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

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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 2participates 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-κF) 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 20207; Qin C et all 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*].

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

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 all 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., Bhadada 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 panc-reas 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 all 2020*].

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 expres-sion of angiotensinconverting enzyme 2, with likelihood of developing "cytokine storm", chronic inflammatory processes of the adipose tissue , changes in dipeptidilpeptidase -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

REFERENCES

1. *Caussy C, Pattou F, Wallet F, Simon C, Chalopin S., et al (2020).* Prevalence of obesity among adult inpatients with COVID-19 in France. Lancet Diabetes Endocrinol. 8(7): 562-564
2. *Chinese Clinical Trial Registry (2020).* ChiCTR2000029765 – A multicenter, randomized controlled trial for the efficacy and safety of tocilizumab in the treatment of new coronavirus pneumonia (COVID-19) 2020 [cited 2020 06/04/2020]. Available from http://www.chictr.org.cn/showprojen. aspx?proj=49409 12.
3. *Di Renzo L, Gualtieri P, Pivari F., et al (2020).* Eating habits and lifestyle changes during COVID-19 lockdown: An Italian survey. J Transl Med. 229
4. *Johnson CL, Dohrmann SM, Burt VL, Mohadjer LK (2014).* National Health and Nutrition Examination Survey: Sample design, 2011-2014. National Center for Health Statistics. Vital Health Stat. 2(162)
5. *Maffetone PB, Laursen PB (2020).* The perfect storm: Coronavirus (Covid-19) pandemic meets overfat pandemic. Front Public Health. 8: 135
6. *Maier HE, Lopez R, Sanchez N, Ng S., et al (2018).* Obesity increases the duration of influenza A virus shedding in adults. J Infect Dis. 218(9): 1378-1382
7. *Misumi I, Starmer J, Uchimura T., et al (2019).* Obesity expands a distinct population of T cells in adipose tissue and increases vulnerability to infection. Cell Rep. 27: 514-24e515
8. *Moser JA, Galindo-Fraga A, Ortiz-Hernández AA., et al (2018).* Underweight, overweight, and obesity as independent risk factors for hospitalization in adults and children from influenza and other respiratory viruses. Infl u Other Respir Viruses. 13: 3-9
9. *Pal R, Bhadada SK (2020*). COVID-19 and diabetes mellitus: An unholy interaction of two pandemics. Diabetes Metab Syndr. 14(4): 513-517

10. *Qin C, Zhou L, Hu Z, Zhang S., et al (2020).* Dysregulation of immune response in patients with COVID-19 in Wuhan, China. Clin Infect Dis. 71(15): 762-768

11. *Ryan PM, Caplice NM (2020).* Is adipose tissue a reservoir for viral spread, immune activation and cytokine amplifi cation in COVID-19. Obesity. 28 (7): 1191-1194

12. *Simonnet A, Chetboun M, Poissy J, Raverdy V., et al (2020).* High prevalence of obesity in Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) requiring invasive mechanical ventilation. Obesity (Silver Spring). 28(7): 1195-1199

13. *Sindhu S, Thomas R, Shihab P, Sriraman D., et al (2015).* Obesity is a positive modulator of IL-6R and IL-6 expression in the subcutaneous adipose tissue: significance for metabolic inflammation. PLoS One. 10: e0133494

14. *Sun P, Lu H, Xu C., et al (2020).* Understanding of COVID19 based on current evidence. J Med Virol. 2020; 10

15. *Zhang H, Penninger JM, Li Y., et al (2020).* Angiotensin-converting enzyme 2 (ACE 2) as a SARS-CoV-2 receptor: molecular mechanisms and potential therapeutic target. Intensive Care Med. 46(4): 586-590

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