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Review Article

Review on Ozone-Based Alternative Medical Therapy

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ABSTRACT

Ozone therapy is an ozone-based alternative medical therapy that involves injecting ozone into the body. Its effects are well-established, repeatable, and safe, with few and easily avoidable negative effects. However, the US Food and Drug Administration (FDA) banned all medicinal applications of ozone in 2003, noting that "ozone is a hazardous gas with no recognised effective medical application". Every therapy has benefits and drawbacks, but in order for a therapy to succeed in the market, benefits must always exceed drawbacks. In recent years, ozone has been criticised and emphasised in connection to therapeutic effectiveness and toxicity. Its usage has become more popular in recent years, it has been emphasised for its potential therapeutic advantages when taken according to well-defined and safe procedures. Ozone therapy is becoming more popular in various parts of the world. Bisleri Trust has initiated activities in India under the platform Ozone Forum of India. Ozone treatment is commonly used in Russia and Cuba, and the therapy is based on the use of low concentrations. The regularisation of ozone therapy is important because it is necessary that the authorities implement the legislative rules in accordance with their spirit and content.

Keywords: Ozone, Ozone therapy, Ozone forum of India, Ozone toxicity, Bisleri trust

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INTRODUCTION

In 1840 Christian Friedrich Schonbein, coined the term Ozone from the Greek word ozein. Ozone is a three-atom based natural gaseous molecule. Ozone therapy is a bio-oxidative therapy in which ozone is used as an agent curing various diseases. Various forms used are gas dissolved in water or oil base depending on the ease (Talukdar A, *et al*., 2015; Baysan A and Beighton D, 2007).

The ozone gas is colourless, has an unpleasant odour. Despite the fact that O_3 has potentially dangerous side effects, researchers feel it has a wide range of medical uses. Due to the introduction of precision medical O_3 generators, clinical trials have only recently been able to investigate the mechanisms, action, and toxic effect of O_3. When present in smog, ozone has the ability to oxidise organic molecules, causing well-known respiratory problems. The gas produced by medical grade equipment is commonly used in medical practise. It is administered in therapeutic doses, but care is taken that inhalation route should not be involved, but it has numbers of health benefits in the prevention of dental caries, blood cholesterol reduction, antioxidative response stimulation, resting muscle oxygenation modification, in hypoxic and ischemic syndromes (Elvis AM and Ekta JS, 2011; Razumovskii SD and Zaikov GE, 1984; Bocci V, 1996).

LITERATURE REVIEW

Despite the fact that ozone was first synthesised in May 1840, it took a long time for ozone therapy to acquire popularity in the medical community. However, since the 1960s, the slow, constant, and increasing use of ozone therapy, mostly in Germany and the former Soviet Union, has rekindled interest in the scientific application of ozone therapy in accordance with previously approved protocols. Ozone therapy grew popular in a number of European countries during the next few decades, most notably Italy, Spain, and lastly Cuba. China became another country where the therapy gained traction after its introduction in 2000. In today's world, therapy is gaining popularity in a number of countries According to the data, ozone therapy is employed in over 50 countries around the world by over 40 national and international organisations, including the International Scientific Committee on Ozone Therapy ($ISCO_3$). Germany now has over 30 000 practising ozone therapists, making it the first country with more than 11,000 practitioners. With 5000 people, China comes in second. With 3500 professionals, Russia ranks third, followed by Italy with 3000.

Dr. Sergei Petrovich Peretyagin is largely credited with developing ozone therapy in Russia. Sergei uncovered the explanation while still a student at the locksmith school. Since then, he's realised the need of acquiring the necessary knowledge and skills to unlock the scientific doors of medicine as a master key. Thanks to his patient and often gruelling labour, Dr. Sergei Peretyagin was able to open many doors in the reluctant health industry to employ modern medical technologies. He has been so successful that ozone therapy is now taught at the university and post-graduate levels in Russian medical centres as normal practise (Quintero R and Schwartz A, 2017).

Physicians are currently treating diseases such as Skin infections, Rheumatism, Respiratory problems, Malignant Tumours, Cerebral Sclerosis, and Cirrhosis of the Liver, Diarrhoea, and Fungal Diseases. Ozone therapy is still a divisive supplementary medicine technique. Various regulatory organisations in United States and Canada have forced numerous physicians and clinics that provide this form of therapy out of business. In other parts of the world, however, this therapy has risen in popularity and validity during the previous 10 years. Ozone therapy is largely available in Mexico, the Bahamas, Cuba, and the Dominican Republic in the Caribbean, and Europe, particularly Germany and Eastern Europe (Ministry of Health, 2005).

It works by various mechanisms like Inactivation of cell membranes of various micro-organisms like bacteria, viruses, fungi, yeast, protozoa, activation of oxygen metabolism, immunostimulating action and action on the human lung. Through the oxidation of phospholipids and lipoproteins, ozone therapy compromises the structure of the bacterial membranes (Pryor WA, *et al*., 1995; Roycroft JH, *et al*., 1977). O_3 limits cell development in fungi at specific stages. By interrupting virus-to-cell interaction *via* peroxidation, it destroys the viral capsid and damages the life cycle of viruses (Bocci V, 1992). It raises the rate of glycolysis in red blood cells. This causes 2, 3 diphosphoglycerate to be stimulated, resulting an increase in the supply of oxygen released to the tissues. Ozone stimulates Adenosine triphosphate (ATP) generation *via* boosting oxidative carboxylation of pyruvate, which initiates the Krebs cycle. The release of interleukin-2 triggered a major reaction of immune reactions (Elvis AM and Ekta JS, 2011) *(Figure 1)*.

Medical ozone can be used locally or parentally. The various ozone application routes can be employed together or separately to provide a synergistic effect (di Filippo C, *et al*., 2010).

The following are some of the parenteral ozone application methods:

• Major Autohemotherapy (AHT major)-The amount of blood to utilise ranges from 50 mL to 100 mL.

• Minor Autohemotherapy (AHT minor)-The amount of blood that should be used is 5 ml.

• Intramuscular injection in the paravertebral region-The conventional paravertebral infiltration involves finding the upper portion of the spinous process and injecting 5 mL of ozone at (10-20) g/NmL into the cervical and dorsal column 1.5 cm.

It can be applied locally in the following ways:

Topical application of water, oil, or ozonized creams- Ozone in water and ozonized oil are used to treat wounds, burns, herpetic lesions, yeast infections, insect bites, dental infections, surgical cavity cleaners, and a variety of diseased lesions at different concentration: high, medium, and low, depending on the goal (to disinfect, to regenerate) and the type of tissue.

Saline Solution with Oxygen- The use of Ozonized Saline Solution (OSS) as a systemic administration of ozone is common in Russian and Ukrainian schools, and the practise is widespread in these two nations.

The Ozone Forum of India, which is supported by the Bisleri Charitable Trust, strives to promote ozone therapy as a cost-effective alternative treatment. The Ozone Forum of India has done extensive study on tuberculosis, cancer, pain management, and COVID-19. Since 2001, it is advocating Ozone Therapy and has reached out to over 1, 50, 000 people around the country. Over 83 training events have been conducted by the Ozone Forum of India, and over 2000 doctors have been taught across the country. Shewri Government Tuberculosis Hospital, LG Hospital in Ahmedabad, and Sion Hospital in Mumbai are among the Forum's partners (Bisleri, 2022) *(Figure 2)*.

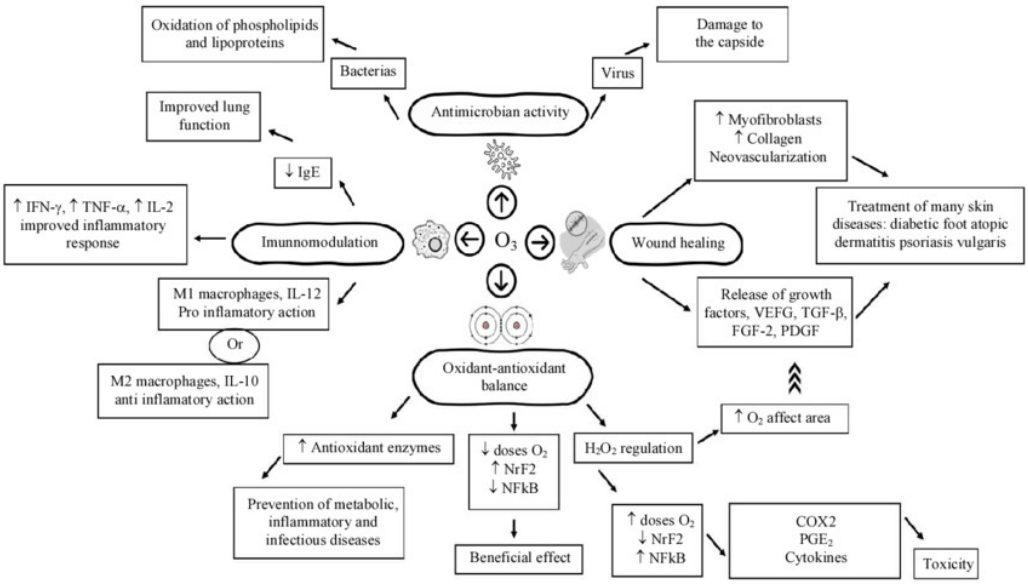

Figure 1: Various mechanism of action of Ozone

Figure 2: Ozone Forum of India, Mumbai

The Ozone Forum of India has conducted two significant trials in the treatment of COVID 19 in collaboration with Lokmanya Hospital in Pune, and the NeuroGen Brain and Spine Institute in Mumbai. Dr. Mili Shah, President, Ozone Forum of India and Trustee, Bisleri Charitable Trust says "In this crisis period of fighting the epidemic and its resurgence, we need to blend understanding of conventional medicine with natural healing techniques. We are pleased to inform that ozone therapy is helpful in COVID 19 patients, as evidenced by both study reports, and is also very cost effective. Its antibacterial properties aid patients in recovering quickly and preventing recurrence (Sharma M and Hudson JB, 2008; Johansson E, *et al*., 2009). The Ozone Forum of India has been investigating this therapy for the past 18 years, and we are only too happy to share our findings in order to aid this pandemic and the greater good of humanity. Our goal is to raise awareness of Ozone Therapy among more doctors and patients, and we've already reached out to over 2400 clinicians around the country who believe in and utilise it successfully." On the occasion of World Tuberculosis Day on March 24, it was reported that integrative medicine primarily works on tuberculosis patients who have been prescribed scientifically established medications, resulting in unpleasant drug reactions. Ozonated water and saline, aids in the recovery of patients and the elimination of pus, while also enhancing their overall health. Most importantly, within a month, patients appetites recover and they restore their weight. In Mumbai, approximately 400 patients received ozone therapy and have been helped to recover. "Tuberculosis causes severe irreversible effects to the lungs," says Dr. Lalit Kumar Anande, who specialises in drug resistance, Tuberculosis (TB) complications, and anti-oxidant therapies. Empyema (Pus in the Chest) is a common complication that requires the introduction of an intercostal tube into the chest to remove the pus. Added to this were the patients' horrible drug-resistance, as well as their mental sadness and severe unpleasant consequences from taking so many antibiotics. The highly quick acting Antimicrobial, Antioxidant, and Anti-Inflammatory characteristics of Ozone therapy in such numerous circumstances helped the patients to survive (Biospectrum, 2022).

Disadvantages of Ozone therapy

One explanation for ozone therapy's lack of popularity in medicine is that its toxicity is equated to that of Reactive Oxygen Species (ROS) (Pryor WA, *et al*., 1995; Donovan DH, *et al*., 1977; Mustafa MG, 1990). In fact, there are significant distinctions because ozone therapy is only used once in a while and can be managed, whereas endogenous ROS production continues unabated throughout life.

The terrain of ROS formation also varies, mitochondria, which converts 95% of inhaled oxygen to harmless water, which are the main source of ROS because at least 3% of oxygen is converted to superoxide. Superoxide dismutase (SOD) disproportionate superoxide to H_2O_2 and can generate dangerous non-specific hydroxyl radical OH in the presence of Fe^{2+}. A 70 kg human produces 0.147 mol or more than 5 g of superoxide per day, while AHT produces less than 18 mg of ozone or less than 0.4% of the minimum daily superoxide output. A small amount of hydrogen peroxide is produced directly by the redox enzyme (NOX) NADPH oxidase. Currently, there is widespread consensus that regular production of hydrogen peroxide is required for cell survival, and the new concept is that "reactive species are not only a tool for cell distress, but also a tool for normal cell physiology." Mitochondrial DNA damage is about 10 times more oxidized than nuclear DNA and permanently damaged, but is explained by the formation of endogenous ROS in mitochondria deeply embedded in cells. Ozone, on the other hand, acts externally on plasma, which contains large amounts of antioxidants. However, the amount of ozone supplied to the blood must reach a certain level in order to produce enough H_2O_2. Only 10% of H_2O_2 migrates from plasma to the cytoplasm of blood cells and has a variety of biological effects. For ozone to work, it is necessary to create a calculated temporary acute oxidative stress that the antioxidant system can quickly correct. Therefore, the formation of peroxy radicals and hydroxyl aldehydes is unmistakable, but the presence of residual OH and HOCl is rapidly neutralized by various antioxidants in plasma. It is noteworthy that all important cellular components such as enzymes, proteins, RNA and DNA are spared during extracellular ozone depletion. Ozone therapy is widely regarded as "barbaric" therapy, especially in the United States, and malicious ozone therapists and quack are doing their best to spread that awareness (Fuccio C, *et al*., 2009).

Regardless of the fact that ozone therapy is frequently used to treat a variety of disorders, doctors should be aware of potential risks. There was a case of sinus arrest, cardiac arrest, and major disc expulsions or huge fragments in the spinal canal, all of which resulted in secondary brain injury. It's possible that the issues go unnoticed. Even rarer are fatal consequences, which are rarely reported. The example of an 80-year-old woman with lower back discomfort caused by a bulging lumbar disc is described. She was given intradiscal O_2-O_3 therapy and died after three treatments. Her death was caused by a pulmonary embolism, based on her clinical symptoms. Her lumbar spine was examined using Computed Tomography (CT) and magnetic resonance imaging, which revealed symptoms of disc arthrosis and a L4-L5 left disc protrusion. Her experience with nonsteroidal anti-inflammatory medications had been mixed. She also had short alleviation from physiotherapy sessions. Her overall health was excellent. She had no other illnesses, and her laboratory tests, as well as a heart examination and chest radiograph, were all normal. She chose O_2-O_3 treatment to alleviate her chronic lumbar discomfort. A periradicular injection of O_2-O_3, corticosteroid, and local anaesthetic was used in conjunction with a L4-L5 intradiscal O_2-O_3 chemonucleolysis. The researchers utilised a fluoroscopy-guided intradiscal mixture of O_2-O_3 (40 g/ml, 4 ml), betamethasone 4 mg, and lidocaine hydrochloride 100 mg. The patient noticed a small reduction in discomfort after the first two administrations. The patient told her family she was having problems breathing just before the third session, in the morning. She didn't mention any other symptoms, including chest pain. The emergency services were notified, and they arrived at her residence in 15 minutes. In the meantime, she had passed out. The patient was unconscious when she arrived at the hospital. The proper reanimation techniques were attempted, but the patient died (Chirchiglia D, *et al*., 2019; Marchetti D and la Monaca G, 2000).

DISCUSSION AND CONCLUSION

Ozone therapy is becoming more popular in various parts of the world. More than 40 national and international ozone groups, as well as more than 30,000 ozone therapists, vouch for this. Authorities are discussing this therapy more regularly. Its practise has been picked up by the media. There have been court cases, and research is being carried out despite restricted funding resources. However, for a variety of reasons, the criteria do not reflect the breadth of ozone therapy's utilisation. When it was outlawed in several regions for several years in outpatient private clinics, such popularity became a hurdle. Ozone is inexpensive, and unlike traditional treatments, it cannot be patented or packaged and marketed easily. The primary goal of ozone therapy is to improve the therapeutic outcomes that pharmacotherapies can provide in a variety of disorders. Would ozone therapy gain support from the pharmaceutical business, at least in terms of building up clinical trial teams, if it is positioned as a potential partner rather than a threat perhaps not; as a result, new avenues for ozone study must be investigated.

REFERENCES

1. Talukdar A, Langthasa M, Barman I. Ozone therapy: Boon to dentistry and medicine. Int J Pre Clin Dent Res. 2015; 2: 59-66.
2. Baysan A, Beighton D. Assessment of the ozone-mediated killing of bacteria in infected dentine associated with non-cavitated occlusal carious lesions. Caries Res. 2007; 41(5): 337-341.

3. Elvis AM, Ekta JS. Ozone therapy: A clinical review. J Nat Sci Biol Med. 2011; 2(1): 66.
4. Razumovskii SD, Zaikov GE. Ozone and its reactions with organic compounds. Studies in organic chemistry. 1984; 15.
5. Bocci V. Does ozone therapy normalize the cellular redox balance?: Implications for the therapy of human immunodeficiency virus infection and several other diseases. Med Hypotheses. 1996; 46(2): 150-154.
6. Quintero R, Schwartz A. The master key of the ozone therapy in Russia by Dr. Sergei Petrovich Peretyagin. Ozone Therapy Global Journal. 2017; 7(1): 91-98.
7. Ministry of Health. Health Technology Assessment- Report: Ozone Therapy. 2005; 6: 42.
8. Pryor WA, Squadrito GL, Friedman M. A new mechanism for the toxicity of ozone. Toxicol Lett. 1995; 82: 287-293.
9. Roycroft JH, Gunter WB, Menzel DB. Ozone toxicity: Hormone-like oxidation products from arachidonic acid by ozone-catalyzed autoxidation. Toxicol Lett. 1977; 1(2): 75-82.
10. Bocci V. Ozonization of blood for the therapy of viral diseases and immunodeficiencies: A hypothesis. Med Hypotheses. 1992; 39(1): 30-34.
11. di Filippo C, Cervone C, Rossi C, di Ronza C, Marfella R, Capodanno P, *et al*. Antiarrhythmic effect of acute oxygen-ozone administration to rats. Eur J Pharmacol. 2010; 629(1-3): 89-95.
12. Bisleri. Ozone Therapy. Bisleri International. 2022.
13. Sharma M, Hudson JB. Ozone gas is an effective and practical antibacterial agent. Am J Infect Control. 2008; 36(8): 559-563.
14. Johansson E, Claesson R, van Dijken JW. Antibacterial effect of ozone on cariogenic bacterial species. J Dent. 2009; 37(6): 449-453.
15. Biospectrum. Ozone therapy making greater impact in controlling COVID-19. Biospectrum. 2022.
16. Pryor WA, Squadrito GL, Friedman M. The cascade mechanism to explain ozone toxicity: The role of lipid ozonation products. Free Radic Biol Med. 1995; 19(6): 935-941.
17. Donovan DH, Williams SJ, Charles JM, Menzel DB. Ozone toxicity: Effect of dietary vitamin E and polyunsaturated fatty acids. Toxicol Lett. 1977; 1(3): 135-139.
18. Mustafa MG. Biochemical basis of ozone toxicity. Free Radic Biol Med. 1990; 9(3): 245-265.
19. Fuccio C, Luongo C, Capodanno P, Giordano C, Scafuro MA, Siniscalco D, *et al*. A single subcutaneous injection of ozone prevents allodynia and decreases the over-expression of pro-inflammatory caspases in the orbito-frontal cortex of neuropathic mice. Eur J Pharmacol. 2009; 603(1-3): 42-49.
20. Chirchiglia D, Chirchiglia P, Stroscio C, Volpentesta G, Lavano A. Suspected pulmonary embolism after oxygen-ozone therapy for low back pain. J Neurol Surg A Cent Eur Neurosurg. 2019; 80(6): 503-506.
21. Marchetti D, la Monaca G. An unexpected death during oxygen-ozone therapy. Am J Forensic Med Pathol. 2000; 21(2): 144-147.