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Ozone: An Emerging Prospect In Dentistry

[1] Megha Gupta
[2] Abhishek

[1] Senior Lecturer, Department Of Pedodontics And Preventive Dentistry, Vyas Dental College, Jodhpur.
[2] General Practitioner

Address For Correspondence:
Dr. Megha Gupta, Senior Lecturer,
Department Of Pedodontics And Preventive Dentistry
Vyas Dental College, Near Kuri Hod, Pali Road,
Jhalamand, Jodhpur - 342005, Rajasthan, India.
Telephone No : +918769395750
Email ID: meghaaguptaa@yahoo.com,
meghamcods@gmail.com

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Abstract
Ozone – a triatomic highly oxidizing agent with high range of therapeutic and antimicrobial properties has been used in medicine for over 100 years. Its bactericide, virucide and fungicide effects are based on its strong oxidation effect with the formation of free radicals as well as its direct destruction of almost all microorganisms. This potentially beneficial agent has been used in dentistry also. Ozone has a wide application in dentistry which includes treatment of carious lesions, root canal disinfection, wound healing impairments after surgical interventions, plaque control, disinfection of dentures etc. There are certain limitations also, which is because of the scarcity of randomized double-blind clinical controlled trials. The objective of this article is to provide an overview of the current applications of ozone in dentistry. Research was based on peer-reviewed sources found through a Medline/Pubmed search and other journals.

Key Words
Ozone, Ozone Therapy, Oxidation, Caries.

Introduction

Ozone (also known as triatomic oxygen and trioxygen O_3, molecular weight 47.98g/mol) is a naturally occurring compound consisting of three oxygen atoms. It is found in nature, in the form of a gas in the stratosphere in a concentration of 1-10 ppm, being continually created from and destroyed into molecular O_2. [1] Ozone in stratosphere has a critical role in both the thermal structure of the stratosphere as well as the ecological framework for life on the Earth's surface. It is one of the most important gases in the stratosphere due to its ability to filter UV rays. This protective layer can be seen as the blue colored sky. [2]

There are three different systems for generating ozone gas:

- **Ultraviolet system:** produces low concentrations of ozone. It is used in esthetics, saunas, and for air purification.
- **Corona Discharge system:** produces high concentrations of ozone. It is the most common system used in the medical / dental field. It is easy to handle and it has a controlled ozone production rate.
- **Cold plasma system:** used in air and water purification. [2]

Historic Background

During World War I, ozone gas was used for treating gaseous post-traumatic gangrene, infected wounds, mustard gar burns and fistulas in German soldiers. [3] Ozone therapy was accepted as an alternative medicine in the U.S.A. from 1880 until 1932. [1] The German chemist Christian Friedrich Schonbein is considered to be the father of ozone therapy (1840). When he passed an electric discharge through water, a strange smell was produced, which he called Ozon, from the Greek word ozein (odor). [3] In dentistry, Dr. E.A. Fisch (1889-1966) was the first dentist to use ozonated water in his practice and introduced it to the German surgeon Dr. Erwin Payr (1871-1946) who used it from that time in surgery and reported his results at the 59th Congress of the German Surgical Society in Berlin(1935). [4]

Earlier, ozone therapy was difficult and limited due to the lack of ozone-resistant materials, such as Nylon, Dacron and Teflon, until 1950 when ozone-resistant materials were manufactured. At that time, Joachim Hansler, a German physicist joined Hans Wolff, another German physician, to develop the first ozone generator for medical use. Their design continues to be the basis for modern equipment. [3]

Properties Of Ozone

Ozone is dependent on systemic conditions like temperature and pressure, and decomposes to pure oxygen with a short half-life. At room temperature, ozone is a blue gas with a characteristic smell that can be noticed in air at a concentration of 2 ppm.

Ozone is thermodynamically highly unstable oxygen compound, which on decomposition produces molecular oxygen, atomic oxygen which is highly reactive; oxidizes all nonnoble metals immediately; and attacks numerous organic compounds as a radical. This makes ozone, apart fro[m] fluorine, one of the strongest oxidants. [5] When dissolved in water, ozone is relatively unstable and decomposition rate depends on quality of water and systemic conditions (temperature, mechanical movement of water, vessel material). [6]

Mechanism Of Action Of Ozone

Ozone can react with blood components (erythrocytes, leukocytes, platelets, endothelial cells and the vascular system) and positively affect oxygen metabolism, cell energy, the immunomodular property, antioxidant defense system, and microcirculation. Ozone, in the gaseous or aqueous phase, has been shown to be a powerful and reliable antimicrobial agent against bacteria, fungi, protozoa and viruses. [7] It is generally accepted that the oxidant potential of ozone induces the destruction of cell walls and cytoplasmic membranes of bacteria and fungi. During this process, ozone attacks glycoproteins, glycolipids, and other amino acids and inhibits and blocks the enzymatic control system of the cell. [8] This results in increase in membrane permeability, the key element of cell viability, leading to immediate functional cessation. Then ozone molecules can readily enter the cell and cause the microorganism to die. [7,9,10]

Also, ozone can attack many biomolecules, such as the cysteine, methionine, and the histidine residues of proteins. [10] By oxidizing the biomolecules featured in dental diseases, ozone has a severely disrupted effect on

cariogenic bacteria, resulting in their elimination. Pyruvic acid, is the strongest naturally occurring acid produced by acidogenic bacteria during cariogenesis. Ozone can decarboxylate pyruvic acid to acetic acid.[11] This also helps in buffering plaque fluid.[12]

Enteroviruses, rotaviruses,[13] hepatitis A[14] and human immunodeficiency viruses[15] are more ozone – sensitive than poliomyelitis and coxackieviruses. The main anti-viral actions of ozone are the change of the capsid and the irreversible destruction of viral DNA. [16] In bacterial cultures, Escherichia coli and Candida albicans are by far more ozone-sensitive than staphylococci. Ozone inhibits their metabolic activity, and the cell walls of the bacteria are primarily damaged. Bacteria can be completely destroyed by ozone-produced antibodies.[17]

Clinical Applications Of Ozone In Medicine

Gaseous pure ozone passes over the mucous membrane of the upper respiratory tracts essentially without absorption and can therefore reach the unprotected bronchioli and alveoli directly.[18] It also oxidizes enzymes, peptides and protein chains of cell membranes leading to the production of free radicals and peroxides. These can lead to vascular – inflammatory damage of the bronchioli and alveoli walls, forming fibrinous coats and destroying surfactants. Long- term exposure to high ozone concentrations can cause an acute collapse of the alveoli and bronchiole and potentially irreversible damage of the alveoli function.[19] Hence, pure ozone is not used for medical purposes.

Medical grade ozone is a mixture of pure oxygen and pure ozone in the ratio of 0.05% to 5% of O_3 and 95% to 99.95% of O_2. Due to the instability of the O_3 molecule medical grade ozone must be prepared immediately before use. Within less than an hour after preparation only half of the mixture is still ozone while the other half is transformed into oxygen. As a result, it is impossible to store ozone over long periods of time. In order to control the decomposition of O_3 into oxygen it can be associated with a vehicle with aqueous properties to promote the conversion more quickly or with a vehicle with more viscous properties to retard the conversion.[20]

The ozone- oxygen mixture is very tissue-friendly, revealing a positive effect on the flow properties of blood. It is based on a structural modification of the erythrocyte membrane that causes an inhibition of the surface Na^+-K^+ adenosinetriphosphatase (ATPase).[21] The effect of ozone on the erythrocytes changes the proteins of the cytoskeleton and increases the elastic molding properties of the membrane. This prevents adhesions between erythrocytes; their improved elasticity facilitates their passage through fine capillaries.[22] Apart from stimulating the blood flow, ozone also has strong bactericide, virucide and fungicide effects, making it possible therapeutic agent in inflammatory and infectious diseases. [23] Ozone can be used to treat a wide range of pathologies because of its high oxidative power and its effect on bacteria, viruses and fungi.

Ozone therapy has been a recognized treatment modality in 16 countries.[1] Its use has been investigated in treatment of ocular diseases (such as optic neuropathies, glaucoma, central retinal vein obstructions, and degenerative retinal diseases), acute and chronic bacterial, viral and fungal infections, ischemic diseases, age-related macular degeneration, orthopedic diseases, and dermatological, pulmonary, renal, hematological and degenerative diseases.[3]

Systemic administration of ozone gas has been carried out using different methods as described below:[3,4]

Major Autohemotherapy

This is an extracorporeal blood treatment with ozone gas followed by the intravenous reinfusion of the patient's treated blood. It is indicated for treatment of arterial circulatory disorders, infections, and for rheumatic arthritis. It is also useful in the promotion of immunoactivation, provides additive therapy for geriatric carcinoma patients.

Autohemothearpy promotes:

- Activation of red blood cell metabolism with an increase of 2,3-diphosphoglycerate and Adenosine Triphosphate (ATP) plus improving O2 release to the tissues.
- Activation of immunocompetent cells with release of cytokines, such as interferons and interleukins.

Minor Autohemotherapy

This is an extracorporeal blood treatment and intramuscular injection. It is indicated for allergies, acne, furunculosis and adjuvant cancer therapy. The mechanism of action deals with a non-specific activation and general stimulation of the immune-system.

Rectal O_3/O_2 Insuflation

This method of administration is indicated for arterial circulatory disorders, general immunoactivation, adjuvant cancer therapy, and hepatitis A,B,C. The effects are virtually equal to those of major autohemotherapy.

Clinical Applications Of Ozone In Dentistry

In dental surgery, ozonated water was used to promote hemostasis, enhance local oxygen supply, and inhibit bacterial proliferation.[24] Theoretically, ozone can reduce the bacterial count in active carious lesions and therefore, it may temporarily arrest the progression of caries, resulting in prevention or delaying the need for tooth restorations.[25] Hence, it has wide potential application in dental field.

Ozone therapy can be used for like treatment of sterilization of cavities, [24, 25, 26] chronic periodontitis,[9] endodontic treatment and root canal disinfection,[27,28] infections after tooth extractions, chronic wound healing impairments after radiotherapy, aphthae, mycoses[29] etc.

CurOzone USA Inc. (Ontario, Canada) developed the HealOzone. Ozicure and HealOzone are the two ozone generating systems commonly used.[20]

Ozone In The Management Of Dental Caries

Ozone is being used for the treatment of carious lesions, but studies have shown varied results. Significant reductions in the number of microorganisms in the carious lesions in vitro was seen after the application of ozone on pit and fissure caries, non-cavitated occlusal carious lesions and primary root caries.[24,26]

Fagrell et al in an in-vitro study, tested the effect of ozone on three different strains of mutans streptococci and one strain of Lactobacilli. They found bactericidal effect of ozone on all the four different strains of bacteria.[30]

Baysan et al, in an in-vitro study assessed the antimicrobial effect of the application of ozone gas on the microflora of infected dentin associated with non-cavitated occlusal carious lesions. The ozone failed to reduce the number of viable bacteria in the underlying infected dentin.[26] In another in vitro study, they showed that application of ozone gas for a period of 10 seconds was capable of reducing the numbers of Streptococcus mutans and Streptococcus sobrinus.[24]

Some authors have suggested an additional hypothesis for the working mechanism of ozone therapy in the treatment of dental caries. They stated that since ozone is a

potent oxidizer, it might promote remineralization of demineralized dentin. [31] However, Zaura et al in their study concluded that the exposure of gaseous ozone had no effect on remineralization and subsequent demineralization of remineralized dentinal lesions.[32]

Ozone In Endodontics

Ozone treatment in endodontics focuses on a high antimicrobial effect while minimizing injury to periapical tissues. Its antimicrobial action has been demonstrated against bacterial strains such as Micobacteria, Staphylococcus, Streptococcus, Pseudomonas, Enterococcus, Escherichia coli and Candida albicans using in-vitro research models.[7,33]

Nagayoshi et al evaluated the effect of ozonated water on Enterococcus faecalis and Streptococcus mutans in contaminated bovine teeth. A significant intratubular decrease of these bacteria was observed.[27] However, Estrela et al concluded that irrigation of infected human root canals with ozonated water, 2.5% NaOCl, 2% chlorhexidine and the application of gaseous ozone for 20 min was not sufficient to inactivate E. faecalis.[28]

Ozone can also be used for the decontamination of root surfaces of teeth avulsed in accidents prior to replantation. Ebensberger et al [34] reported that two-minute irrigation of the avulsed teeth with non-isotonic ozonated water might lead not only to a mechanical cleansing, but also decontaminate the root surface, with no negative effect on periodontal cells remaining on the tooth surface. There is a slight increase in the proliferation rate under ozone influence. Hence, ozone has its future in tooth transplantation or replantation also.[35]

Ozone In Prosthodontics

Microbial plaque accumulating on the fitted surfaces of dentures is composed of several oral microorganisms, mainly Candida albicans. Denture plaque control is essential for the prevention of denture stomatitis.[20]

Arita et al [7] assessed the effect of ozonated water in combination with ultrasonication on Candida albicans. Following exposure to flowing ozonated water (2 or 4 mg/l) for one minute they found no viable C albicans suggesting the application of ozonated water might be useful in reducing the number of C albicans on denture bases.

In another study, gaseous ozone revealed a more effective antimicrobial action than ozonated water and thus is more recommendable for disinfection of dentures.[36]

Suzuki et al examined the effectiveness of ozone cleaning on the surface of removable partial denture alloys (Co-Cr, Au-Ag-Pt, and Au-Cu-Ag-Pd). Ozone had little influence on the oxidation of dental alloys, unlike acid-electrolyzed water and the commercial denture cleaners.[37]

Ozone In Periodontics

Ozonated water (4mg/l) was found effective for killing gram-positive and gram-negative oral microorganisms and oral Candida albicans in pure culture as well as bacteria in plaque biofilm and therefore might be useful to control oral infectious microorganisms in dental plaque.[9]

In implant dentistry, the use of ozone is currently being investigated for the decontamination of the implant surface in peri-implant therapy.[38]

Ozone In Oral And Maxillofacial Surgery

Ozonated water is suitable for prophylactic applications against infections after osteotomies. Since ozone improves the rheological properties of erythrocytes and facilitates oxygen release in the tissues, it leads to vasodilatation of vessels and improved supply of blood to ischemic zones. Hence, it is useful in wound healing impairments post radiotherapy treatment, after surgical interventions like tooth extractions or implant dentistry.[29]

Ozone can be used as an alternative to hyperbaric oxygen therapy after the removal of the bone sequestra. [39] Its action is based on the enormous oxidation strength and on the fact that bacteria can be more easily recognized and destroyed by granulocytes and the complement system after contact with ozone. There is an increase in the phagocytosis performance of polymorphonuclear cells in the presence of ozone.[40,41]

Ozone Toxicity

Ozone inhalation can be toxic to the pulmonary system and other organs. The known side effects are epiphora, upper respiratory tract irritation, rhinitis, cough, headache, occasional nausea and vomiting. However, complications caused by ozone therapy are infrequent. In the event of an ozone intoxication, the patient must be placed in the supine position, inhale humid oxygen, and take ascorbic acid, Vitamin E and nacetylcysteine. Further, because of its high oxidative power, all materials that come in contact with the gas must be ozone resistant such as glass, silicon and Teflon.[20]

Ozone Therapy Containdications[20]

The following are contraindications for use of ozone therapy:

- Pregnancy
- Glucose-6-phosphate-dehydrogenase deficiency
- Hyperthyroidism
- Severe anemia
- Severe myasthenia
- Active hemorrhage

Conclusion

Since its introduction in 1840, ozone therapy is proving to be a new therapeutic modality with great benefits to the patients. The potent antimicrobial power of ozone, along with its capacity to stimulate the circulatory system and modulate the immune response, makes it a therapeutic agent of choice in the treatment of medical pathologies and infectious oral diseases.

Oxidative effect of ozone on the microbiota has been shown in several studies. However, varied results that have been obtained from different studies. This divergence of the study outcomes may be related to the methodological differences linked to the lack of in vitro and in vivo, long term randomized controlled trials and double blind studies.

The clinical application of ozone has not achieved strong level of efficacy and cost-effectiveness. There is good evidence of in vitro biocompatibility of aqueous ozone with human oral epithelial cells, gingival fibroblast cells and periodontal cells. Further, the use of ozone is an easy and painless treatment modality. There is still a need for the highest level of evidence, ie well designed; double-blind randomized clinical trials to justify the routine use of ozone as a treatment modality in dentistry. Scientific support, as suggested by demonstrated studies, show ozone to be a potential use in dentistry.

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