



## **PHYSIOPATOLOGICAL MECHANISMS OF OZONE IN THE TREATMENT OF COVID-19 ACTIVITIES**

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The biochemical and pharmacological characteristics lead to consider ozone important in the treatment of COVID-19. In fact, by reacting with biological substrates, it induces the synthesis of 4-hydroxynonenal, signal transducer that determines a greater resistance to prooxidant agents and an important response to oxidative stress.

The 4-HNE causes the release of Nrf2, transcription factor inducer in turn of several antioxidant enzymes including: SOD, CAT, HO-1. While SOD is involved in counteracting some neurodegenerative aspects, HO-1 modulates NF-KB, resulting in reduced expression of pro-inflammatory cytokines and induction of anti-inflammatory cytokines. The dual role of antioxidant and anti-inflammatory allows ozone to modulate IL-6 preventing the occurrence of the "cytokinetic storm", a critical event in COVID-19 infection.

### **IMMUNITARY ACTIVITIES**

Ozone reacting with PUFA, in addition to aldehydes, induces hydroperoxides which, spreading rapidly in the cells of the immune system, bioregulate the signal transduction, increasing the release of immunoactive cytokines. This is achieved by involving NFAT (Nuclear Factor of Activated Cells), a transcription factor linked to cytokines that support lymphocytes and macrophages that are fundamental constituents of the primary defense barrier. The bioregulation activity on the Immune System exerted by ozonized blood auto-haemifusion is well known.

### **ANTIVIRAL ACTIVITIES**

Lerner and Wentworth, in 2002 showed that our body is able to produce ozone endogenously to protect itself from infectious agents, involving neutrophil cells and antibodies of the immune system that, by producing ozone, exploit its oxidizing power to destroy the cell walls of bacteria and viruses. The lipidic molecules components of the pericapsid that envelops the virus, represent an ideal target for ozone; in fact, Byron K. Murray et al have shown substantial reductions in viral infectivity determined by the lipid peroxidation of the capsid caused by exposure to ozone. This prevents the virus from attacking the cellular receptor and therefore its replication. It is interesting to remember that the Ministry of Health in 1993 confirmed the antiviral and antibacterial activity of ozone in the blood.

## OXYGEN SATURATION

Another important characteristic of ozone in therapy against COVID-19 infection is the ability to counteract critical hypoxemia caused by this virus.

Experiments carried out with the collaboration of the University of Pavia and the Polytechnic of Turin using NIRS spectroscopy have shown an increase in oxygenation represented by an increase in the concentration of oxygenated haemoglobin and constant values of non-oxygenated haemoglobin. From a clinical point of view it translates into a powerful response to the dramatic drop in saturation values with relative recovery in para-physiological areas.

## ANTITROMBOTIC ACTIVITY

The protection of the endothelium by ozone is well known. Several publications have highlighted how endothelial cells, in contact with ozonized blood, induce NO synthesis. The cells contain the constitutive Nitoxide synthetase, which can be stimulated by ozone to synthesize Nitroxide, useful in cases of increased demand on the part of the body. This characteristic, together with the greater deformability of erythrocytes, facilitates metabolic exchanges, reduces blood viscosity and platelet aggregability. Under the metabolic aspect there is a greater availability of ATP at mitochondrial synthesis, an increase in P50 st and a reduction in the affinity of HbO<sub>2</sub> with the following greater bioavailability of tissue oxygen. In COVID-19 the presence of diffuse thrombi is highlighted and the ozone characteristics described seem to be suitable to counteract this problem.

## CONCLUSIONS

The characteristics of COVID-19 infection are expressed with different levels of severity, from the asymptomatic positive subject to the most serious cases requiring intensive care and mechanical ventilation. It is a pathology that involves in addition to the lungs different organs and districts, nervous axis, myocardium, vascular tree, hepatic entero tract, creating a metabolic syndrome. We therefore thought it was useful to propose and practice ozone therapy because of its physiopathological characteristics that seem suitable and specific in the treatment of this serious pathology. When news of the first cases of infection in the city of Wuhan, a Consensus Conference was urgently called among the members of the Scientific Committee of SIOOT because, aware of the mechanisms of action of ozone, it seemed useful to verify the possible intervention in this case.

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