



Dr. Joseph Varon - Research Inquiry #19

Ozone therapy for Post-Covid-19 Syndrome | 23.04.24

Research Inquiry

What is the role of ozone therapy in the treatment of vaccine-related injury and post covid-19 syndrome?

Conclusions

- There is no **peer-reviewed scientific evidence** supporting the effectiveness or safety of ozone therapy for COVID-19 vaccine-related complications.
- There is scant very low-quality evidence possibly supporting **ozone therapy for long-COVID**.
- Ozone therapy has been rec explored for **pain-related conditions** such as fibromyalgia and refractory headaches, with beneficial effects.
- Reported **side effects** following ozone administration **through autohemotherapy** include tingling in the lips and tongue, nausea, a metallic taste in the mouth, fatigue, and a diffuse erythematous skin rash.

Important Note - Neither the services nor the research report constitute medical advice of any kind and are not intended to be a substitute for professional medical advice.



Meta Medical Findings

Introduction

Ozone therapy has been traditionally employed in the field of alternative medicine to treat various infectious diseases, likely due to its antioxidant effects and its ability to deliver oxygen to oxygen-starved tissues. It has also been studied during the COVID-19 pandemic, and despite showing some potential benefits for patients in the acute phase, it has not been incorporated into the current COVID-19 treatment guidelines ^[1].

It is important to note that ozone is not an approved therapy in the US, and the Food and Drug Administration (FDA) stated in 2019 that “Ozone is a toxic gas with no known useful medical application in specific, adjunctive, or preventive therapy.”^[2] While Ozone therapy is available in several European countries such as Spain and Greece^[3], it is not recognized by the EU regulations as a medical treatment^[4].

Ozone for vaccine-related injury

There are non peer-reviewed websites suggesting that ozone may relieve the side effects of COVID-19 vaccine-related injury.

Ozone for long covid-19 syndrome

The most common method of ozone delivery used in studies is autohemotherapy, where ozone is administered through the re-infusion of the patient's own blood after it has been treated with an O₂/O₃ gas mixture ^[5].



Only two studies have reported the effects of ozone treatment for long-COVID. Additionally, only one of these studies has been published in a peer-reviewed journal. The table below provides a summary of both studies:

Study	Study design	Intervention	Outcome	Results	Adverse events
Tirelli et al. [6] (2021)	One arm prospective study (n=100)	Autohemotherapy 2-3 times/week for 3 weeks	Reduction in Fatigue Severity (FSS) Scale	The median FSS score dramatically decreased from 7 to 2 ($p < 0.0001$). 36% of the cohort experienced the maximum reduction in the FSS score, from 7 to 1.	Not reported.
Baranova et al. [7] (2021)	Non-randomized controlled trial (n=42)	10 sessions of treatment with ionized saline and autohemotherapy	- Subjective: Post-COVID-19 Functional Status (PCFS) scale. - Objective: oxygen saturation, C-reactive protein, ferritin, D-dimer, urea and creatinine, 6-minute walk test	Twice as many participants in the ozone group ($n = 18$) reached the study's endpoints compared to the control group ($n = 9$), ($P < 0.01$)	Not reported.



Study Details

- **Oxygen-ozone autohemotherapy may help to recover normal functionality and to relieve pain and discomfort in post-COVID sequelae** - preliminary results of a non-controlled interventional study [\[6\]](#) were published in *European Review for Medical and Pharmacological Sciences* (Q1, Impact factor 3.3) in 2021. The study included a cohort of 100 patients suffering from post-COVID-19 fatigue who were treated with ozone autohemotherapy. The patients were evaluated with a 7-scoring system Fatigue Severity Scale (FSS) before and after undergoing therapy.
 - 02 -03 autohemotherapy treatments each week for 2–3 weeks. Following treatments, patients were interviewed with FSS at least one week following the last session, to avoid placebo effects.
 - The median FSS score decreased from 7 to 2 ($p < 0.0001$).
 - 36% of the cohort experienced the maximum reduction in the FSS score, from 7 to 1.
 - The limitations of the study include the absence of information about the patients, such as their medical background. In addition, the cohort consisted solely of Caucasian participants, which restricts the applicability of the findings to other ethnic groups.
 - No information regarding the safety or adverse events were published.
- **Ozone therapy may be effective as a recovery tool** - a non-randomized controlled interventional study [\[7\]](#) published in *Zaporozhye medical journal* (non-indexed journal) in 2021 included 42 long COVID-19 patients who underwent rehabilitation after community-acquired polysegmental pneumonia associated with SARS-CoV2 infection. Twenty-one patients received an intravenous ozone therapy, consisting of an alternate-day infusion of 200 ml ozonized saline and autohemotherapy for 10 sessions.



- **Patients in the intervention group had a significant improvement in various functional outcomes**, as indicated by the Post-COVID-19 Functional Status (PCFS) scale, with noticeable reductions in symptoms like **dyspnea, general weakness, improved sleep quality**, and emotional state ($P < 0.01$).
- By the 20th day of treatment, 18/21 in the ozone treatment group had functional limitations rated between 0 to 1 on the PCFS scale, indicating minor to no limitations in daily activities. In contrast, only 9 of 21 in the control group experienced similar improvement.
- Patients receiving ozone therapy exhibited a notable improvement in their tolerance to physical activity during a 6-minute walk test. By the 20th day, patients in the treatment group had higher scores on the test (520 vs. 405 meters, $p < 0.01$), despite starting the study with similar baseline measurements.
- Adverse effects directly associated with ozone therapy are not mentioned in the article.
- The study's limitations include a relatively small sample of patients, and a focus on short-term outcomes that may not reflect long-term effects or safety of ozone therapy.

Safety profile

Reported side effects following ozone administration through autohemotherapy include tingling in the lips and tongue, nausea, a metallic taste in the mouth, fatigue, and a diffuse erythematous skin rash ^[8].

Ozone therapy for pain-related conditions

The table below summarizes data on ozone therapy's use for various pain-related conditions, including fibromyalgia and headache.

Condition	Study	Study design	Intervention	Outcomes	Adverse events
Fibromyalgia	Sucuoğlu et al. ^[9] (2023) Q2, IF 1.6	Randomized controlled trial (n=54)	Autohemotherapy for 10 sessions	Significant post-treatment improvements in (FIQ subscales (feel good, fatigue) and subjective sleep quality, sleep latency, and sleep disturbances compared to the control group (p< 0.05).	No adverse events or complications were observed.
Fibromyalgia	Tirelli et al. ^[10] (2019) Q2, IF 3	Non-controlled interventional trial (n=65)	Autohemotherapy or ozone rectal insufflations	An improvement of at least >50% of symptoms was observed in 45 patients (70%).	No adverse events or complications were observed.
Fibromyalgia	Türkyılmaz et al. ^[11] (2021) Q3, IF 1.8	Cross-sectional study (n=40)	Autohemotherapy for 13 sessions	Significant improvement in fibromyalgia impact questionnaire (FIQ) and SF-36 scores was observed in all periods compared to the previous period (P < .05).	No adverse events or complications were observed.
Refractory headache	Clavo et al. ^[12] (2013) Q1, IF 1.5	Interventional trial (n=5)	Autohemotherapy	Despite a very small sample size , the analysis showed that following ozone treatments, the median number of headache episodes was significantly lower (p = 0.04)	No adverse effects were observed with the treatment aside from ecchymosis at the site of injection.



Insomnia and myofascial pain syndrome	Shen et al. ^[13] (2022) Q2, IF 2.9	Randomized controlled trial (n=118)	Autohemotherapy for three weeks	Compared with the control group, the ozone therapy group had significantly improved sleep quality, pain, and negative mood at different time points.	No adverse complications were observed in either group.
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