

OZONE THERAPY - BEATING THE ODDS

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Article Received on 12/06/2020

Article Revised on 02/07/2020

Article Accepted on 22/07/2020

ABSTRACT

Ozone (O₃) is a triatomic molecule, an allotropic form of oxygen that acts as an oxidant and oxidizer. It acts as an air pollutant and a constituent of urban smog, if it is present at the ground level; as a protective layer from ultraviolet rays when present in earth's upper atmosphere and as a medicine, when used on humans. Ozone has been used in medical field for more than 100 years but its use in dentistry has just begun to be explored. Its application in medicine and dentistry for the treatment of 260 different pathologies shows promising and better results as compared to conventional or conservative treatments alone. Its special antimicrobial property without the danger of antibiotic resistance which is prevailing in today's era, gives us a new ray of hope in effective treatment outcomes with minimal side effects. Ozone has a wide application in dentistry which includes treatment of carious lesions, as an effective agent against wound healing impairments after surgical interventions, root canal irrigation and disinfection, plaque control, disinfection of dentures etc. It has shown promising results in all the fields of dentistry in some way or the other. This molecule has the power to change the face of dentistry in a miraculous way. This article is a brief review consisting of the details of ozone therapy, its role and fate in dentistry.

KEYWORDS: Antimicrobial, Anti-inflammatory, COVID-19, Dentistry, Immunomodulatory, Ozone.**INTRODUCTION**

The word Ozone (O₃) is derived from the Greek word 'ozein' (odorant) due to its characteristic smell. E. A. Fisch, a German dentist, was the first person to use O₃ for disinfection and also to aid healing in his own practice.^[1] Dr Edwin Parr, a Swiss dentist who in the 1920's, started to use O₃ as part of his disinfection system and surgeries.^[2] Ozone used in medical field is essentially a composition of 0.1–5% ozone and 95–99.6% pure oxygen.^[3] Today, ozone therapy has shown success and miraculous outcomes with managing wound healing post surgery, dental caries, premalignant lesions like oral lichen planus, periodontal problems like gingivitis and periodontitis, halitosis, postoperative complications as osteonecrosis of the jaw, post-surgical pain, plaque and biofilm, root canals disinfection, dentin hypersensitivity, temporomandibular joint disorders and teeth whitening.

Antimicrobial properties**Bacteria**

The strong antimicrobial property of ozone is due to strong oxidizing potential which degrades the unsaturated fatty acids which makes up the cytoplasmic membranes.^[4,5] Ozone hampers the germination process, by damaging the spore's inner membrane.^[6] Ozone

directly inactivates bacterial toxins, while antibiotics do not. There is always a probability for the development of resistance against antibiotic but not against ozone.

Virus

Viruses which have a lipid outer envelope are sensitive to ozone.^[7,8] Ozone shows damage to polypeptide chains and envelope proteins of virus and impaired the viral attachment capability, and also causes breakage of viral RNA.^[9]

Protozoan & Fungi

Ozone shows cell inhibitory process to inhibits the protozoan and fungal cell growth at certain stages.^[12]

Effect on blood componenets**Effect on RBC's**

Ozone inhibits agglutination or clumping of blood without affecting its oxygen carrying capacity and flexibility.^[10] It stimulates the production of natural free radical scavengers of the blood i.e. glutathione peroxidase, catalase, superoxide dismutase etc.^[11]

Effect on WBC's

Ozone acts as a weak cytokine like IL2, IL6, IL8, TNF- α and TGF- β .^[12,15] Ozone acts on cellular membranes in

humans and reacts with its unsaturated fatty acids, forming hydrogen peroxides (H_2O_2), which acts as one of the most significant cytokine inducers.^[16]

Effect on Platelets

When blood is subjected to ozone, then H_2O_2 is generated which activates phospholipase A2, phospholipase C, lipo-oxygenases and cyclo-oxygenases, and thromboxane synthetase with increase in level of intracellular calcium, release of prostaglandin components, and thromboxane A2 and therefore helps in platelet aggregation.^[17,19]

Actions on other biological tissues

A. Immunomodulatory Effect

Ozone has been detected in the proliferation of immune complement cells, synthesis of immunoglobulins, activate the macrophages and allows sensitization of the antigens for its phagocytosis. Immune system depression has been seen with increase in concentration of ozone and immune stimulation has been seen with low or optimum concentration of ozone.

B. Antihypophylic Effect

It improves the oxygen carrying capacity of erythrocytes, increases the aerobic cellular metabolism, activation of aerobic process i.e. krebs cycle, glycolysis, oxidation of fatty acids and blood coagulopathies can be treated.

C. Anti-inflammatory Effect

Inflamed site has a positive charge whereas, ozone has a negative charge which attracts the positive inflammation site to show its anti-inflammatory effect. It causes production of inflammatory mediators such as leukotrienes, prostaglandins and interleukins.

D. Biosynthetic Effect

It activates protein synthesis and also increases the powerhouse of the cells that is the mitochondria and protein synthetic cell organelles such as ribosomes.

Forms of ozone administration

Gaseous ozone

Ozone in gaseous form can be generated from the open system or a sealed suction system. There are adverse effects if ozone is inhaled in an open system, so the sealed suction system is usually used. Ozone gas is led to a handpiece fitted with silicon cup.

Adverse effects of open system ozone on inhalation

Epiphora
Rhinitis
Cough
Headache
Nausea and vomiting

Ozonated water

Ozone dissolved in water can be used as

1. mouthwash

2. drinking to kill off microbes such as bacteria, viruses, and fungi for various issues such as halitosis or periodontal diseases.
3. In dental unit water supply lines for its direct usage.

Ozonated water is a safer alternative to gaseous ozone. It shows disinfectant and sterilizing effect, hemostatic effect in hemorrhages, accelerated wound healing with improved oxygen supply.

Ozonated oil

Ozonated oils are pure plant extracts. It is more convenient and provide greater permeation on external application.

Uses of ozone in different fields of dentistry

Oral medicine

Ozonated oil applied on viral infections such as herpes labialis, causing lesions on the skin. It also showed positive effect on mandibular osteomyelitis and demonstrated faster healing than the conventional protocols.^[20] It stimulates the healing of tissues through circulatory prompting, inhibit bacterial super infections due to its powerful oxidant property. In case of lichen planus, gaseous ozone has been proven to be effective in increasing wound healing after a high-dose radiotherapy. Resolution of the symptoms were seen and shows the ray of hope in replacing steroids as the mode of treatment.^[21] Temporomandibular joint dysfunction and sinusitis have shown positive results with ozone therapy mainly because of their anti-inflammatory and anti microbial properties. Muscle trigger points may also be areas where application of ozone can effectively reduce pain.

Oral & Maxillofacial Surgery

Ozone in the form of oil and water has been used in alveolitis and avascular osteonecrosis of jaw and has shown encouraged healing and control of opportunistic infections.^[20]

Periodontics

Culprits of most of the gum diseases causing gingivitis and periodontitis are the gram-negative bacteria, such as *Porphyromonas gingivalis*, *Porphyromonas endodontalis* etc. These microorganisms are more sensitive to ozonated water than gram-positive oral streptococci and *Candida albicans* in pure culture.^[22] Ozone has a great effect on bacterias releasing volatile sulphur compounds leading to halitosis. Ozonated water is used in ultrasonic cleaning system containing different experimental solutions. It results in antibacterial activity against *Staphylococcus aureus*.^[23]

Prosthodontics

Denture stomatitis is one of the main enemies of prosthodontists. Ozonated water (2 or 4 mg/L) for 1 min can reduce the number of *C. albicans* on denture bases although exposure to gaseous ozone is more effective.^[24]

Endodontics

Ozone has been used to remove biofilm or plaque in a gaseous or aqueous form, and its associated bacteria.^[25] On exposure with ozone for 60 seconds, cariogenic microflora, such as *Streptococcus mutans*, *Lactobacillus casei*, and *Actinomyces naeslundii* have been deactivated.^[26] While exposure for 80 seconds on deep cavities reduces the residual microbial load significantly.^[27] After 10 seconds exposure on a lesion by ozone gas at 2100 ppm, followed by 5 seconds application of xylitol and fluoride followed by a 6 month follow up, lesion significantly rehardened.^[28] In hypersensitivity, following therapy, ozone along with mineral wash, fluoride and other mineralizing agents was effective in reducing dentinal hypersensitivity by occluding the dentinal tubules.^[29,30] In root canal treatment, studies have shown that ozone due to its antimicrobial effect used in the form of gas or water can disinfect the canals and leave them clean for a year and is most effective when there is the least amount of organic debris in the canal.^[31] In case of teeth whitening, studies have shown that ozone reduces the yellowish tinge of tetracycline-stained teeth.^[32] A combination of 38% hydrogen peroxide and ozone resulted in more whiter teeth than 38% hydrogen peroxide alone.

Pedodontics

Ozone therapy being painless and fast, children are more compatible with this treatment. Also due to its remineralizing and antimicrobial effects, as mentioned above, this agent can readily be used as an anti caries agent and in conjunction with pit and fissure sealants.

Contraindications of ozone^[21]

- a. Alcohol intoxication
- b. Anemia
- c. Autoimmune disorders
- d. Hemorrhage
- e. Hyperthyroidism
- f. Myasthenia gravis
- g. Myocardial infarction
- h. Ozone allergy
- i. Pregnancy

Fate of ozone therapy in dentistry and medicine

As explained above, ozone seems to be a wonder molecule, being biocompatible, safe, quick to apply and with positive outcomes. It does not show much negative or adverse effects as compared to conventional treatments used alone. In contrast with traditional medicine modalities such as antibiotics and disinfectants, ozone therapy is quite economical and tolerant to patient. With every passing day, new modalities in the treatment of various diseases are being discovered, this is especially done so as to overcome the drawbacks of conventional treatment. Ozone is one of them and it can be said with no doubt that in upcoming days with more clinical research and trials, new and unknown properties of ozone as a therapeutic molecule will be discovered. It

surely has the power to become the face of dentistry and medicine in the near future.

The coronavirus outbreak has been labelled a pandemic by the World Health Organization (WHO) and no specific treatment or a vaccine against it has yet proven to be effective. Ozone therapy can be a promising tool for both prevention and treatment of COVID-19 infection by various possible mechanisms. The oxidative stress created by ozone in the body to stimulate the peripheral phagocytic cells, activate the antioxidant system and restore the immune system is thought to be effective for the prevention of COVID-19 infection. However, more trials need to be performed to use ozone in this new infection in future.

CONCLUSION

Ozone therapy is more advantageous in contrast to the present conventional therapeutic modalities. It is a minimally invasive and conservative approach, quite inexpensive, painless therapy which increases the acceptability and compliance of patient with minimal adverse effects. Positive outcomes also instill confidence in the clinicians to perform best treatment possible. It is truly a paradigm shift in dental practice. Ozone therapy does not differentiate in age of the patients i.e. a single therapy can be used in children as well as adults without alteration. In spite of all these positive effects, still more in vivo randomized and well controlled clinical trials are the requirement of the day to establish it as a standard therapy.

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