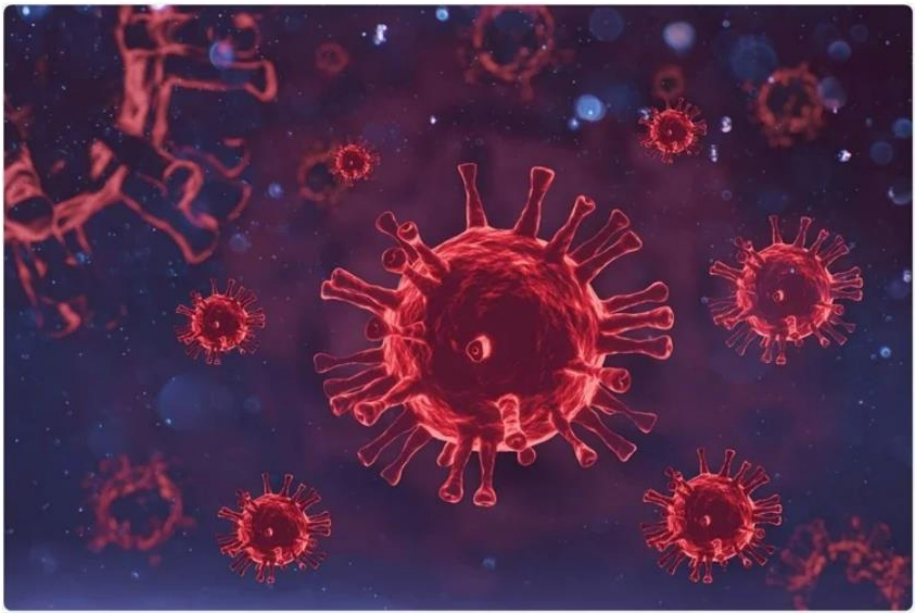
# For Treatment of the COVID-19, Potential Therapeutic Targets of Hydrogen?

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has led to the ongoing global pandemic. The pathophysiological process of COVID-19 is an excessive inflammatory response in the host after the viral infection.



Multiple therapies have been tested to alleviate symptoms of this disease; however, no specific and effective treatment exists. Hydrogen therapy has been included in a new treatment plan for COVID-19 in China.

A review of a study led by academician Zhong Nanshan, in China, on COVID-19 treatment by inhalation of a mixed gas composed of hydrogen and oxygen.

This article also describes the pathophysiology of COVID-19, summarizes therapeutic effects and underlying mechanisms of hydrogen on the critical disease, and analyzes the feasibility and potential therapeutic targets of hydrogen in treating COVID-19.

## Mechanisms of COVID-19

In COVID-19, the excessive activation of the immune cells and persistent inflammation caused by the viral infection generate large amounts of reactive oxygen species (ROS). After SARS-CoV-2 infection, its replication depends on the energy metabolism of the host cells, while the glycolytic pathway of the host cells is significantly enhanced, resulting in the production of a large number of ROS.

In the course of COVID-19, the impact of SARS-CoV-2 infection and ROS produced by the above two pathways lead to diffuse alveolar damage. This impedes alveolar gas exchange and causes dyspnea and hypoxemia. Hence, the lung is more prone to secondary infection.

## Hydrogen Therapy

Hydrogen therapy targets both inflammatory storms and ROS. Hydrogen, the lowest density gas known, has the smallest molecular mass and a degree of reducibility. Previously, hydrogen therapy has been tested in UV radiation-induced squamous cell carcinoma, end-stage colorectal cancer, parasitic liver diseases, cerebral ischemia-reperfusion injury, Parkinson's disease, soft-tissue injuries,

insulin resistance, rheumatoid arthritis, tumors, sepsis, and organ injury. Hydrogen therapy has demonstrated efficacy in the treatment of inflammatory damage.

Initially, the hydrogen used in clinical trials was mainly in a non-gaseous form. Clinical studies have shown that drinking hydrogen-rich water (HRW) is safe and well-tolerated; HRW containing 7 ppm H2 could protect the vascular endothelium from ROS.

Other forms of hydrogen that have been used are – hydrogen-rich saline injection containing 1 ppm H2, hydrogen-rich tablets, and hydrogen-rich oral capsules.

Recently, clinical trials have also confirmed the therapeutic effects of hydrogen gas inhalation. Therapeutic effects of inhalation of hydrogen gas have been demonstrated in patients with acute severe tracheal stenosis, end-stage colorectal cancer, acute cerebral infarction, postcardiac arrest syndrome after acute myocardial infarction, and non-small cell lung cancer. However, evidence relating a direct effect of hydrogen on viruses is lacking.

Currently, COVID-19 hydrogen therapy involves inhalation of a mixture of hydrogen and oxygen (66% hydrogen; 33% oxygen) at 6 L/min through the nasal cannula by using a Hydrogen/Oxygen Generator. Evidence suggests that H2-O2 inhalation for 7.7 hours, according to the standard of care, significantly improved the severity of COVID-19 within two days, including dyspnoea scale, chest distress, chest pain, cough scale, and resting oxygen saturation, when compared to control group of patients who received daily standard of care with oxygen therapy.

These benefits are likely conferred due to lower inhalation resistance after hydrogen/oxygen mixture inhalation. In another instance, a multicentre, randomized, double-blinded, parallel-group, controlled trial showed that inhalation of a hydrogen/oxygen mixture could significantly improve acute exacerbation of chronic obstructive pulmonary disease (COPD) symptoms, including – dyspnoea, cough, and expectoration, better than only oxygen therapy-with acceptable safety and tolerability profile.

## Potential Targets of Hydrogen in COVID-19

### *Neutrophils*

It has been found that inhalation of hydrogen gas can reduce the infiltration of the neutrophils in lung tissue and can aid in alleviating inflammatory damage to the lung tissue in the disease states.

Evidence suggests that hydrogen gas inhalation improved inflammatory cell infiltration-induced lung structural damage and enhanced the survival rate in severe septic mice modelled with caecal ligation and perforation.

In addition, in a rat model of the haemorrhagic shock and resuscitation, briefly inhaling 2% hydrogen gas after haemorrhagic shock and resuscitation minimized the degree of lung injury via reducing the infiltration of inflammatory cells into the lung tissue.

### *Macrophages*

Hydrogen reduces monocyte adsorption by the endothelial adhesion molecules under inflammatory response, thus preventing blood-borne monocytes from passing through the vascular endothelium and activating into the macrophages that cause an excessive inflammatory response. Hydrogen therapy can stabilize the function of macrophages and prevent damage caused by excessive activation and phagocytic defects.

***Cytokines***

Hydrogen reduces airway inflammation by reducing cytokine levels. The use of hydrogen gas can reduce the destructive cytokine storm and lung injury caused by SARS-CoV-2 in the early stage of COVID-19 and stimulate sputum drainage and ultimately reduce the incidence of severe disease.

***Reactive Oxygen Species***

In COVID-19, ROS and inflammatory response may be co-dependent. Hydrogen may either work by removing toxic ROS directly or indirectly improving the antioxidant activity of the body. Hydrogen therapy renders both anti-inflammatory and antioxidant effects and thus may aid in preventing disease progression in COVID-19.

***Adjunctive Therapy***

The main reason for COVID-19-related respiratory disorders is that SARS-CoV-2 attacks the pulmonary capillary endothelial cells and triggers an immune response. Hydrogen therapy may inhibit tissue damage by the inflammatory cells at all the stages of the inflammatory response.

Despite its potential efficacy and safety for use as adjunctive therapy, the mechanism of hydrogen alleviating symptoms of patients with the COVID-19 needs to be further clarified.

**Source:**

https://www.news-medical.net/news/20211112/Potential-therapeutic-targets-of-hydrogen-for-treatment-of-the-COVID-19.aspx