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COVID-19 and Antihistaminic Medicines - Improving the Health of Millions by Strategically Disseminating a "Simple but Potential Solution"

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Abstract

This article aims to present the analysis of pathophysiological mechanism of COVID-19 as conclusion of review based on the available literature and research about COVID-19 and to help support the treatment protocol of COVID-19 patients based on the established pathophysiology of COVID-19 hyper inflammation. The proposed changes relate to the use of antihistamines in the prevention and treatment as well as changing the procedures of mechanical ventilation of the patient.

Introduction:

The proposal to adapt the new procedures is dictated by the targeting of the COVID-19 symptom development mechanism, which has not been taken into account in the public discourse so far, and whose key is the activation of mast cells, which are part of the immune system, and the release of histamine, which acts as a mediator of inflammatory processes, the highest concentration of which occurs in the skin, lungs, nasal mucosa and stomach. **[**1**]**

The SARS-CoV-2 virus after entering the body initiates the activation of mast cells to release large amounts of histamine from the granules, which by affecting the H1, H2, H3, H4 receptors **[**2,3,4**]**, causes an allergic and pseudo-allergic reaction called histamine intolerance (HIT) **[**5,6,7,8**]**. Avalanche histamine ejection and stimulation of the above-mentioned receptors, among others leads to: bronchospasm, cough, shortness of breath, increase in platelet aggregation, decrease in saturation, tachycardia, vasodilation and increase in their permeability, edema, diarrhea, hypotension, characteristic severe fatigue, fever, headache, neurological changes, as well as multi-organ changes including hyper inflammation in the lungs, intestines, heart, kidneys, liver **[**9**]**. The above symptoms of a systemic inflammatory reaction are also observed in the developing COVID-19 and its complications **[**10**]**.

The consequence of the unstoppable cascade of the histamine reaction is a decrease in saturation and breathing difficulties, which leads to the need for oxygen therapy and in the advanced stage to the mechanical ventilation, which extremely often leads to ventilator associated pneumonia (VAP) **[**11,12,13,14**]**. Patients, with bypassed nose air flow aerodynamics **[**15**]**, in most cases are ventilated with cold **[**16,17**]** and dry air **[**18,19**]**, regarding its difference with body temperature, the air reaches excessively high pressures in the lungs due to Charle's Law **[**20**]**, these physical factors leads to nonspecific degranulation of mast cells and the release of further doses of histamine **[**21,22**]**, provoked respiratory and other symptoms **[**23,24,25,26,27**]**. For proper oxgen- CO2 exchange in lungs there is required temperature 37°C and 100% humidity (44mg/L) **[**28,29,30**]**. The colder air together with too high pressure and viruses, among other, are activators for mast cells **[**31,32,33,34,35**]** that are massively present in the lungs **[**36,37**]**. As a result, it leads to irreversible damage to the pulmonary parenchyma such as inflammation, fibrosis and barotrauma **[**38,39,40,41**]**.

Histamine exerting a physiological effect through its four H1-H4 receptors coupled with G-protein, entering the bloodstream, causes a systemic inflammatory response syndrome and multi-organ failure that can lead to life-threatening conditions or even death, and in cases of chronic could initiate autoimmune diseases **[**42,43,44,45,46,47**]**.

Conclusion:

Based on analyzes of the literature, available to date, in the fields of COVID-19 and the treatment of patients with viral diseases, histamine intolerance and others, as well as experts consultations in the field of pulmonology, anesthesiology, allergology, physics, chemistry, technical issues of ventilators, genetics, with current and past research published about histamine, confirmed cases, it can be concluded that antihistamines **[**48,49**]**, blocking H1-H4 receptors, used preventively, at the first symptoms and during the development of the disease, can stop the cascade of reactions in the form of a storm histamine- cytokine **[**50,51**]**, thus the progression of COVID-19 and protect many patients from mechanical ventilation.

Considering presented hypothesis of histamine pathophysiology, the Indian Premiere Medical Institute has incorporated antihistamine in the treatment protocol of COVID-19 patients. In UAE also significant improvements has been observed in the symptomatology of COVID-19 patients viz cough, throat irritation and breathlessness after application of antyhistamines. Although histamines levels were not measured but addition of antihistamines with consequent improvement in symptoms reflects involvement if histamine pathway in COVID-19 pathophysiology and systemic inflammatory response, which was also confirmed in the ICU cases of the hospital in Wieliszew in Poland.

Recommendations:

Among the well-established inflammatory mechanism of COVID-19 induced multi-organ dysfunction including prothrombotic stage, hypercoagulability, cytokine storm and direct vascular injury, we suggest role of histamine mechanism also as a significant contributory cause of inflammatory organ dysfunction. Consider replacing the passive Heat Moisture Exchanger (HME) **[**52,53,54**]** with an active Moisture Heater (HH) on ventilators, as required device in each ventilator to warm and humidify of the air up to requisite levels **[**55,56**]**, revise also if the volume of air is setting to the appropriate base of the patient body mass (not total body mass) **[**57**]**. In addition, attention should be paid to the level of histamine neutralizing enzymes such as DAO and HMNT, provide them if possible and support their synthesis with supplementation **[**58**]**.

Of course, the use of the established hypothesis and research does not automatically guarantee obtaining the same results in all patients and the further extensive research work including large randomized controlled trails should be carried out on large number of COVID-19 patients to establish the exact role of histamine and beneficial effects of targeted antihistaminic medicine to prevent the COVID-19 induced inflammatory multi-organ damage.

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