Biomeditsinskaya Khimiya, 2023 vol. 69, issue 4, pp. 240–247.

CLINICAL-DIAGNOSTIC STUDIES

ALPHA-2 MACROGLOBULIN ACTIVITY IN SARS-CoV-2 INDUCED INFECTION AND IN THE POST-COVID-19 PERIOD

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The universal proteinase inhibitor α_2-macroglobulin (α_2-MG) exhibiting antiviral and immunomodulatory activities, is considered as an important participant in the infectious process. The activity of α_2-MG in the new coronavirus infection and post-covid syndrome (long COVID) has not been studied yet. We examined 85 patients diagnosed with community-acquired bilateral polysegmental pneumonia developed under conditions of a new coronavirus infection SARS-CoV-2. For assessment of the post-COVID period, 60 patients were examined 5.0±3.6 months after the coronavirus infection. Among these patients, 40 people had complications, manifested in the form of neurological, cardiological, gastroenterological, dermatological, bronchopulmonary symptoms. The control group included 30 conditionally healthy individuals with a negative PCR result for SARS-CoV-2 RNA and lack of antibodies to the SARS-CoV-2 virus. The α_2-MG activity in serum samples of patients with coronavirus infection dramatically decreased, up to 2.5% of the physiological level. This was accompanied by an increase in the activity of the α_1-proteinase inhibitor, elastase- and trypsin-like proteinases by 2.0-, 4.4- and 2.6-fold respectively as compared with these parameters in conditionally healthy individuals of the control. In the post-COVID period, despite the trend towards normalization of the activity of inhibitors, the activity of elastase-like and especially trypsin-like proteinases in serum remained elevated. In overweight individuals, the increase in the activity of trypsin-like proteinases was most pronounced and correlated with an increase in the antibody titer to the SARS-CoV-2 virus. In the post-COVID period, the α_2-MG activity not only normalized, but also exceeded the control level, especially in patients with dermatological and neurological symptoms. In patients with neurological symptoms or with dermatological symptoms, the α_2-MG activity was 1.3 times and 2.1 times higher than in asymptomatic persons. Low α_2-MG activity in the post-COVID period persisted in overweight individuals. The results obtained can be used to monitor the course of the post-COVID period and identify risk groups for complications.

Key words: alpha-2-macroglobulin; alpha-1-proteinase inhibitor; trypsin-like proteases; elastase-like proteases; post-COVID period

DOI: 10.18097/PBMC20236904240

INTRODUCTION

Alpha-2-macroglobulin (α_2-MG) is a high molecular weight glycoprotein acting as an inhibitor of proteolytic enzymes [1]. It exhibits a wide specificity, inhibiting activities of serine, cysteine, aspartyl proteinases, and metalloproteinases.

Proteinases play an important role in the pathogenesis of coronavirus infection. To penetrate the body, the virus employs such human proteinases as membrane trypsin-like (TMPRSS, ADAM17, furin), intracellular cysteine (cathepsins), and extracellular serine proteinases (trypsin, elastase, Hageman factor, thrombin, etc.) [2]. Proteinases hydrolyze (prime) the spike protein S, providing binding to the receptor (angiotensin-converting enzyme 2; ACE2), fusion of the virus with cell membranes, and development of the infection [3]. Mutations of the virus with appearance of new sites for hydrolysis by additional enzymes increase the contagiousness of the virus [4]. In the presence of concomitant pathology associated with inflammation and activation of neutrophil elastase and plasma proteinases, susceptibility to viral infection increases with the development of a severe form of COVID-19 [5, 6].

α_2-MG is involved in the body defense against viral, fungal, and bacterial infections by blocking enzyme activities and preventing pathogen penetration into the cell [1, 7]. The inhibitory potential of α_2-MG is relatively small, but it is a necessary addition to the functions of the α_1-proteinase inhibitor (α_1-PI, α_1-antitrypsin), which provides 90% of the inhibitory activity of blood plasma. Both α_1-PI and α_2-MG have a wide range of regulatory properties, including immunomodulatory ones. At the same time, complexes of α_2-MG with proteinases have a short half-life (1-3 min), while complexes with α_1-PI are eliminated from the circulation for much

longer time (hours) and the effects are delayed [8]. In addition to proteinase inhibition, α_2-MG binds cytokines IL-6 and IL-18, IL-4 and IL-10, participates in the activity of the immune system [8, 9]. α_2-MG is involved in antigen presentation and antibody formation; it regulates reactions of nonspecific humoral immunity by binding hydrolases, lysozyme, and properdin. Interacting with cytokines, α_2-MG acts as a mediator of nitric oxide synthesis and NO-induced macrophage cytotoxicity [7]. The intensity of the immune response depends on α_2-MG concentrations. Its deficiency results in appearance of the phenomenon of areactivity and its excess causes suppression due to blocking of the major histocompatibility complex [10]. α_2-MG plays an important role in hemostasis as a thrombin inhibitor [11]. Determination of the α_2-MG complex with thrombin can be used to assess thrombinemia.

The antiviral and immunoregulatory properties make α_2-MG and α_1-PI, important factors in the pathogenesis of coronavirus infection associated with hyperinflammation, cytokine storm, thrombophilia, thrombosis and its complications. The study of α_2-MG activity during SARS-CoV-2 infection and in the post-COVID period is of both theoretical and practical importance. A meta-analysis (n=50) showed a ubiquitous prevalence of complications following COVID-19. The health consequences of the post-COVID syndrome seem to be quite long-term [12], this determines the importance of studying diagnostic and prognostic parameters, including the balance of inhibitor and proteinase activity.

The aim of the study was to determine the activity of α_2-MG, α_1-PI, as well as trypsin- and elastase-like proteinases in COVID-19 and in the post-COVID period (long COVID).

MATERIALS AND METHODS

85 patients (46 women and 39 men) aged 46±8.5 years with a diagnosis of community-acquired bilateral polysegmental pneumonia developed under conditions of a new SARS-CoV-2 coronavirus infection were examined. They were hospitalized in the Tomsk Medical and Sanitary Unit No. 2 in the period from March 16 to June 5, 2021. Mild pneumonia was diagnosed in 69.9% patients, moderate and severe in 3.6% and 26.5% of patients, respectively. Diagnostics and treatment of patients were carried out in accordance with the interim guidelines for the prevention, diagnosis and treatment of a new coronavirus infection (COVID-19) of the Ministry of Health of the Russian Federation. SARS-CoV-2 RNA was detected using nucleic acid amplification methods in nasopharyngeal swabs. The severity of acute respiratory distress syndrome (ARDS) was assessed by the ratio of the partial pressure of arterial oxygen to the fraction of inhaled oxygen (PaO_2/FiO_2). 47% of patients had ARDS (pO_2 less than 95%), as well as respiratory failure (RF) of varying severity. Concomitant diseases included arterial hypertension, type 2 diabetes mellitus, obesity. The prescription of glucocorticoids was required in 18% of patients (Table 1). The mortality rate of patients infected with SARS-CoV-2 was 9.4% (8 people).

To assess the development of complications of COVID-19, 60 people (47 women and 13 men) were examined 5.0±3.6 months after the coronavirus infection. It should be noted that 62.5% of individuals were vaccinated. In all examined persons, the body mass index (BMI) was measured as the ratio of weight (kg) to height (m). According to the international classification, excess body weight is verified with a BMI in the range of 25.0-29.9, obesity — with a BMI ≥30.0 (WHO, 1997). An increased body mass index was detected in almost 50% of the examined. In 40 people (66.7%) aged 36.8±6.7 years in the post-COVID period, complications were identified in the form of neurological, dermatological, gastroenterological, cardiological, and bronchopulmonary symptoms (Table 2).

All primary data on patients and the control group are given in supplementary materials.

The control group included 30 conditionally healthy individuals (18 women and 12 men) aged 56.8±6.7 years. These individuals had a negative PCR result for SARS-CoV-2 RNA, and no antibodies to the SARS-CoV-2 virus were detected in their serum samples.

Table 1. Clinical and anamnestic characteristics of patients infected with SARS-CoV-2

Criterion		Patients with this criterion (%)	Patients without this criterion (%)
Acute respiratory distress syndrome		40 (47.0%)	45 (53.0%)
Arterial hypertension		51 (60.0%)	34 (40.0%)
Diabetes mellitus type 2		14 (16.5%)	71 (83.5%)
Obesity		6 (7.1%)	79 (92.9%)
Respiratory failure	Grade I	18 (21.2 %)	49 (57.6%)
	Grade II	8 (9.4%)	
	Grade III	10 (11.8%)	
Treatment with glucocorticoids (dexamethasone i/v bolus)		16 (18.8%)	69 (81.2%)

Table 2. Percentage of clinical symptoms in the post-COVID period

Symptoms	Manifestations	%
Dermatological	dry skin, hair loss	90
Gastroenterological	gastrointestinal tract disorders, nausea	55
Neurological	cognitive disorders, headache, arthralgia, thoracalgia, anosmia, ageusia	43
Cardiological	sudden changes in blood pressure, postural orthostatic tachycardia syndrome, dizziness	30
Bronchopulmonary	dyspnea	5

Determination of the Activity of Proteinase Inhibitors in Serum

The α_2-MG activity was determined by the residual arginine-esterase activity of the trypsin-α_2-MG complex [13]. Briefly, 0.05 ml of 0.1% trypsin solution (SAMSON-MED, Russia) was added to 0.1 ml of blood serum diluted 10 times. After incubation for 5 min at 25°C and addition of 0.1 ml of 0.3% soybean trypsin inhibitor solution (Sigma-Aldrich, USA), the samples were incubated for 5 min and 1 ml of 1.5 mM N-benzoyl-L-arginine-ethyl ester solution (BAEE, Sigma-Aldrich) was then added. The increase in optical density at 253 nm was measured on a spectrophotometer (United Products and Instruments, USA). The activity of α_1-PI was assessed by the inhibition of BAEE hydrolysis by trypsin [13]. Two experimental samples were prepared, one of which contained 1.9 ml of 0.05 M Tris-HCl buffer and 0.1 ml of 0.01% trypsin solution, and the second one contained 1.8 ml of 0.05 M Tris-HCl buffer, 0.1 ml of 0.01% trypsin solution, and 0.1 ml of serum diluted 50 times. After incubation for 5 min at 25°C and adding 1 ml of 1.5 mM BAEE solution, an increase in optical density was measured at 253 nm. The activity of proteinase inhibitors was expressed in inhibitory units (IU) per 1 ml of serum (IU/ml). One IU corresponds to the amount of inhibitor that inhibits cleavage of 1 μmol BAEE in 1 min.

Determination of Proteinase Activity

The activity of trypsin-like and elastase-like proteinases was assessed by the hydrolysis, respectively, of BAEE and *p*-nitrophenyl ester of N-butyloxycarbonyl-L-alanine (BANE, Sigma-Aldrich) [14]. To determine the activity of elastase-like proteinases, 0.2 ml of 10-fold diluted serum and 2.7 ml of 0.05 M sodium phosphate buffer (pH 6.5) were mixed in a spectrophotometer cuvette. After adding 0.1 ml of 0.01 M BANE in acetonitrile, the increase in optical density was measured at 347.5 nm. Activity was expressed in nmol BAE/min per 1 ml of serum. To measure the activity of trypsin-like proteinases, 1.9 ml of 0.05 M Tris-HCl buffer (pH 7.8), 1 ml of 1.5 mmol/l BAEE solution were added to 0.1 ml of 10-fold diluted serum, and the increase in optical density was measured at 253 nm. The activity of trypsin-like proteinases was expressed in nmol BAEE/min per 1 ml of serum.

Determination of the Antibody Content to SARS-CoV-2

The content of antibodies to SARS-CoV-2 was determined using an enzyme immunoassay kit (Vector Best, Russia).

Statistical data processing was carried out using the Kolmogorov-Smirnov test, Mann-Whitney test, Spearman correlation analysis. Differences were considered as statistically significant at $p<0.05$. Results are presented as median and quartiles, Me (Q_{25}; Q_{75}).

RESULTS

The serum activity of α_2-MG in patients with coronavirus infection dramatically decreased and represented only 2.5% of the control level. At the same time, the activity of α_1-PI, trypsin-like, and elastase-like proteinases demonstrated 2.0-fold, 4.4-fold, and 2.6-fold, respectively, compared with the control group (Table 3). A higher activity of trypsin-like proteinases was observed in patients with ARD: 546.0 (264.81; 655.20) nmol BAEE/min·ml versus 207.5 (117.39; 464.10) nmol BAEE/min·ml in patients without ARDS. In the cases of lethal outcome, the activity of trypsin-like proteinases was maximal and represented 582.86 (505.05; 750.80) nmol BAEE/min·ml.

In the post-COVID period, the α_2-MG activity increased and significantly exceeded the control level. Although the α_1-PI activity and elastase-like activity decreased as compared to the hospital period, they still remained higher than the control. It should be noted that the activity of trypsin-like proteinases in the post-COVID period did not decrease; moreover, it even increased, exceeding the values obtained in the acute phase of infection (by 1.7 times) and the control (by 7.4 times) (Table 3).

In general, COVID-19 is characterized by a developed imbalance in proteinase inhibitors, including a decrease in the α_2-MG activity and an increase in the α_1-PI activity; this imbalance is accompanied by an increase in the activity of elastase-like and, especially, trypsin-like proteinases. In the post-COVID period, despite the normalization of the level of proteinase inhibitors, increased activity of trypsin-like proteinases is still detected in the serum.

Table 3. Activity of α_2-MG, α_1-PI and proteinases in acute and post-COVID periods

Parameter	Control n=30	COVID-19 n=85	Long COVID n=60
α_2-Macroglobulin, IU/ml	2.2 (1.7; 2.5)	0.055* (0.03; 0.09)	3.11*/** (2.0; 3.6)
α_1-Proteinase inhibitor, IU/ml	27.3 (20.7; 27.3)	54.8* (34.9; 78.96)	39.9*/** (21.8; 52.3)
Trypsin-like proteinases, nmol BAEE/min·ml	45.5 (45.5; 90.3)	200.1* (62.8; 518.7)	335.7*/** (163.9; 531.8)
Elastase-like proteinases, nmol BANE/min·ml	93.9 (90.3; 109.6)	245.7* (163.8; 330.3)	125.6** (54.6; 382.2)

*/** – Statistically significant difference with control and between groups, respectively (p<0.05).

Table 4. Inhibitory coefficients and correlation coefficients ($r_{x,y}$) between proteinases and inhibitors

Coefficient	Control	COVID-19	Long COVID
Elastase-like proteinases / α_2-macroglobulin	42.70 $r_{x,y}$= 0.172	4500 $r_{x,y}$ = -0.215	40.40 $r_{x,y}$ = 0.689
Trypsin-like proteinases / α_2-macroglobulin	20.70 $r_{x,y}$ = -0.039	4002 $r_{x,y}$ = -0.156	107.90 $r_{x,y}$ = 0.076
Elastase-like proteinases / α_1-proteinase inhibitor	3.40 $r_{x,y}$ = 0.066	4.50 $r_{x,y}$ = -0.013	3.15 $r_{x,y}$ = -0.605*
Trypsin-like proteinases / α_1-proteinase inhibitor	1.67 $r_{x,y}$ = 0.163	3.65 $r_{x,y}$ = -0.422*	8.41 $r_{x,y}$ = -0.143

In order to evaluate the "proteinase-inhibitors" system, the inhibitory coefficients of the ratio of the proteinase activity to their inhibitors were calculated. An increase in the coefficient indicates a decrease in the inhibitory activity under conditions of high proteinases activity. This is considered as an impaired control of blood proteinases.

α_2-MG is able to control the activity of elastase-like proteinases: the coefficient in the acute phase of infection demonstrated a 105-fold increase, while in the post-COVID period it decreased and did not differ from the control level. However, in the case of trypsin-like proteinases, the α_2-MG control impaired: the coefficient increased by 193 times, and in the post-COVID period it remained 5 times higher than in the control. Similar dynamics was revealed for α_1-PI, which controlled the activity of elastase-like proteinases and could not regulate the increase in the activity of trypsin-like proteinases (Table 4).

An imbalance in the activity of inhibitors may underlie uncontrolled proteolysis followed by damage of organs and tissues. In this regard, at the next stage, the α_2-MG activity was analyzed depending on the clinical manifestations of the post-COVID period. It has been found that the α_2-MG activity in patients with neurological and dermatological symptoms was higher (Table 5). Proteinase activity did not depend on the presence/absence of clinical symptoms, with the exception of trypsin-like activity, which was increased in dyspnea and represented 896.0 (867.20; 924.80) nmol BAEE/min·ml.

Comorbid pathology has a significant impact on the course of coronavirus infection and post-covid syndrome. The activity of inhibitors and proteinases was analyzed depending on the presence of overweight and obesity, which were detected in 50% of the examined patients. In individuals with BMI>25, a decrease in α_2-MG activity was observed under conditions of increased activity of trypsin-like proteinases (Table 6).

Correlation analysis revealed an inverse relationship between the α_2-MG activity and BMI. The strength of the relationship increases in the presence of clinical manifestations (correlation coefficient was -0.421, p<0.05). On the contrary, the direct correlation was found between the activity of trypsin-like proteinases and BMI (the correlation coefficient was 0.372; p<0.05). A positive relationship was also found between the activity of trypsin-like proteinases and the content of SARS-CoV-2 antibodies (the correlation coefficient of 0.518). It should be noted that the concentration of antibodies was higher in patients with post-COVID symptoms than in asymptomatic patients in the post-COVID period: 838.0 (631.4; 856.7) BAU/ml versus against 643.5 (468.3; 838.9) BAU/ml, respectively.

Table 5. α_2-MG activity (IU/ml) in patients with various symptoms in the post-COVID period

Symptoms	Absent	Present
Neurological	n=23 2.72 (2.02; 3.18)	n=17 3.66 (3.31; 4.05)*
Cardiological	n=28 2.91 (2.07; 3.645)	n=12 3.52 (3.15; 3.72)
Bronchopulmonary	n=38 3.14 (2.12; 3.70)	n=2 3.745 (3.57; 3.92)
Dermatological	n=4 1.77 (1.485; 2.21)	n=36 3.275 (2.54; 3.76)*
Gastroenterological	n=18 3.24 (2.09; 3.93)	n=22 3.19 (2.38; 3.70)

* – Statistically significant difference between groups (p<0.05).

Table 6. Activity of proteinases and their inhibitors in patients with different values of the body mass index (BMI)

Parameter	BMI <25 n=31	BMI >25 n=29
α_2-MG, IU/ml	3.275 (2.82; 3.68)	2.540 (1.77; 3.52)*
α_1-PI, IU/ml	44.10 (32.30; 54.80)	29.75 (20.83; 49.24)
Elastase-like proteinases, nmol BANE/min·ml	363.09 (72.35; 578.76)	109.20 (54.60; 327.60)
Trypsin-like proteinases, nmol BAEE/min·ml	300.30 (136.50; 374.01)	382.20 (303.70; 683.20)*

* – Statistically significant difference between groups (p<0.05).

DISCUSSION

It is known that α_2-MG and α_1-PI play an important role in protecting the body from excessive activation of proteolysis [8]. α_2-MG inhibits activities of the main proteases released from stimulated human neutrophils, in particular, neutrophil elastase [9].

Overflow and activation of neutrophils in the lungs during COVID-19 leads to the formation of neutrophil extracellular traps (NETs), the release of neutrophil proteinases, which are known to be involved in tissue damage and promote the spread of infection [15]. In addition to α_2-MG, the proteolytic activity of neutrophil elastase is regulated by α_1-PI, which plays a protective role against COVID-19. It is known that a mutation in the α_1-PI gene (*SERPINA-1*) contributes to a more severe course of coronavirus infection. For example, high mortality from COVID-19 in Italy (Lombardy) is associated with a high frequency of the deficient α_1-PI allele in people living in this territory [16].

In this study, an increase in the α_1-PI activity was accompanied by a decrease in the inhibitory activity of α_2-MG in serum; this is consistent with the literature data on the reciprocal mode of changes in these inhibitors during pathological processes [1, 7]. α_2-MG is known as a negatively reacting "acute phase protein" [10]. The wide range of inhibitory activity of α_2-MG is due to its unusual mechanism of action, which is based on the creation of a tetrameric "trap cell" around active proteases thus limiting protease interaction with high-molecular-weight substrates but retaining their ability to hydrolyze low-molecular-weight substrates [9]. In contrast to α_1-PI, which completely inhibits the activity of proteinases, α_2-MG partially retains their lytic activity. The α_2-MG structure contains receptor-binding domains (RBDs), involved in α_2-MG interaction with cell surface receptors. In native α_2-MG, these domains are hidden, but during α_2-MG binding to proteinases RBDs are exposed to the surface of the α_2-MG-proteinase complex and this promotes its uptake by cells by means of LRP-1 (low-density lipoprotein receptor-related protein-1) [9, 10]. In our case, a decrease in the α_2-MG activity may be associated with increased elimination of proteinases from the bloodstream and a decrease in the pool of native α_2-MG in the circulation.

Decreased biosynthesis of α_2-MG in chronic inflammation may contribute to the sanitation of affected tissues via proteolysis [17]. However, under conditions of hyperproteolysis, which is characteristic of coronavirus infection, excessive activity of proteinases has a more damaging effect than a protective one. For example, the activity of elastase- and trypsin-like proteinases demonstrated 2–4-fold increase during the acute period of the infection (Table 3). An increase in the activity of trypsin-like proteinases reflects

the phenomena of blood plasma hyperproteolysis with the activation of thrombin, plasmin, renin, kallikrein, components of the complement system and can be considered as an integrative indicator of the risk of developing cardiovascular events, thrombophilia, or hemophilia [6].

In the post-COVID period, the level of inhibitors normalizes: the α_2-MG activity increased while α_1-PI decreased, as compared with the acute period. However, compared with the control, the level of activity of proteinase inhibitors remained high (Table 3); this was accompanied by an additional increase in the activity of trypsin-like proteinases. The inhibitory coefficients of the ratio of trypsin-like proteinases to α_2-MG and α_1-PI in the post-COVID period remained high as compared to conditionally healthy individuals of the control group (Table 4). Taking into consideration that the activity of the proteolytic enzymes in the post-COVID period remains high, this can be considered as an unfavorable factor. The high activity of elastase-like proteinases (including neutrophilic) may also indicate the presence of an inflammatory process [5].

Taking into consideration the fact that the activity of the proteolytic enzymes in the post-COVID period remains high, the level of the α_2-MG activity can be considered as an indicator of the presence of inflammatory, including autoimmune processes, affecting the skin and nervous system; this is accompanied by the appearance of dermatological and neurological symptoms (Table 5). It has been previously found that SARS-CoV-2 provokes the development of autoimmune diseases. In this context altered α_2-MG activity can be both a consequence and one of the reasons for the development of autoimmune reactions in some patients.

It is known that α_2-MG acts as a neuromodulator by binding neuropeptides, myelin basic protein and amyloid peptides [17]. In the context of the development of neurodegenerative diseases it is also important that α_2-MG binds zinc ions [18]: zinc ion accumulation in neurodegenerative processes is generally recognized [17]. At the same time, hyperinflammation can lead to damage of α_2-MG molecules, disruption of their functional activity and affinity for receptors, as well as to the synthesis of autoantibodies to this protein [1].

It is known that the activity of α_2-MG and α_1-PI inhibitors can change in obesity. Our study has shown an inverse relationship between α_2-MG activity and BMI, which is consistent with literature data [19]. In contrast to α_2-MG, the activity of α_1-PI decreases, probably due to an increase in leptin content and the development of leptin resistance in obese patients [20].

High activity of trypsin-like proteinases and a decrease in the α_2-MG activity were found in overweight excess body weight (Table 6), which may be associated with an increase in proteolysis during a nonspecific inflammatory reaction. It is assumed that overweight people have a higher level of inflammation due to increased synthesis of pro-inflammatory cytokines in adipose tissue [21]. In the post-COVID period, a positive relationship was found between the activity of trypsin-like proteinases and antibodies to SARS-CoV-2. The antibody concentrations were higher in patients with complications. Probably, a high level of antibodies and an increased activity of trypsin-like proteinases are a consequence of the intensity of the immunological process and inflammation during the acute period of coronavirus infection.

CONCLUSIONS

In coronavirus infection, reciprocal changes in the activity of α_2-MG and α_1-PI are observed under conditions of the increased activity of elastase- and trypsin-like proteinases. In the post-COVID period, despite the normalization of the level of inhibitors, the activity of elastase-like and especially trypsin-like proteinases remained elevated. In overweight patients, a decrease in the α_2-MG activity and an increase in the activity of trypsin-like proteinases were found proportionally to the increase in the level of antibodies to SARS-CoV-2. The high activity of α_2-MG in the post-COVID period is accompanied by appearance of neurological and dermatological symptoms. The results obtained can be used to monitor the course of the post-COVID period and detection of risk groups for complications.

FUNDING

The work was supported by the Siberian State Medical University.

COMPLIANCE WITH ETHICAL STANDARDS

All subjects included in the study signed an informed consent to participate in it. The study was approved by the Ethics Committee at the Siberian State Medical University (protocol No. 8785 dated September 21, 2021).

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

Supplementary materials are available in the electronic version at the journal site (pbmc.ibmc.msk.ru).

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Received: 26. 05. 2023.
Revised: 13. 06. 2023.
Accepted: 29. 06. 2023.

АКТИВНОСТЬ АЛЬФА-2-МАКРОГЛОБУЛИНА ПРИ ИНФЕКЦИИ SARS-CoV-2 И В ПОСТКОВИДНОМ ПЕРИОДЕ

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Универсальный ингибитор протеиназ α_2-макроглобулин (α_2-МГ) обладает противовирусными и иммуномодулирующими свойствами, что делает его важным участником инфекционного процесса. Активность α_2-МГ при новой коронавирусной инфекции и постковидном синдроме (long COVID) не изучена. Обследовано 85 пациентов с диагнозом внебольничная двусторонняя полисегментарная пневмония на фоне новой коронавирусной инфекции SARS-CoV-2. Для оценки постковидного периода было обследовано 60 человек через 5,0±3,6 месяцев после перенесенной коронавирусной инфекции. Из них 40 человек имели осложнения, проявляющиеся в виде неврологических, кардиологических, гастроэнтерологических, дерматологических, бронхолёгочных симптомов. В контрольную группу были включены 30 практически здоровых лиц с отрицательным результатом ПЦР на РНК SARS-CoV-2 и отсутствием антител к вирусу SARS-CoV-2. Активность α_2-МГ в сыворотке крови пациентов с коронавирусной инфекцией сильно снижалась, составляя всего 2,5% от физиологического уровня, что сопровождалось увеличением активности α_1-протеиназного ингибитора, эластазо- и трипсиноподобных протеиназ соответственно в 2,0 раза, 4,4 раза и в 2,6 раза по сравнению с показателями практически здоровых лиц. В постковидном периоде, несмотря на тенденцию к нормализации активности ингибиторов, активность эластазоподобных и особенно трипсиноподобных протеиназ в сыворотке крови оставалась повышенной. У лиц с избыточным весом увеличение активности трипсиноподобных протеиназ было наиболее выражено и коррелировало с увеличением титра антител к вирусу SARS-CoV-2. В постковидном периоде активность α_2-МГ не только нормализовалась, но и превышала уровень контроля, особенно у лиц с дерматологическими и неврологическими симптомами. При жалобах неврологического характера активность α_2-МГ была в 1,3 раза, а при дерматологических симптомах — в 2,1 раза выше, чем у лиц, не предъявлявших жалоб. Низкая активность α_2-МГ в постковидном периоде сохранялась у лиц с избыточной массой тела. Полученные результаты могут быть использованы для мониторинга течения постковидного периода и выявления групп риска развития осложнений.

Полный текст статьи на русском языке доступен на сайте журнала (http://pbmc.ibmc.msk.ru).

Ключевые слова: альфа-2-макроглобулин; альфа-1-протеиназный ингибитор; трипсиноподобные протеиназы; эластазоподобные протеиназы; постковидный период

Финансирование. Работа выполнена при финансовой поддержке Сибирского государственного медицинского университета.

Поступила в редакцию: 26.05.2023; после доработки: 13.06.2023; принята к печати: 29.06.2023.