



PATHOGENETIC MECHANISMS OF SEVERE COURSE OF CORONA VIRAL INFECTION IN OBESE PATIENTS

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Receive 02.08.2021; accepted for printing 15.06.2021

Abstract

Obesity is one of the most serious diseases resulting in disability and high mortality. The problem of obesity existed before COVID-19 (Corona Virus Disease 2019) pandemic. It is proved that patients with obesity are most at risk to get infected and having a severe course of the infectious disease. In the contemporary world combination of obesity and a new corona viral infection is of a special significance. The increased risk of severe consequences of COVID-19 in people with obesity is also determined by the high reliability of developing “a cytokine storm”. Obesity is a source of chronic inflammation as it is accompanied by the production of pro-inflammatory cytokines and an increase of acute phase proteins. At present many peculiarities of the course of corona viral infection are revealed against the background of obesity. Among them are: presence of severe respiratory failure, high risk for developing respiratory distress syndrome, thrombosis and thrombo-embolic complications, as well as worsening of chronic cardio-vascular diseases. In the current situation questions of conservative treatment, considering the mechanisms of virus penetration into the cell, peculiarities of its pathophysiology and interaction with the human organism, obtain a special actuality.

KEYWORDS: obesity, Corona Virus Disease, complications, cytokine storm

Obesity is one of the most serious diseases resulting in disability and high mortality. The problem of obesity existed before COVID-19 (Corona Virus Disease 2019) pandemic. According to the World Health Organization (WHO, 2016) data, about 13% of adult population of the planet (11% men and 15% women) suffered from obesity [Johnson CL et al 2014].

It is proved that patients with obesity are most at risk to get infected and having a severe course of the infectious disease. Researchers have confirmed a higher risk of hospitalization in case of associating a viral infection in patients with obesity, especially in the group of patients with morbid obesity [Moser J.A et al 2018].

In the contemporary world combination of obesity and a new corona viral infection is of a special

significance. Epidemic COVID-19 started in December 2019 in Uxan city (China) and has reached the scale of an extreme situation spreading like lightning across all the countries of the world. The cause was the new corona virus SARS-CoV-2, which brings to a severe acute respiratory syndrome (Severe Acute Respiratory Syndrome Coronavirus 2). One of the causes of an increased risk of COVID-19 consequences in obesity is angiotensin-transforming enzyme 2 (ACE 2) activity [Sun P et al 2020]. It is determined that in case of overweight expression of genes, responsible for ACE 2 protein formation, becomes activated [Zhang H et al 2020]. This is the very protein that is “entrance gates” through which virus SARSCoV-2 penetrates into the cell. ACE 2 participates in the regulation of arterial pressure at the expense of the inhibition of renin-angiotensin system activity, vasodilatation, increase of natriuresis and inhibition of the inflammatory process activity. ACE 2 is also a receptor of SARS-CoV-2, inter-acting with amino-acid and integrin transporters. Expression occurs mainly in smooth muscular cells, in the cells of endothelium,

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acinuses of the pancreas, canalicular epithelium of the kidney, as well as in the adipocytes [Ryan P.M., Caplice N.M 2020]. As a target for viruses in the fatty tissue can serve adipocytes themselves and other cells (stromal cells, endothelial cells, macrophages and lymphocytes). The analysis of the risk for getting infected with different viruses among the population has shown not large spreading of SARS-CoV-2 in obesity [Misumi I et al 2019]. However, taking into account the high affinity for the receptors on target cells, among them adipocytes as well, we can consider hematogenic way of spreading in the fatty tissue, which increases the risk for this contingent of patients of getting ill.

The increased risk of severe consequences of COVID-19 in people with obesity is also determined by the high reliability of developing “a cytokine storm”.

Obesity is a source of chronic inflammation as it is accompanied by the production of pro-inflammatory cytokines and an increase of acute phase proteins. Patients with obesity have a higher activity of the nuclear factor transcription (NF- κ B) and a higher expression of pro-inflammatory cytokines, such as the factor of necrosis of α , interleukin -1 tumor (IL-1) and interleukin -6 (IL-6), which are key in the pathogenesis of the metabolic syndrome [Caussy C et al 2020; Maier H.E et al 2018]. “Cytokine storm”, occurring in many respiratory viral infections, including COVID-19, is manifested by the activation of interferon, interleukin, chemokine production, tumor necrosis factor

[Caussy C et al 2020; Qin C et al 2020]. Thus, the balance between for- and against inflammatory mechanisms is of crucial importance for maintaining lung tissue homeostasis. The impairment of one or several regulatory elements or their absence, presumably, can promote “cytokine storm” in the lungs or in other tissues (for

example, fatty), where aberrant activation of cytokines exists [Maffetone P.B., Laursen P.B. 2020].

The study of the “cytokine storm” has shown that IL-6 supports the activation of several cytokines during many days after the initial immune response [Chinese Clinical Trial Registry 2020]. The randomized multicenter investigation has shown that COVID-19 IL-6 was a strong independent predictor of lethal issues. Human adipose tissue is the main source of IL-6 and its receptor IL-6R [Sindhu S., 2015], that is why it can provide reservoir for IL-6 activation and cascade transfer of signals in viral infection. Spread of the virus from the affected organs into its surrounding adipose tissue can take several days followed by prolonged release of the virus, which contributes to the delayed “cytokine storm” by affecting tissues of the patient with COVID-19. Thus, the key role of IL-6 in mediating the response of the acute phase and its value as a prog-nostic biomarker in sepsis and different severe injuries of organs, is proved [Simonnet A., et al 2020]. In this regard inhibition of IL-6 has been recommended for treating COVID-19 and tocilizumab test results – awaiting [Chinese Clinical Trial Registry 2020].

One of the pathogenetic mechanisms of obesity is insulin-resistance, which afterwards can bring to the dysfunction of β -cells, development of carbohydrate metabolism disturbance, including diabetes mellitus which is directly related to the severe course of corona viral infection [Pal R., Bhaddada S.K. 2020].

Complex regulation of metabolism, necessary for complicated cellular interaction and effective protection of the patient’s organism, is impaired and brings to functional deficit. Virus SARS-CoV-2 can destroy β -cells of the pancreas by penetrating into them through the interaction with angiotensin converting enzyme II (ACE II). Finally, COVID-19 is often accompanied by hypokalemia which is due to the inhibition of the pulmonary ACE II, decrease of angiotensin II degradation and then increase of aldosterone secretion. Hypokalemia, in its turn, can worsen glycemia control in patients with diabetes mellitus types 1 and 2 [Di Renzo L., et al 2020].



To overcome it is possible, due to the uniting the knowledge and will of all doctors in the world

Understanding the mutual aggravating effects of obesity and COVID-19 determines the need for preventive actions directed to decreasing risks not only of unfavorable issues of corona viral infection, but also of developing and progressing chronic diseases, as well as decreasing the general immune response of the organism. One of the important steps for achieving this goal is to lose weight.

Thus, at present the problem of obesity against the background of new corona viral infection pandemic obtains a special significance (value). On the one hand, prevalence of obesity among population is steadily increasing, on the other hand, it is proved that obese people belong to the risk group of getting infected and having severe course of COVID-19. It is due to the presence of high expression of angiotensin converting enzyme 2, with likelihood of developing "cytokine storm", chronic inflammatory processes of the adipose tissue, changes in dipeptidylpeptidase -4, which bring to metabolic disorder

in the adipose tissue and immune mechanisms of antiviral protection. Patients with COVID-19 and obesity often require hospitalization in ICU and intensive therapy department and connection to the device of artificial ventilation of the lungs. At present many peculiarities of the course of corona viral infection are revealed against the background of obesity. Among them are: presence of severe respiratory failure, high risk for developing respiratory distress syndrome, thrombosis and thrombo-embolic complications, as well as worsening of chronic cardio-vascular diseases. All this, in the end, brings to the development of severe multi-organic failure which is a cause of death in such patients. In the current situation questions of conservative treatment, considering the mechanisms of virus penetration into the cell, peculiarities of its pathophysiology and interaction with the human organism, obtain a special actuality

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*Our journal is registered in the databases of Scopus,
EBSCO and Thomson Reuters (in the registration process)*



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Copy editor: Tatevik R. Movsisyan

Printed in "collage" LTD
Director: A. Muradyan
Armenia, 0002, Yerevan,
Saryan St., 4 Building, Area 2
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