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Ozone therapy in chronic diseases; a narrative review of the literature

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ABSTRACT

Nitric oxide (NO) has various physiological and biochemical effects. In many biological systems of the body, NO acts as a messenger molecule via cyclic guanosine monophosphate (cGMP), which affects the body cells. NO is synthesized in the body from the L-arginine amino acid by the NO synthases enzyme. This enzyme consists of three major isoforms including neurotransmitter, endothelial and inductive types. According to the results of numerous studies, the administration of ozone as a complementary therapy of the diseases is a less complicated and cost-effective way. Over the past forty years, the results of ozone therapy have been satisfactory and without any problems. Ozone therapy affects various diseases. For example, in treatment for vascular diseases and some degenerative diseases, it has an ameliorative impact. Regarding kidney disease, still many experimental or clinical studies are necessary to find its improvement/anti-oxidative effect.

Review

Implication for health policy/practice/research/medical education:
Ozone therapy in treatment of various diseases such as vascular diseases and diabetic foot has an ameliorative impact. Regarding kidney disease, still many experimental or clinical studies are necessary to find its improvement/anti-oxidative effect.

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Introduction

NO (nitric oxide) is a gas with a short half-life (several seconds) with various physiological and biochemical effects. In many biological systems of the body, NO acts as a messenger molecule via cyclic guanosine monophosphate (cGMP), which affects the body cells. Nitric oxide is synthesized in the body from the L-arginine amino acid by the nitric oxide synthases enzyme. This enzyme consists of three major isoforms including neurotransmitter, endothelial and inductive types (1). Ozone therapy, or in particular, the original one (O3-AHT) has been used for almost 40 years. The first report on ozone therapy was published by Wolff in 1974 (2). Although ozone therapy is currently used throughout the world, it has not been legally accepted in all countries as a traditional medicine. About two decades ago, nitrogen oxides (NO) and carbon monoxide (CO) were discovered as toxic pollutants of the air or gases resulted from cigarette smoke. Today, however, they are considered as essential gases because NO and CO are the agents of great physiological actions in the body (3,4). Toxic compounds and their effects in the body are constantly changing while, their toxicity is dose dependent. Ozone therapy leads to improvement of circulation and oxygen delivery in ischemic tissues due to increased levels of intraerythrocytic 2, 3-DPG. Increasing metabolism by improving oxygen delivery, adjustment of cell antioxidant enzyme and induction of HO-1 and HSP70, activating the immune system and increasing the growth factor release. By stimulating the neuroendocrine system, ozone therapy, may result in promoting health in most patients. Additionally, it may activate neuroprotective system (2). Ozone therapy does not produce acute or late complications.

Ozone therapy affects the improvement of various diseases. For example, it is the most appropriate treatment for vascular diseases and some degenerative diseases,

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while acute and chronic infectious diseases such as HIV infection and chronic C hepatitis cannot be treated by ozone (2,5).

The results of studies on peripheral obstructive arterial diseases (POADs) showed that 13 to 18 sessions of ozone therapy led to improved blood flow to the peripheral arteries (2).

Considering that, the constant obstruction of the limb arteries due to atherosclerosis, diabetes, or Buerger's disease can lead to reduced blood flow to the limb, therefore ozone application can result in an increase in limbic blood circulation (2,6). Ozone initially leads to the activation of glycolysis by increasing adenosine triphosphate (ATP) and 2,3-phosphoglycerate (2, 3-DPG). As a result, the hemoglobin-oxidative sigmoid binding curve moves to the right and increases the oxygen emission in ischemic tissues (1-3). Ozone has different effects on biological systems in the body. In the cardiovascular system, it acts as a blood vessel relaxant derived from endothelium (endothelium derived relaxing factor; EDRF) (1,7). It plays a role in the central nervous system as a neurotransmitter in neutrophil cytotoxicity, platelet aggregation, bloodstream, synaptic transmission, and long-term memory enhancement (8,9). It plays a role in ovulation and menstruation, capacity building and sperm motility (1). It also plays a protective role in the digestive system and is effective in secretion, absorption and gastrointestinal movements (10). In the immune system it has anti-viral, antimicrobial, immune-suppressant and cytotoxic and cytoprotective effects (8). It is also administered as a lung vascular relaxant and bronchodilator in infants with chronic pulmonary hypertension and in patients with acute respiratory distress syndrome and during cardiac surgery and also organ transplantation (1). Ozone can have antimicrobial properties in gaseous forms and ozonated solutions. In this case, high concentrations of ozone are used. In addition, ozone can also enhance the phagocytic system in this state (11). Other studies have also shown the effect of this substance on the elimination of protozoa, such as giardia and its cyst (12). Ozone induces fibrinolytic properties at low concentrations, and increases the thrombotic properties of the blood at high concentrations in the form of external use (11). At high concentrations, it can have anti-inflammatory effects. This substance can have extensive anti-inflammatory effects by controlling the nucleus factor related to the kappa translation (NFκB) and inducing the nuclear factor erythroid 2-related factor 2 (Nrf2). Nuclear factor-κB (NF-κB), induces several inflammatory processes while, Nrf2 has known, to have anti-inflammatory effects (2, 13). Low concentrations of NF-κB can cause oxidation of binary bonds of prostaglandins and other arachidonic acid derivatives. This change, unlike what was said about high concentrations of ozone, can induce inflammatory processes. Ozone has an analgesic and antioxidant effect. In other words, ozone leads to increased activity of antioxidant enzymes such as catalase, superoxide dismutase and glutathione peroxidase. Antioxidant properties are the basis for the administration of this substance in the treatment of diseases associated with increased oxidative stress such as diabetes and diabetic foot. Ozone also helps neutralize oxidant and toxic substances (14). Ozone is also administered in treating age-related macular degeneration (ARMD) patients, a treatment that can dramatically improve the patient's quality of life. A study by Sweet et al showed that ozone is not able to reach cancer cells in the body. On the other hand, some studies have shown that ozone has an effect on liver or lung metastasis (2). Ozone is most commonly used in children to treat primary caries lesions of the tooth. This method eliminates tooth decay and can cause tooth rejuvenation (15,16). Chronic diseases lead to increased living costs, decreased well-being, depression and quality of life. The results of a study showed that after ozone therapy, spotting, pain, itching, heavy legs, insomnia, appetite, or weakness in vision is severely reduced, while general welfare and quality of life are increased (17). Insulin or ozone therapy alone can significantly reduce the effects of diabetes, but the combination of insulin and ozone is more effective in controlling diabetes than mono-therapy. The results of a recent study showed that ozone supplementation in diabetic rats reduces the levels of oxidative stress markers and the activity of renal antioxidant enzymes. Ozone therapy may be useful for the treatment of diabetic patients, especially by mediating antioxidant responses (18). The results of another study after receiving 200 mg of ozone for twenty days showed that in the case group, blood glucose and oxidative stress have decreased in comparison to the control group. Additionally, the superoxide dismutase has also increased. Accordingly, diabetic wounds have recovered more, and the amputation in the case group was lower than the control group (19). Ozone also has extensive local application in infections of skin or mucosal lesions. Importantly, compared to antibiotics, ozone therapy leads to significant improvement in infectious diseases and skin lesions (20). Ozone affects back pain and leads to pain relief (21).

Common ways to treat by ozone

Major autohemotherapy with ozone/oxygen mixtures

In this method, neutral glass bottles (sterile and vacuumed with anticoagulant) are used. These bottles are filled with 50-100 mL of venous blood belonging to the patient. The blood immediately combines with specific concentration and volume of ozone based on the type of disease and the stage of disease progression and then returns to the patient's body through the vein (11,12,22).

Minor autohemotherapy with ozone/oxygen mixtures

This method is administered to create an excitatory effect in cases of immune system weakness. Following

the application of this simple procedure, 5-10 mL of venous blood combines with a specific concentration and a volume of ozone, then is injected muscularly into the patient (2,7).

Subcutaneous, intradermal, intra-muscular and intra-articular injections

In all of these methods, an ozone-oxygen mixture is used in the gas phase. The administration of ozone in these conditions has anti-inflammatory and analgesic effects too(23).

Rectal insufflations with ozone/oxygen mixtures

These injections are carried out with a Janet syringe and with the help of a poly vinyl chloride tube while the patient is lying down to the left and has bent his knees toward his abdomen. Two hours before the enema is performed, the bowels are prepared for the patient. Rectal enema is performed with a mixture of ozone and oxygen at a concentration of 10-10 mg/L while, a volume of 1000-150 mL depends on the underlying pathology and its course, and also the stage of the disease (11, 12).

Vaginal insufflations with ozone/oxygen mixtures, are conducted with ozone concentration of 2-2.5 mg/L in ozone/oxygen mixtures with the gas rate of 0.5 to 1 L/min for 5-10 minutes (11,12).

Ozone bagging

This method has the greatest effect on the treatment of septic ulcers, bedsore and burns. Before doing the procedure, the involved lower limb is moistened with water or saline and then inserted into an air tight plastic bag and completely fastened. First, the air is completely removed from the bag and then the bag is filled up with the gas mixture until it reaches the doubled pressure and it remains in the same state for 15-20 minutes. In patients afflicted to vascular diseases, if the skin surface is not involved ozone is used at a high concentration of 1-8 mg/L. In cases with purulent ulcers, the wound should be covered with saline or ozonated water. To disinfect the wound in this method the concentration of ozone at the beginning is 1-5 mg/L, and in the stage of the granulated tissue formation reduces to 1-2 mg/L (1, 2).

Ozonated water

Ozone mixed with water at a concentration of 5 mg/L in a glass bottle. Ozonated water is widely used in the treatment of surgical ulcers and in gynecology. Ozonated water is used, like drinking water via the mouth, in the stomach and intestinal diseases such as esophagitis, gastritis and ulcers. It is also used for inflammation of the intestine for enema. In the context of oral diseases, ozonated water is used as mouthwash to disinfect the oral cavity in stomatitis and dental injuries. One of the important points in using this mixture is to apply it within 90 minutes of its preparation (2).

Ozonated oil

Antimicrobial activity of ozonated oil is several hundred times more than saline. For ozonation, pure sunflower, olive or olive corn are used. Ozone and vegetable oil are mixed at different concentrations and times.

Ozonated oil should be away from direct sunlight, thus it will be kept in dark glass bottles. It can be used for four months in room temperature if the proper conditions for its maintenance are met and it can be used for up to two years if stored in a refrigerator. The amount of consumed ozonated oil is one teaspoonful orally in 20-90 minutes before each meal and 2-4 times a day, which can be gradually increased to one tablespoonful 2-4 times a day (11).

Contraindications of ozone therapy

First, all cases with blood coagulation disorders. Second, bleeding of organs. Third, thrombocytopenia. Fourth, allergy to ozone. Fifth, hemorrhagic or apoplectic stroke and finally, sixth is ozone intolerance (11,12).

Conclusion

According to the results of numerous studies, the administration of ozone as a complementary therapy of the diseases is a less complicated and cost-effective way. Over the past forty years, the results of ozone therapy have been satisfactory and without any problems.

Authors' contribution

Primary draft by AHD. MMA, edited the paper. MAD, finalized the edit and completed. All authors read and signed the final manuscript.

Conflicts of interest

The author declared no competing interests.

Ethical considerations

Ethical issues including plagiarism, double publication, and redundancy have been completely observed by the authors.

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References

1. Mirzaei F, Khazaei M. Role of nitric oxide in biological systems: A systematic review. J Mazandaran Univ Med Sci. 2017;27:192-222.
2. 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. doi: 10.1186/2045-9912-1-29.
3. Morse D, Sethi J, Choi AM. Carbon monoxide-dependent signaling. Crit Care Med. 2002;30:S12-S7.
4. Nakao A, Sugimoto R, Billiar TR, McCurry KR. Therapeutic antioxidant medical gas. J Clin Biochem Nutr. 2009;44:1-13. doi: 10.3164/jcbn.08-193R.
5. Kazancioglu HO, Erisen M. Comparison of low-level laser

therapy versus ozone therapy in the treatment of oral lichen planus. Ann Dermatol. 2015;27:485-91. doi: 10.5021/ad.2015.27.5.485.
6. Isik A, Peker K, Gursul C, Sayar I, Firat D, Yilmaz I, et al. The effect of ozone and naringin on intestinal ischemia/reperfusion injury in an experimental model. Biomed Res Int. 2015;21:38-44. doi: 10.1155/2015/598980.
7. Zhao Y, Vanhoutte PM, Leung SW. Vascular nitric oxide: Beyond eNOS. J Pharmacol Sci. 2015;129:83-94. doi: 10.1016/j.jphs.2015.09.002.
8. Choudhari SK, Chaudhary M, Bagde S, Gadbail AR, Joshi V. Nitric oxide and cancer: a review. World J Surg Oncol. 2013;11:118. doi: 10.1186/1477-7819-11-118.
9. Ying L, Hofseth LJ. An emerging role for endothelial nitric oxide synthase in chronic inflammation and cancer. Cancer Res. 2007;67:1407-10. DOI:10.1158/0008-5472.CAN-06-2149.
10. Wiest R, Groszmann RJ. The paradox of nitric oxide in cirrhosis and portal hypertension: too much, not enough. Hepatology. 2002;35:478-91. DOI: 10.1053/jhep.2002.31432.
11. Izadi M, Joneidi Jafari N, Heydary B, Asadi P, Olmedo J, Marques J. The role of ozone in the treatment of chronic wounds. J Mil Med. 2014;16:105-13.
12. Izadi M, Adib Zadeh A, Rezaeean M, Jamaran H, Babayee Z, Farnia S. Evaluation of ozone effectivity on removal of giardia cysts in water. J Mil Med. 2008;10:113-8.
13. DASTAN SAM, MASOODI H, SALEHI A. Use of ozone to treat wounds. Cumhuriyet Science Journal. 2015;36:1365-73.
14. Bocci V, Zanardi I, Huijberts MS, Travagli V. Diabetes and chronic oxidative stress. A perspective based on the possible usefulness of ozone therapy. Diabetes Metab Syndr. 2011;5:45-9. doi: 10.1016/j.dsx.2010.05.014.
15. Bocci VA. Scientific and medical aspects of ozone therapy. State of the art. Arch Med Res. 2006;37:425-35. doi: 10.1016/j.arcmed.2005.08.006.
16. 16.Nogales CG, Ferrari PH, Kantorovich EO, Lage-Marques J. Ozone therapy in medicine and dentistry. J Contemp Dent Pract. 2008;9:75-84.
17. Bocci V, Zanardi I, Travagli V. Oxygen/ozone as a medical gas mixture. A critical evaluation of the various methods clarifies positive and negative aspects. Med Gas Res. 2011;1:6. doi: 10.1186/2045-9912-1-6.
18. Bocci V, Zanardi I, Travagli V. Ozone: a new therapeutic agent in vascular diseases. Am J Cardiovasc Drugs. 2011;11:73-82. doi: 10.2165/11539890-000000000-00000.
19. Martínez-Sánchez G, Al-Dalain SM, Menéndez S, Re L, Giuliani A, Candelario-Jalil E, et al. Therapeutic efficacy of ozone in patients with diabetic foot. Eur J Pharmacol. 2005;523:151-61. doi: 10.1016/j.ejphar.2005.08.020.
20. Valacchi G, Lim Y, Belmonte G, Miracco C, Zanardi I, Bocci V, et al. Ozonated sesame oil enhances cutaneous wound healing in SKH1 mice. Wound Repair Regen. 2011 ;19:107-15. doi: 10.1111/j.1524-475X.2010.00649.x.
21. Murphy K, Elias G, Steppan J, Boxley C, Balagurunathan K, Victor X, et al. Percutaneous treatment of herniated lumbar discs with ozone: investigation of the mechanisms of action. J V I R. 2016;27:1242-50. e3.
22. Travagli V, Zanardi I, Bernini P, Nepi S, Tenori L, Bocci V. Effects of ozone blood treatment on the metabolite profile of human blood.Int J Toxicol. 2010 ;29:165-74. doi: 10.1177/1091581809360069.
23. Bromberg PA. Mechanisms of the acute effects of inhaled ozone in humans. Biochim Biophys Acta. 2016;1860:2771-81. doi: 10.1016/j.bbagen.2016.07.015.

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