

# Could the minor autohemotherapy be a complementary therapy for healthcare professionals to prevent COVID-19 infection?

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## Abstract

**Aim:** Coronavirus disease (COVID-19) poses a public health threat to the whole world and healthcare professionals also had difficulties in protecting themselves. Ozone therapy is an alternative and complementary treatment method that is theoretically accepted as an inactivated and immunogenic vaccine. We aimed to evaluate the effectiveness of minor autohemotherapy in the COVID-19 pandemic on protection and anxiety in healthcare professionals.

**Materials and Methods:** The minor autohemotherapy was performed on the healthcare professionals' weekly/six times. A general questionnaire, the Worry and Anxiety questionnaire, and the International Physical Activity Questionnaire-Short Form (IPAQ-SF) were used at the beginning and after 6 weeks from the beginning.

**Results:** The study was started with 89 healthcare professionals and finished with 73 in total. The IPAQ- SF score was  $718.11 \pm 507.49$  (median 583, low) before treatment, and decreased to  $462.67 \pm 250.65$  (median 437, low) after treatment. The WAQ score was  $34.79 \pm 13.27$  (median 36) before treatment and decreased to  $22.19 \pm 11.22$  (median 21) after treatment. The median of the pre-treatment scores for both scales was statistically different from the median of the post-treatment scores ( $p < 0.001$ ).

**Conclusion:** None of the healthcare professionals who performed the minor autohemotherapy had become sick or had COVID-19 positive test results. The results of our study reveal that healthcare professionals who were applied minor autohemotherapy worry and anxiety decreased despite decreasing physical activity levels of individuals.

**Keywords:** Anxiety; ozone therapy; pandemic; physical activity; prevention

## INTRODUCTION

Coronavirus disease (COVID-19) due to a new subtype emerging in China and reported from various countries poses a public health threat to the whole world. COVID-19 has been declared a pandemic by WHO on March 11, 2020 (1). It is essential to identify methods that show antiviral activity to prevent infection and spread in the face of the COVID-19 pandemic (2). Nearly 2 million people were died due to COVID-19 according to WHO since pandemic started (3). Restrictions were done to avoid the spread of the virus all over the world. Inactivity were occurred. Most works were done by healthcare professionals. More difficult working conditions, fear of illness, and also limitations in lifestyles have occurred. The healthcare professionals may have thought that they might have a shortage of supplies to protect themselves or that they

were left alone in an environment of fear created by an epidemic of unknown treatment for which they did not have sufficient knowledge. Due to these stresses depression and anxiety symptoms were seen at different levels in healthcare professionals (4).

Ozone (O<sub>3</sub>) is a gaseous unstable molecule consisting of 3 oxygen atoms (5). The main task of the ozone present in the atmosphere is to protect people from UV rays (6). However, it is known to have a toxic effect on the human eye and lungs, depending on concentration, temperature, humidity, and exposure time. (7). Even so, it has been widely used in infection treatments since World War I (8) or even before (6). The three main effects of ozone therapy, which is an alternative treatment method, are shown as antimicrobial (9), antioxidant / oxidant balance (10) and immunomodulatory (10-12). It has been shown

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that ozone therapy has an amazing treatment effect, especially in cases where the inflammatory process is intense and the immune system is at the forefront in laboratory studies. Private ozone therapists have treated or suppressed autoimmune diseases that have been never reported in medical journals in all over the world (13). Also Ozone therapy is performed effectively in serious and various infectious diseases such as HIV and chronic hepatitis C infections treated with ozone therapy combined with the appropriate dosages of antiviral drugs (13,14), and mouth and dental infections (15) that have been reported. There are different forms of application: major autohemotherapy, minor autohemotherapy, intravaginal, intrarectal, intramuscular and subcutaneous (10). Ozone therapy is an alternative and complementary treatment method that is theoretically accepted as an inactivated and immunogenic vaccine. The main problem is uncertainty of the ideal ozone concentration, number of application, and choose of application method in the usage of strengthening immune system (13).

In the light of all this information, we aimed to evaluate the effectiveness of minor autohemotherapy in COVID-19 pandemic on protection and anxiety in healthcare professionals.

## **MATERIALS and METHODS**

### **Subjects**

Eighty-nine healthcare professionals who work in our hospital and do not have symptoms of COVID-19 between 23 March and 15 May 2020 were included in the study. Our hospital has a capacity of 1500 bed and consists of separate building complexes on the same campus. When this protection program started, suspicious or positive COVID-19 patients were in only one building (with a capacity of about forty patients) in our hospital, and all healthcare professionals we received under the protection program were not working in this clinic. However, as the outbreak progressed, the COVID clinic was inadequate and these clinics and building numbers were increased. Healthcare professionals, who we started to program, also took part in these areas. The healthcare professionals of the COVID-19 clinics were on duty for 24 hours and rested for 72 hours. We did not end the protection program of these healthcare professionals. In addition to healthcare professionals of the newly created COVID-19 clinics, we also included the healthcare professionals of the anesthesia, emergency, and otolaryngology clinics, who are at the highest rate of coming across with COVID-19 patients, as healthcare professionals in the COVID-19 clinic.

Although we applied the same preventive complementary treatment to our own clinic staff, we excluded our clinicians and nurses from the study to prevent bias.

Inclusion criteria of the study were; being a healthcare professional at our hospital, and do not have symptoms of COVID-19 infection. Exclusion criteria of the study were; the glucose 6 phosphate dehydrogenase enzyme

deficiency, pregnancy, using of angiotensin converting enzyme (ACE) inhibitor, hyperthyroidism, the bleeding disorders, unstable cardiovascular diseases, presence of chronic pancreatitis and missing follow-ups.

The local ethics committee approved the study protocols. (Date: 30.06.2020, Number: 2020-223)

Each volunteer who was enrolled in this program has signed informed consent of ozone therapy.

### **Minor Autohemotherapy (MIH)**

We have decided to do ozone therapy to healthcare professionals in our hospital to contribute to the protection due to the antiviral and immune-enhancing properties of ozone therapy after the announcement of the first COVID-19 case in Turkey. However, we evaluated that the minor autohemotherapy is more suitable due to the high cost and the possibility of increased virus risk depending on the application time of the major autohemotherapy. There is no consensus on the dosage or the number of applications for other causes of disease (16), and the method of this application had been determined by us because there is no standard for the COVID-19 infection also.

5 ml of blood was taken to the ozone resistant syringe from the volunteers. After mixing with 5 cc ozone, a period of time was waited to dissolve in blood and then react with biological molecules. Then it was injected slowly to gluteus muscle. The ozone was applied in the first week at a dose of 10mcgr / ml with a weekly dose increase of 1mcgr / ml. This application were done six times.

In addition, we suggested that not to use all antioxidant supplements, especially vitamins C and E on the day of MIH, due to reducing the effectiveness of ozone. We also recommended that foods rich in antioxidant molecules not be consumed in large quantities at that time to increase this complementary treatment.

### **Assessments and Outcomes**

We used a general questionnaire, the Worry and Anxiety questionnaire and the International Physical Activity Questionnaire-Short Form (IPAQ-SF) for assessing protection, worry and anxiety levels of the healthcare professionals. These questionnaires were administered at the beginning and at the 6<sup>th</sup> week of the study. Volunteers were asked for side effects at every control.

The General Questionnaire: This questionnaire was prepared by us to evaluate the protection level of the MIH. It consists of 22 questions totally. The first 9 questions include the demographic data and the other 13 questions include the COVID-19 symptoms, test, diagnosis, contact status, smoking, chronic disease, medicine usage, exercise status, ozone information and use of the volunteer.

The Worry and Anxiety Questionnaire (WAQ) was used to evaluate worry and anxiety states. The first question is the issues that cause concern for the person. The other 10 questions are 9-point Likert type and each question is 8

points. It is scored between 0-80 points (17). The Turkish version of the WAQ is shown to be a valid and reliable questionnaire (18).

The International Physical Activity Questionnaire-Short Form (IPAQ-SF) was based on calculating the MET (metabolic equivalent) value spent by evaluating at least 10 minutes of physical activities in the last seven days in terms of frequency, duration (minutes) and intensity. 1 MET indicates the amount of oxygen uses by the person while sitting, at rest.

The questionnaire consists of 4 parts. These are intense physical activities, moderate physical activities and walking sections. The individual spends 8.0 MET in "intense physical activities", "4.0 MET in moderate physical activities, and 3.3 MET in" walking ". In calculation, total MET value is obtained by multiplying MET values from the related activity group by minutes and frequency (days). The multiplied values are finally summed and the total physical activity value is obtained. Accordingly, those with a weekly MET value below 600 are considered to be low in physical activity, those between 601 and 3,000 are moderate, and those above 3,000 are considered high (19). The Turkish version of the IPAQ is shown to be a valid and reliable questionnaire (20).

### Statistical Analyses

Statistical Package for Social Sciences software (IBM 20.0) was used. The nominal variables were presented as number, percent and frequency, and continuous variables were presented as mean  $\pm$  SD. The comparison of continuous variables spread with the normal spread was done using Kolmogrov Smirnov test. Wilcoxon signed rank test was used to compare related groups. Cramer's V coefficient was used to evaluate the relationship between the questions of COVID 19 test application and contact with ozone therapy.  $p < 0.05$  was considered statistically significant.

## RESULTS

The study was started with 89 healthcare professionals and finished with 73 in total (Figure 1). 74% (n = 54) of the professionals are female and 26% (n = 19) are male. The majority of the professionals, 63% (n = 46), are in the age group 41 and above, and 37% (n = 27) are in the 26-40 age group, and there is no staff under the age of 26 among the participants. 45.2% (n = 33) of the healthcare professionals stated that they have been in their current position for 15 years and more, and 50.7% (n = 37) stated that their total work experience is 20 years and more. In addition, 38.4% (n = 28) of the healthcare professionals are nurses, followed by assistants and patient registrar with 13.7% (n = 10) rates (Table 1).

The distribution of the healthcare professionals participating in the study according to the units they work in was also examined. The participants of the research work in 32 different units. It has been determined that the majority of 15.1% (n = 11) of the participants work in the

otolaryngology unit. This is followed by medical genetics with 9.6% (n = 7), underwater medicine and hyperbaric medicine with 8.2% (n = 6), sports medicine with 6.8% (n = 5) and cardiology with 5.5% (n = 4).

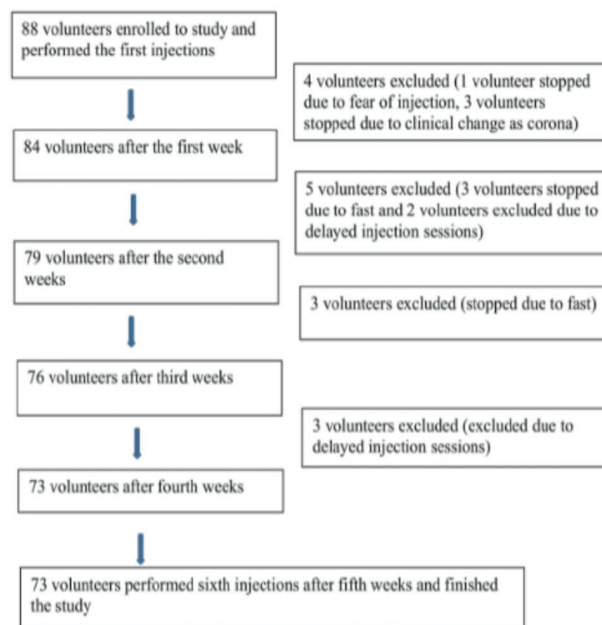


Figure 1. Study Flowchart

Table 1. Demographics of the healthcare professionals

		Frequency	Percent
Gender	Female	54	74
	Male	19	26
Age (year)	26-30	11	15.1
	31-35	5	6.8
	36-40	11	15.1
	41 and higher	46	63
Education	High School	14	19.2
	Associate Degree	5	6.8
	Licence	29	39.7
	Graduate	21	28.8
Time to work in the current position (year)	Doctorate	4	5.5
	0-2	17	23.3
	3-5l	9	12.3
	6-8	2	2.7
	9-11l	4	5.5
	12-14	4	5.5
	15 and higher	33	45.2
Time of the total work experience (year)	New started	4	5.5
	0-3	3	4.1
	4-7	12	16.4
	8-11	5	6.8
	12-15	5	6.8
	16-19	11	15.1
	20 and higher	37	50.7

Title	Nurse	28	38.4
	Assistant	10	13.7
	Patient registrar	10	13.7
	Medical secretary	9	12.3
	Health officer	5	6.8
	Physiotherapist	4	5.5
	Technician	4	5.5
	Specialist	1	1.4
	Midwife	1	1.4
	Audiologist	1	1.4
	Total	73	100

**Table 2. The information about the general health status of the healthcare professionals**

		Frequency	Percent
Did you experience fever, cough, shortness of breath or nasal congestion recently?	Yes	5	6.8
	No	68	93.2
Do you smoke?	Yes	23	31.5
	No	50	68.5
Weekly exercise frequency (day)	None	37	50.7
	1-2	25	34.2
	3-5	7	9.6
	Everyday	4	5.5
Do you have chronic diseases?	None	47	64.4
	Diabetes	2	2.7
	Hypertension	2	2.7
	Lung diseases	2	2.7
	Rheumatological	3	4.1
	Other	17	23.3
Medicines that you use	None	48	65.8
	Nonsteroid anti-inflammatory drugs	1	1.4
	Angiotensin converting enzyme inhibitors	1	1.4
	Other	23	31.5
	Total	73	100

In order to obtain information about the general health status of the healthcare professionals, some questions about the health status of the healthcare professionals participating in the research were asked. Accordingly, it was determined that 93.2% (n = 68) of the healthcare professionals did not experience fever, cough, shortness of breath or nasal congestion recently. It was determined that the majority of the healthcare professionals who participated in the study did not smoke (68.5%, n = 50), had no chronic disease (64.4%, n = 47) and did not use any medicines (65.8%, n = 48). However, it was determined that the majority of the healthcare professionals did not exercise any day of the week (50.7%, n = 37), only 34.2% (n = 25) of them exercised 1-2 days a week (Table 2).

In the research, some questions are included to evaluate the thoughts of the healthcare professionals about ozone therapy. It has been determined that 95.9% (n = 70) of the healthcare professionals have not received ozone treatment before, however 74% (n = 54) have knowledge about ozone treatment. In addition, it was found that 63% (n = 46) of the healthcare professionals were not aware of the recently published articles about ozone therapy. The rate of healthcare professionals who believed that ozone therapy would help protect the virus was 93.2% (n = 68).

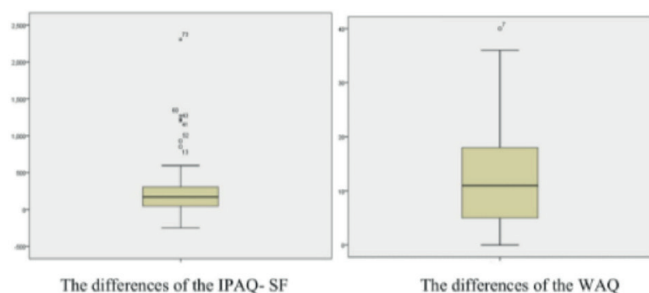
**Table 3. COVID-19 and healthcare professionals**

		Pretreatment		Posttreatment	
		Frequency	Percent	Frequency	Percent
Has the COVID-19 test applied to you?	Yes	5	6.8	44	60.3
	No	68	93.2	29	39.7
Have you contacted patients with the diagnosis-possibly diagnosed of COVID-19?	No	68	93.2	50	68.5
	1 time	0	0.0	5	6.8
	1-2 times per week	4	5.5	16	21.9
	3-4 times per week	1	1.4	1	1.4
	Everyday	0	0.0	1	1.4
Sum		73	100	73	100

Finally, the general questionnaire includes four questions about COVID-19. These four questions were answered by the healthcare professionals both before and after ozone therapy. It was observed that none of the healthcare professionals were followed up due to COVID-19 either before or after treatment. It was also observed that none of the healthcare professionals were diagnosed with COVID-19 either before or after treatment. However, as can be seen from Table 3 whether the COVID-19 test is



applied to the healthcare professionals and whether the healthcare professionals come into contact with patients with COVID-19 - possible diagnoses differed before and after the treatment. According to Table 3, while the rate of healthcare professionals who were tested for COVID-19 before ozone therapy was only 6.8% (n = 5), the number of healthcare professionals who received COVID-19 tests after ozone therapy was 60.3% (n = 44). The relationship coefficient between these two variables was found as Cramer's  $V = 0.566$  and since  $p < 0.001$ , this relationship between the variables was found to be statistically significant. Likewise, 93.2% (n = 68) of the healthcare professionals before the minor autohemotherapy stated that they did not come into contact with the patients with COVID-19 -possible diagnosis, and only 5.5% (n = 4) contacted the patients in question 1-2 times a week. It was observed that these rates were 68.5% (n = 50) and 21.9% (n = 16), respectively after the minor autohemotherapy. Again, the relationship between these two variables was found to be statistically significant (Cramer's  $V = 0.330$ ,  $p = 0.003$ ).



**Figure 2.** The differences of the IPAQ- SF and the WAQ

The working time of healthcare professionals in COVID-19 clinics was  $14.81 \pm 19.93$  days (minimum 0, maximum 45 days). The IPAQ- SF and WAQ scores were applied to 73 healthcare professionals participating in the study both before and after ozone therapy. The scores of each healthcare professional from these two scales were calculated separately before and after treatment. The IPAQ- SF score was  $718.11 \pm 507.49$  (median 583, low) before treatment, and decreased to  $462.67 \pm 250.65$  (median 437, low) after treatment. The WAQ score was  $34.79 \pm 13.27$  (median 36) before treatment, and decreased to  $22.19 \pm 11.22$  (median 21) after treatment. It has been tested whether there is a statistically significant difference between the pre-and post-treatment scores of the healthcare professionals, in other words, whether ozone treatment has a significant effect on the scale scores. Prior to this test, it was tested whether the difference series obtained by calculating the difference between these scores before and after these scores are suitable for normal distribution. For this, Kolmogorov-Smirnov normality test was used. According to the test results, it was determined that both the difference series related to the IPAQ- SF (statistic = 0.224, sig. <0.001) and the WAQ (statistic = 0.128, sig. = 0.005) were not suitable for the normal distribution. Therefore, related-samples Wilcoxon

signed rank test, which is a non-parametric method, was used to test whether ozone therapy has a significant effect on scale scores. The median of the pre-treatment scores for both scales was statistically different from the median of the post-treatment scores ( $p < 0.001$ ). The differences of the IPAQ- SF and the WAQ is shown in Figure 2.

## DISCUSSION

The COVID-19 pandemic has forced all healthcare professionals both physically and spiritually in terms of working conditions. These difficult situations of healthcare professionals were frequently reflected on both social media and television. In this process, we conducted this study to protect the health of healthcare professionals and reduce their anxiety and worries. None of the healthcare professionals who performed the minor autohemotherapy had become sick or had COVID-19 positive test results in this study. The results of our study reveal that healthcare professionals who were applied minor autohemotherapy worry and anxiety decreased despite decreasing physical activity levels of individuals. In fact, worry and anxiety levels would have increased in these conditions without minor autohemotherapy applications. Although health professionals have more contact with COVID-19 patients due to an increase in patient number than baseline, test positivity has not been determined, but indeed the expectation is being an increase in the positive test results.

The success achieved with ozone treatment methods, which are widely used today, is potentially due to triggering some protective and repair systems existing in the organism. In fact, when ozone is applied to human, it damages by oxidizing organic molecules that make up the cellular structures of the body (21). This is an inverse situation and difficult to understand. However, this triggers critical mechanisms that mediate beneficial effects as a result of this cellular damage that ozone initially made. The damage occurring in the cells that contact with the ozone and the damaged molecules released into the cellular environment as a result of this damage, strongly trigger the defense and repair mechanisms that are responsible for preventing and repairing the damage. This strong defense and repair response that emerged shows effectiveness against all pathologies present in the organism, regardless of the actual reason that triggered it. Such responses developed in the organism are called non-specific (nonspecific) responses. Owing to this non-specific response, every pathology existing in the organism simultaneously takes its share from the healing effects of the antioxidant and immune system and other repair mechanisms. As can be seen, the treatment logic is similar to the stimulation of the immune system with vaccines. In vaccination, harmful microorganisms are given to the body that killed or weakened or some antigenic structures and the immune system is triggered. Not all work is done by the vaccine itself, it is the immune system, one of the potential defense mechanisms triggered by it. Similarly, especially the antioxidant system, the anti-inflammatory system (22), the immune system (23), and secreted

growth factors (24) play a role in the treatment process following the ozone application. Based on this opinion, it is theoretically accepted that minor autohemotherapy may be appropriate to induce oxidation of free viral components, which can represent an inactivated and immunogenic vaccine, using ozone concentrations close to 90 µg / mL per mL of blood (16,25,26). However, there is no study that proves this in the literature. Our study was made by accepting the same theory, but unlike this theory, the method of this application had been determined by us and the dose we used was starting with 10 gammas and increasing each week. Ozone therapy is useful not in one session, sessions are needed to perform its effect on immunity (13), we preferred 6 sessions and we routinely use increasing doses to follow-up the side effects. 5-10 ml venous blood combined with ozone is the simplest way for minor autohemotherapy (15). We used 10 ml venous blood and ozone combination, similarly. The low dose ozone (10-20 µg/ml) acts as a stimulator of the immune system (27). We use low dose ozone concentration similar to this study. We have shown that minor autohemotherapy applied in this way is effective to prevent viral outbreaks.

COVID-19 occurs by affecting immunity (28). Physical activity is known to strengthen the immune system (29), reducing the risk of disease that endangers excess weight gain and immune function (30,31). However, it is preferred to stay at home in order to prevent the spread of the virus all over the world. Exercise is also an effective treatment to reduce symptoms of depression (32). Aerobic exercise has a positive effect on patients diagnosed with anxiety disorder (33). However, being limited movement causes both weight gain (34) and worry, anxiety, depressed mood, and depression (35). When we started our study, some restrictions had already been brought to our lives due to the pandemic. Therefore, the already low levels of physical activity decreased even more. The expected anxiety increase with decreasing physical activity level could not be determined due to ozone application.

## LIMITATIONS

The limitation of our study are that the evaluation could not be made with immunological parameters and performed not with major autohemotherapy. Considering that our first priority was to prevent the pandemic, it was more important to minimize contact time and number, so we did not use major autohemotherapy. We needed more financial support for immunological parameters and we did not want to lost time.

## CONCLUSION

The results of our study to protect the health and reduce their worry and anxiety of healthcare professionals in this process are promising. No volunteer had become sick or had positive test results. Of course, we cannot say that ozone therapy provides sufficient protection alone, but in cases of pandemic or illness with unknown treatment, measures taken to protect healthcare professionals may help at least protecting their mental health. For this purpose, minor autohemotherapy seems to be a

preferable cheap, simple and easily applicable protection method. Further studies are needed to show the effects of minor autohemotherapy alone on the immune system and psychological conditions.

*Competing Interests: The authors declare that they have no competing interest.*

*Financial Disclosure: There are no financial supports.*

*Ethical Approval: This study was ethical approval of The Ethics Committee of the Health Sciences University, Turkey. Study Number: 2020-223 Date:30.06.2020.*

## REFERENCES

1. Park SE. Epidemiology, virology, and clinical features of severe acute respiratory syndrome -coronavirus-2 (SARS-CoV-2; Coronavirus Disease-19). Clin Exp Pediatr 2020;63:119-24.
2. Fantini J, Di Scala C, Chahinian H, Yahi N. Structural and molecular modelling studies reveal a new mechanism of action of chloroquine and hydroxychloroquine against SARS-CoV-2 infection. Int J Antimicrob Agents 2020;55:105960.
3. WHO Coronavirus Disease (COVID-19) Dashboard [Internet]. Available from: [https://covid19.who.int/?gclid=Cj0KCQiAk53-BRD0ARIsAJuNhpvucu3GDZTU6eOhWLR3RbvLgXwxDYO4MTjTebiBguxm4ly99-mLtgkaAsflEALw\\_wcB](https://covid19.who.int/?gclid=Cj0KCQiAk53-BRD0ARIsAJuNhpvucu3GDZTU6eOhWLR3RbvLgXwxDYO4MTjTebiBguxm4ly99-mLtgkaAsflEALw_wcB)
4. Bohlken J, Schömig F, Lemke MR, et al. COVID-19-Pandemie: Belastungen des medizinischen Personals [COVID-19 Pandemic: Stress Experience of Healthcare Workers - A Short Current Review]. Psychiatr Prax. 2020;47:190-7.
5. Bocci V. Ozone as Janus: This controversial gas can be either toxic or medically useful. Mediators Inflamm 2004;13:3-11.
6. Elvis AM, Ekta JS. Ozone therapy: A clinical review. J Nat Sci Biol Med 2011;2:66-70.
7. Ozler M, Oter S, Korkmaz A. TAF Prev Med Bull 2009;8:59-64.
8. Ozkan H, Ekin S, Uysal B, et al. Evaluation and comparison of the effect of hypothermia and ozone on ischemia-reperfusion injury of skeletal muscle in rats. J Surg Res 2015;196:313-9.
9. Ozturk B, Kurtoglu T, Durmaz S, et al. The effects of ozone on bacterial growth and thiol-disulphide homeostasis in vascular graft infection caused by MRSA in rats. Acta Cir Bras 2017;32:219-28.
10. Pivotto AP, Banhuk FW, Staffen IV, Daga MA, Ayala TS, Menolli RA. Clinical Uses and Molecular Aspects of Ozone Therapy: A Review. Online J Biol Sci 2020;20:37-49.
11. Bocci VA. Scientific and medical aspects of ozone therapy. State of the art. Arch Med Res 2006;37:425-35.
12. Bocci V. The case for oxygen-ozonotherapy. Br J Biomed Sci 2007;64:44-9.
13. Sagai M, Bocci V. Mechanisms of Action Involved in Ozone Therapy: Is healing induced via a mild oxidative stress? Med Gas Res 2011;1:29.

14. Suarez JCC, Serrano YM, Peña MRC, Carballosa DRD. The immune response behavior in HIV-AIDS patients treated with ozone therapy for two years. *Journal of Ozone Therapy (JO3T)* 2018;2:1-9.
15. Dayani MA, Dehkordi AH, Miraghajani M. Ozone therapy in chronic diseases; a narrative review of the literature. *J Renal Inj Prev* 2019;8:195-8.
16. Bocci V, Travagli V, Zanardi I. The failure of HIV vaccines: A new autovaccine may overcome some problems. *Med Hypotheses* 2009;72:662-4.
17. Gosselin P, Ladouceur R, Pelletier O. Evaluation of an individual's attitude toward daily life problems: The negative problem orientation questionnaire. *J Ther Comport Cogn* 2005;15:141-53.
18. Akyay A. Anxiety and Anxiety Scale, Negative Attitude towards Problems Scale and Cognitive Avoidance Scale, Turkish adaptation, validity and reliability. (Master thesis). Uskudar University, Social Sciences Institute, Istanbul, 2016.
19. Lee PH, Macfarlane DJ, Lam TH, Stewart SM. Validity of the International Physical Activity Questionnaire Short Form (IPAQ-SF): A systematic review. *Int J Behav Nutr Phys Act* 2011;8:115.
20. Saglam M, Arikan H, Savci S, et al. International physical activity questionnaire: Reliability and validity of the Turkish version. *Percept Mot Skills* 2010;111:278-84.
21. Bocci V, Borrelli E, Travagli V, Zanardi I. The ozone paradox: Ozone is a strong oxidant as well as a medical drug. *Med Res Rev* 2009;29:646-82.
22. Bocci V, Luzzi E, Corradeschi F, et al. Studies on the biological effects of ozone: 4. Cytokine production and glutathione levels in human erythrocytes. *J Biol Regul Homeost Agents* 1993;7:133-8.
23. Larini A, Bocci V. Effects of ozone on isolated peripheral blood mononuclear cells. *Toxicol In Vitro* 2005;19:55-61.
24. Valacchi G, Bocci V. Studies on the biological effects of ozone: 10. Release of factors from ozonated human platelets. *Mediators Inflamm* 1999;8:205-9.
25. Martínez-Sánchez G, Schwartz A and Donna VD: Potential Cytoprotective Activity of Ozone Therapy in SARS-CoV-2/COVID-19. *Antioxidants* 2020;9:389.
26. Bocci V, Zanardi I, Travagli V. Ozonation of human HIV-infected plasmas for producing a global vaccine: How HIV-patients may help fight the HIV pandemia. *Virulence* 2010;1:215-7.
27. Viebahn-Hänsler R, Leon Fernández OS, Fahmy Z. Ozone in Medicine: The Low-Dose Ozone Concept—Guidelines and Treatment Strategies. *Ozone: Science and Engineering* 2012;34:408-24.
28. Thevarajan I, Nguyen THO, Koutsakos M, et al. Breadth of concomitant immune responses prior to patient recovery: A case report of non-severe COVID-19. *Nat Med* 2020;26:453-5.
29. Nieman DC, Wentz LM. The compelling link between physical activity and the body's defense system. *J Sport Health Sci* 2019;8:201-17.
30. Laddu DR, Lavie CJ, Phillips SA, Arena R. Physical activity for immunity protection: Inoculating populations with healthy living medicine in preparation for the next pandemic. *Prog Cardiovasc Dis* 2020;S0033-0620:30078-5.
31. Fletcher GF, Landolfo C, Niebauer J, et al. Promoting physical activity and exercise: JACC health promotion series. *J Am Coll Cardiol* 2018;72:1622-39.
32. Cooney G, Dwan K, Mead G. Exercise for depression. *JAMA* 2014;311:2432-3.
33. Aylett E, Small N, Bower P. Exercise in the treatment of clinical anxiety in general practice - a systematic review and meta-analysis. *BMC Health Serv Res* 2018;18:559.
34. Fallon K. Exercise in the time of COVID-19. *Aust J Gen Pract* 2020;49:1-2.
35. Chen P, Mao L, Nassis GP, et al. Returning Chinese school-aged children and adolescents to physical activity in the wake of COVID-19: Actions and precautions. *J Sport Health Sci* 2020;9:322-4.