

# COVID19 and ozone therapy (ver 1.2)

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## INTRODUCTION.

SARS-Cov2 has a mean incubation period of 5 days, although it can reach up to 2 weeks.

Infected patients evolve differently and extreme cases die after 10 days of being infected. Most patients ask for medical help after 5 days of suffering a catarrhal syndrome that worsens. They usually remain in-hospital for 3 weeks before discharge but according to age and concomitant pathology, 10% go to ICU. The prognosis there is also related with age and concomitant diseases as indicated by WHO<sup>1</sup>.

## Ozone therapy and viral diseases.

Bocci and cols.<sup>2</sup> tested *in vivo* effects of ozone in patients with different infections and discovered the following facts:

1- Ozone improves lung and peripheral tissue oxygenation and gases exchange because of peripheral vase-dilatation mediated by nitrosotyols and enhanced glucolysis in erythrocytes that produce more ATP and secondary higher 2,3-DPG levels (Bohr effect) and more elasticity because an optimal functioning of Na/K+ membrane pump<sup>2</sup>.

2- Ozone modulates the NRF2<sup>3</sup> and this produces three effects. First<sup>4</sup>, normalize the redox balance through the increase in antioxidants in cytoplasma, mitochondria and finally, plasma, mainly glutatione peroxidase, but also glutatione reductase, NADPH and SOD. Second<sup>5</sup>, induces the production of HO-1, a protective enzyme, together heat-shock proteins like HSP60, HSP70 and HSP90. Third<sup>6</sup>, activates the NFKbeta that modulates the production of pro-inflammatory interleukines in inflammated tissues.

All three effects contribute to restore the normal functioning of the inflammated tissues and decrease the amount of plasma interleukines.

## Ozone administration ways.

Ozone for systemic diseases should be used in a systemic way<sup>1</sup>:

A. Indirect Endovenous Administration (IEV). As ozone is a gas, it cannot be directly injected into the blood mainstream, to avoid gas embolism. Special medical devices have been manufactured and EU certificated by different manufacturers to allow ozone dissolve into the patients' blood risk free. For details on this technique, please read World Federation of Ozone Therapy - WFOT's book<sup>2</sup>.

Based on the information from the three Chinese Hospitals<sup>7,8,9</sup> that are presently performing and official clinical trial and also on the protocol presented and pre-accepted in Università della Sapienza in Rome, the proposed treatment will be:

- 100 mL of blood and 100 mL of ozone gas at 30 mcgr/mL concentration.
- In-hospital patients: each 12 hours application for minimum 14 weeks.
- ICU patients: each 8 hours until the patients starts improving; later, each 12 hours application til discharge to in-hospital care.

B. Rectal Inssuflation (RI). Rectal inssuflation is not so exact as IEV but it can be the only option for patients where peripheral veins don't allow the previous technique. For details on this technique, please read World Federation of Ozone Therapy - WFOT's book<sup>2</sup>.

We propose the following protocol:

- Day 1: 100 mL at 30 mcgr/mL concentration.
- Day 2: 150 mL at 30 mcgr/mL concentration.
- Day 3 - 14: 200 mL at 30 mcgr/mL concentration.

- In-hospital patients: each 12 hours application for minimum 14 weeks.
- ICU patients: each 8 hours until the patients starts improving; later, each 12 hours application til discharge to in-hospital care.

### **Complementary treatments to ozone administration.**

To help ozone effect, it is advisable although not mandatory, the administration during the ozone treatment of:

- Vitamine C: 3 gr each 12 hours, 6 hours after ozone administration. 1 gr each 12 hours is standardize in Italy and Spain protocols for COVID19.
- Glutathione: 600mg each 12 hours, 6 hours after ozone administration. This substance is administered because ozone effect is partially based on it and old patients may have a low blood glutathione level.

### **TRIAL DESIGN.**

#### **Purpose:**

1. Enhance respiratory function.
2. Stop the blood interleukine storm.
3. Limit patients needing ICU.
4. Shorten the time in hospital.

#### **Inclusion criteria:**

1. Confirmed patients (or legal guardian) sign a written informed consent form.
2. Aged from 18 to 80 years, male or female.
3. Patients with positive detection of 2019 Novel Coronavirus Pneumonia fluorescence RT-PCR in respiratory specimens or blood samples.
4. Mild ill and severe ill patients NOT IN ICU are grouped based on the "Handbook of COVID-19 Prevention and Treatment".

#### **Exclusion criteria:**

1. Patients who may be transferred to other hospitals that are not included in the trial within 72 hours.
2. G-6PD defect (Major Favism).
3. Pregnancy, especially early pregnancy.
4. Patients who continually use immunosuppressant, or are organ transplant recipients within 6 months.
5. Patients who are receiving other clinical trials.

#### **Interventions:**

WE SHOULD RANDOMIZE the patients going for control IEV or RI groups:

1. Control group. 60 patients. Conventional treatment.
2. Mild ill patients: 15 patients. Conventional treatment + ozone protocol A (IEV).
3. Mild ill patients: 15 patients. Conventional treatment + ozone protocol B (RI).
4. Severe patients: 15 patients. Conventional treatment + ozone protocol A.
5. Severe patients: 15 patients. Conventional treatment + ozone protocol B.

#### **Outcomes:**

1. Primary:
  1. Chest CT or XRay: interstitial pattern.
  2. Whole blood cell analysis: leucocytes recount.
  3. Oxygenation index: SpO2.
  4. Inflammation index: PCR. (optional: IL6, procalcitonin, ferritin, D-dimer)
  5. Fever: axillary temperature.

2. Secondary:
  6. Recovery rate.
  7. Conversion rate of severe patients.
  8. Mortality rate.

## REFERENCES

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- <sup>1</sup> WHO. Clinical management of severe acute respiratory infection when Novel coronavirus (2019-nCoV) infection is suspected: Interim Guidance. WHO/nCoV/Clinical/2020.2
- <sup>2</sup> Bocci V. Ozone: A new medical drug. Netherlands: Springer; 2011.
- <sup>3</sup> Baeza J, Cabo JR, Gómez M, et al. WFOTs Review on Evidence Based Ozone Therapy. World Federation of Ozone Therapy. 2015:1–116.
- <sup>4</sup> Bocci V, Valacchi G. Nrf2 activation as target to implement therapeutic treatments. Front Chem. 2015;3:4.
- <sup>5</sup> Pecorelli A, Bocci V, Acquaviva A, et al. NRF2 activation is involved in ozonated human serum upregulation of HO-1 in endothelial cells. Toxicol Appl Pharmacol. Feb 15 2013;267(1):30-40.
- <sup>6</sup> Re L, Martinez-Sanchez G, Bordicchia M, et al. Is ozone pre-conditioning effect linked to Nrf2/EpRE activation pathway in vivo? A preliminary result. Eur J Pharmacol. Nov 5 2014;742:158-162.
- <sup>7</sup> Guangjian N, Hongzhi Y. Clinical study for ozonated autohemotherapy in the treatment of Novel Coronavirus Pneumonia (COVID-19). ChiCTR2000030165. Academy of Medical Engineering and Translational Medicine, Tianjin University. 2020-02-24. <http://www.chictr.org.cn/showprojen.aspx?proj=49947>
- <sup>8</sup> Linlin H, Xiangdong C. A randomized controlled trial for the efficacy of ozonated autohemotherapy in the treatment of Novel Coronavirus Pneumonia (COVID-19). ChiCTR2000030006. Union Hospital, Tongji Medical College, Huazhong University of Science and Technology. 2020-02-19. <http://www.chictr.org.cn/showproj.aspx?proj=49737>
- <sup>9</sup> Huiling H, Tong X. A multicenter randomized controlled trial for ozone autohemotherapy in the treatment of novel coronavirus pneumonia (COVID-19). ChiCTR2000030102. Tianjin Huanhu Hospita. 2020-02-23. <http://www.chictr.org.cn/showproj.aspx?proj=49747>