemia - 24 (41.3%), physical inactivity - 25 (43.1%).

When analyzing complaints and clinical symptoms, it turned out that the patients were dominated by complaints of pain in the heart, increased blood pressure, increased heart rate, shortness of breath during exercise and other symptoms indicated in Table 1.

The obtained clinical data indicate the predominance in the post-COVID period of such symptoms as: weakness and fatigue, increased blood pressure with the presence of LVH on the ECG, the appearance of headaches and angina pectoris. Thus, in 15 patients (35.7%) out of 42 patients with elevated A/D, who had not previously suffered from hypertension, there were sharp jumps in A/D, pulse, ventricular and supraventricular arrhythmias, tachycardia (including orthostatic tachycardia).

Table 1

Picture of clinical symptoms of post-covid syndrome

№	Symptoms	Abs (n=58)	%
	Pain in the heart according to the scale of verbal assessment of pain syndrome	38	65,5
2.	Shortness of breath on the TF scale	15	25,8
3.	Arterial hypertension (AH)	42	72,4
4.	Degree of hypertension (average values)	138/72 мм.рт.ст.	-
5.	Headache	25	43,1
6.	Dizziness	15	25,8
7.	Weakness, fatigue	44	75,8
8.	Pulse (averages)	87 уд/мин	-
9.	Availability HLV	42	72,4
10.	Signs of impaired blood supply on the ECG	23	39,6
11.	Rhythm disturbances (various extrasystoles)	18	31,0
12.	Pulse oximetry	98,1±1,16	-
13.	The presence of wet rales	12	20,6
14.	Liver enlargement	23	39,6
15.	Edema of the lower extremities	11	18,9

Persistent weakness and shortness of breath may indicate a decrease in cardiac function (Table 2). It mainly concerns patients who have recovered from moderate and severe forms of covid infection. Thus, 42 patients with heart pain and high blood pressure were diagnosed with coronary artery disease with hypertension of various degrees, and all of them underwent an echocardiographic (EchoCG) study for the differential diagnosis of CHF (table 2).

A certain dynamics of echocardiographic parameters in patients in the pre- and post-COVID period was noted. Within a short time, some patients moved from the group with preserved LVEF to the group with low EF, which indicates an aggravation of CHF as a result of a coronavirus infection. All patients with an established diagnosis of coronary artery disease and hypertension received drug therapy in accordance with the clinical guidelines of 2020 (JHypertension. 2020;75:1334–1357). Long-lasting shortness of breath can also be a sign of the development of fibrosis of the lung tissue, and this is the most dangerous, because this change is already irreversible.

Table 2
Echocardiographic parameters of heart remodeling in CHF in the post-surgery period

Indicators	Group 1 low LVEF (<40%), n=9	Group 2, intermediate LVEF (41–49%), n=12	Group 3, saved LVEF (>50%), n=21
EDS, sm	6,1±0,05	5,8±0,2**	4,7±0,03###
EDV, ml	198,2±4,6	185,4±6,2**	131,2±1,5###
ESS, sm	4,9±0,05	4,6±0,1**	3,3±0,03###
ESV, ml	119,3±3,8	101,9±4,5***	51,7±1,0###
LVEF, %	39,9±0,2	45,4±0,4***	61,1±0,4###
E/A, unit	2,01±0,05	1,08±0,2*	0,95±0,05###
THIS, sm	1,06±0,1	1,08±0,2	1,1±0,2#
THPWLV, sm	1,1±0,2	1,2±0,2*	1,2±0,2#
LVMI, g/m ²	249,9±5,6	215,9±5,7***	184,5±4,2###

Note: - reliability of the difference between the indicators of the 1st and 2nd groups: * - p<0.05; ** - p<0.01; *** - p<0.001; Reliability of differences in indicators of groups 1 and 3: # - p<0.05; ## - p<0.01; ### - p<0.001; EDS - end diastolic size; EDV- end diastolic volume; FSS- final systolic size; ESV- end systolic volume; LVEF- left ventricular ejection fraction; E/A – coefficient of early and late diastolic filling; THIS - thickness of the interventricular septum; THPWLV - thickness of the posterior wall of the left ventricle; LVMI- left ventricular myocardial mass index;

In order to make it easier for the doctor to choose a therapeutic regimen, after recovery, patients are recommended to: control lung function, blood pressure and heart rate, do breathing exercises, spend more time outdoors; with muscle weakness, slowly and gradually increase physical activity; take vitamin-mineral and amino acid complexes (the most important vitamins are A, D, E, C).

In light of the latest recommendation [10], we recommended a dietary supplement called GLUTAREDOX to 58 patients with post-COVID syndrome. This food supplement is a powerful detoxifying agent and is a cofactor of the phase II detoxification enzyme - glutathione-s-transferase, which detoxifies a wide range of toxic compounds, including heavy metals. It has a pronounced antioxidant effect, that is, it inactivates a large number of free radicals and restores the oxidized forms of vitamins E and C, DNA strands and oxidized proteins damaged by free radicals. One tablet of glutaredox contains: Glutathione - 250 mg, Vitamin C - 40 mg, L-cystine - 50 mg and selenium - 55 mcg. Taking Glutaredox for one month showed positive changes in some indicators of the clinical condition of patients with post-COVID syndrome, as shown in Table 3.

Table 3
Indicators of the effect of complex therapy with Glutaredox on clinical parameters in patients with post-covid syndrome

Clinical symptoms	Before treatment with Glutaredox,	After treatment with Glutaredox	P

	(n, %)	after 1 month of treatment, (n, %)	
Headache	25 (43,1%)	19 (32,7%)	p<0,05
Dizziness	15 (25,8%)	11 (18,9%)	p<0,05
Weakness	44 (75,8%)	36 (62,0%)	p<0,01
Fast fatiguability	44 (75,8%)	31 (53,4%)	p<0,01
muscle weakness	30 (51,7%)	25 (43,1%)	p<0,05

Antioxidant therapy has a beneficial effect on many diseases characterized by inflammation caused by impaired redox homeostasis.[3,4,5,].

In the context of inflammatory diseases, systemic oxidative stress is defined as a decrease in the total level of free thiols (free cysteine sulfhydryl groups in proteins such as albumin, as well as low molecular weight free thiols such as cysteine, glutathione, homocysteine and related species). A recent study suggested that low molecular weight systemic thiols may play a role in inflammatory and oxidative stress pathways involved in both chronic obstructive pulmonary disease (COPD) and CVD [6].

A study of the acute antihypertensive effect of antioxidants in patients with hypertension and diabetes showed that the antioxidant GSH exhibits a significant hypotensive effect, probably due to the control exercised over the interaction of nitric oxide with free radicals [2]. From our side, the hypothesis put forward continues to find its clinical confirmation.

Conclusion:

The review outlined describes how SARS-CoV-2 can disrupt the balance of high activity of the renin-angiotensin system in the lungs through ACE2 downregulation followed by free radical-mediated inflammation and reveals the protective role of GSH. This biochemical approach to COVID-19 disease opens up new avenues for further research aimed at understanding the molecular mechanisms involved.

Several pieces of evidence presented in our biochemical analysis suggest that low GSH levels may be one of the main causes of the excessive inflammatory response associated with severe COVID-19 symptoms and indicate that an increase in GSH in the body may reduce the number of symptomatic patients. Future clinical studies of GSH levels in patients with COVID-19 may be a starting point to explore this possibility.

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