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OZONE THERAPY –A MILESTONE IN DENTISTRY ; A REVIEW

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ABSTRACT: Ozone therapy is be defined as a versatile bio-oxidative therapy in which oxygen/ozone is administered via gas or dissolved in water or oil base to obtain therapeutic benefits. Ozone being considered as a perfect substance for use in dental procedures, is nowadays taking the pathway of conventional dentistry in following a minimally invasive and conservative application to dental treatment. But still in developing countries its awareness and popularity are less due lack of knowledge. Thereby, purpose of this systematic review was to make the clinicians aware about its effectiveness and the biological effects of ozone therapy in all fields of dentistry.

Keywords – Ozone, Ozone therapy, Ozonated water, Ozonated oil.

I. INTRODUCTION

Atmospheric air is composed of nitrogen (71%),oxygen (28%), and other gases (1%) including ozone.[1,2] Ozone is a gas with the chemical formula O_3,and is an activated, trivalent form of oxygen[3] having a molecular weight of 47,98 g/mol. Being present in upper layer of atmosphere it is highly unstable structure due to the presence of mesomeric states,[4-7]giving off nascent oxygen to form oxygen molecule depending on systemic conditions like temperature and pressure.[7,8]It is one of the most important gases in the stratosphere present in a concentration of 1–10 ppm and is being continually created from and destroyed into molecular O.[9,10]Due its ability to filter UV rays, ozone is critical for the maintenance of biological balance in the biosphere thereby, protecting the living organisms from the harmful ultraviolet rays as it forms a blanket surrounding the earth at altitudes of 50,000 to 100,000 ft.[11] This protective layer being heavier than air hence, falls downward to earth from such high altitudes. It's a natural self cleansing mechanism of the earth as ozone purifies the air and combines with any pollutant that it comes in contact.[11-14]Ozone is blessed with the oxidative capacity to prevent, repair and heal the human cell damage caused by any pathogen.[4] Hence, can be used widely in both medicine and dentistry in the form of ozone therapy. Ozone therapy is recognized to be versatile bio-oxidative therapy in which oxygen/ozone is administered via gas or dissolved in water or oil base to obtain therapeutic benefits.[15] The ozone therapist determines the complete dosage of ozone according to the medical/dental indication and condition of the

patient.[16] Being a gas, ozone has the penetrative effect on such tissues and spaces that are not accessible. Thereby, introduction of ozone therapy has truly changed the way dentistry was before.[17]

HISTORY- Ozone therapy has a long history of research and clinical application with humans. In 1840, a German chemist Christian Friedrich Schonbein first discovered ozone gas on passing electrical discharge through water which he called Ozen from the Greek word ozein(Odor). He is considered as father of Ozone therapy.[7] In 1870, Landler used ozone gas in medicine by purifying blood in test tubes The first dentist to use ozone therapy in his practice was E.A. Fisch in the 1930's, to aid in disinfection and wound healing during dental surgeries.[14,18-19]

II. OZONE PRODUCTION

Oxygen molecules in the air combine to form ozone under the influence of factors such as ultraviolet radiation(from the sun), electrical discharges (lightning) and intense physical stress on water (such as in areas of waterfalls and ocean waves crashing onto rocks).There are three different systems for generating ozone gas by Ozone generators for medical usage – a. **Ultraviolet System** which produces low concentrations of ozone, used in esthetics , saunas, and for air purification. b. **Cold Plasma System** which used in air and water purification. c. **Corona Discharge System** which manufactures high concentrations of ozone and is the most common system used in the medical/dental field.[20-22]

III. MODES OF OZONE ADMINISTRATION:-

For therapeutic purposes ozone is administered in various forms like ozone gas, as an aqueous solution, oil or as ozonated water. **Ozone Gas** is most frequently used in restorative dentistry and endodontics. **Ozone aqueous Solution is** useful for disinfection and sterilization. It shows hemostatic effect in cases of hemorrhage and is helpful in accelerated wound healing. It also improves oxygen supply and support of metabolic processes. **Ozonated Water** may be useful to control oral infections and various pathogens.[20-22] Dr. Kramer[23] postulated that it can be used in a number of different ways: 1.as a mouth rinse (especially in cases of gingivitis, periodontitis, thrush or stomatitis); 2. as a spray to cleanse the affected area, and to disinfect oral mucosa, cavities and in general dental surgery; 3.as an ozone/water jet to clean cavities of teeth being capped, receiving root canal therapy, and in treating painful gingivitis and stomatitis. **Ozonized Oils** are pure plant extracts, through which pure oxygen and ozone are passed to form a thick gel containing ozonides. They are effective antimicrobials.

IV. MECHANISM OF ACTION OF OZONE

There are several known actions of ozone, such as antimicrobial (bactericidal, viricidal, and fungicidal), immuno-stimulating, immune modulatory, anti-inflammatory, biosynthetic (activation of the metabolism of carbohydrates, proteins, lipids), bioenergetic, antihypoxic, analgesic, haemostatic, etc.[24]Presence of 20 and 40 µg/ml ozone per ml of blood can induce the following biological responses[5]:

1.Antimicrobial Effect- Effect on Bacteria, Virus, Fungus, Protozoa

Bacteria :By the process of ozonolysis bacterial cell membranes are damaged and intra cellular proteins get oxidated by ozone leading to loss of organelle function. This action is selective to microbial cells. Human body cell having good antioxidative ability is thereby, not affected. Ozone is effective in antibiotic resistant strains with accelerated efficiency in acidic PH environment. **Viruses:** Ozone makes the infected cell intolerant to peroxides and changes the activity of reverse transcriptase thus hampering viral protein synthesis. **Fungal & Protozoa:** cell growth is inhibited by ozone at certain stages.[5,11,24-25]

2. Immunostimulating Effect- Ozone reactivates the immune system by influencing cellular and humoral immune system through macrophage activation and Cytokine release which in turn boost immune system thereby, making it useful in patients with low immune status and immunodeficiency. Ozone in high concentration causes immune-depressive effect whereas in its low concentration it shows immune-stimulating effect. [5,11,24-25]

3. Anti–Inflammatory & Analgesic Action- Ozone has a dual action mechanism: analgesic and anti-inflammatory due to its way of acting on diverse targets. It decreases the production of mediators of the inflammation by helping in the synthesis of biologically active substances such as interleukins, leukotrienes and prostaglandins which are beneficial in reducing inflammation and pain and promoting wound healing. The infection or inflammation is positively charged (acidic) and ozone is negatively charged (basic) so the chemistry of infection and inflammation attracts ozone to the area. In addition, it causes the oxidation (inactivation) of metabolic mediators of pain and improves local blood microcirculation, with an improvement in the oxygen delivery to the tissues, essential for the generation of anatomic structures; the elimination toxins and in general to the resolution of the physiological disturbance that generated the pain .[5]

4. Anti-hypoxic Action- Ozone acts by changing the rheological properties of the blood and it accelerates the speed of glycolysis of the erythrocyte .It brings about the rise of Po2 in tissues and improves transportation of oxygen in blood resulting in change of cellular metabolism activation of aerobic processes (Glycolysis, Kreb's cycle, B-oxidation of fatty acids) and use of energetic resources. Also, acts as a super-oxygenator, bringing oxygen to tissues, assisting body in its natural healing process.[5]

5. Biosynthetic Effect- Protein synthesis mechanism is activated by ozone with increased amount of mitochondria and ribosomes in cells that leads to increase in functional activity and regeneration potential of tissues and organs. Ozone releases vasodilators (nitric oxide) that are responsible for dilatation of arterioles and venules and intensifies remineralization potential by acting on the organic substance of mineralized tooth tissues.[5,11,24-25]

V. USE OF OZONE IN MEDICINE AND DENTISTRY

Scientific literature has jotted down medicinal indications of ozone therapy namely in external ulcers and skin lesions, arterial circulatory disorders, immunodeficiency and immune dysbalance ,chronic forms of hepatitis B and C, supportive therapy in cancer and rheumatoid arthritis and in inflammatory conditions such as knee arthrosis or gonarthrosis.[4,6] The use of ozone in dentistry is gaining its place in every day's dental practice and is used in almost all fields of dentistry.

Uses in Oral medicine- Ozonated water or oils are helpful in treating soft tissue lesions like herpes, aphthae, removable denture ulcers, cuts, cheilitis, candidiasis, cysts and traumatic wounds because ozone acts as a disinfectant and has accelerated healing properties. Oral lichen planus can be treated by tissue insufflation injection, cupping and ozonated oil applications. Chemotherapy and radiotherapyinvariably causes mucositis when administered in patients suffering from carcinomatous lesions. Ozone therapy is useful in mucositis cases as it enables the patient to eat normally, and improves the quality of life during oncological therapeutic interventions when applied in both aqueous and gaseous forms.[4,9,12,14,21,22,24,26,27] Intra-articular administration of ozonated water has been found to be a successful alternative therapy for the management of different joint diseases like Temporomandibular joint disorders.[5]

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Uses in Endodontics and Conservative dentistry:

Dental caries - Ozone gas when applied to carious lesion for 10-20 sec causes a reduction of about 99% of microorganisms. Ozonated water and gaseous ozone have strong antimicrobial activity against E. faecalis and S. mutans infections. Hence, it can be used as an adjuvant in caries therapy.[4,9,12,14,21,22,24,26,27]

Root canals –Ozone has bactericidal and effervescent properties and hence, ozone oils can be used to sterile the root canal systems and to clear the canals of necrotic debris. These oils are ozonated sunflower oil or olive oil or groundnut oil. This ozone oil irrigation is more quick and efficient in canal sterilization than that conventional irrigation by the sodium hypochlorite and sodium peroxide combination. [22]

Bleaching - In discolored non vital teeth, ozone can be used for bleaching. Once the bleaching agent is placed on the inner aspect of the root canal treated tooth, the crown is irradiated with ozone for minimum of 3-4 mins. This ozone treatment bleaches the tooth within minutes and provides good esthetic result.[4,9,12,14,21,22,24,26,27]

Hypersensitive Teeth- Noncarious hypersensitivity is caused by factors like attrition, erosion, abfraction, bite pressure, and gum recession. Ozone is helpful in removing the smear layer which prevents the penetration of ionic calcium and fluorine deep into the dentinal tubules. Thus, it opens up the dentinal tubules, broadens their diameter, and allows calcium and fluoride ions to flow into tubules easily, and effectively to plug dentinal tubules, preventing the fluid exchange through these tubules. Quick relief is reported from root sensitivity after ozone spray for 60 seconds followed by mineral wash onto the exposed dentin in a repetitive manner.[12]

Cracked Tooth Syndrome: Crack in the tooth is explored and it is exposed to ozone for 60 – 120 sec and later sealed with an intermediate restoration like GIC8. [27]

Uses in Periodontics-Use of ozonated water is helpful in periodontal therapy as it is effective in reducing count of both gram+ve and gram-ve bacteria in dental plaque. Ozonated oil is used as a therapeutic agent in treatment of acute necrotizing ulcerative gingivitis. Ozonated water is used to irrigate sulci and pockets during scaling and surgical procedure thus reducing preoperative bacterial load. It is also used for LASER therapy during ultrasonic debridement. Pretreatment rinsing with ozonated water is used in routine minor recall treatment cases, such as gingivitis, irrigation of the periodontium and insufflation of any periodontal pockets. Local ozone application serve as potent atraumatic, antimicrobial agent to treat periodontal disease nonsurgically and is an important tool during supportive periodontal therapy.[4,9,12,14,21,22,24,26,27]

Ozone in Implantology - Ozone helps in bone regeneration. During implant placement, the socket is prepared and ozone is bubbled into the prepared socket for about 40 seconds followed by placement of implant into the socket. This prevents infection and accelerates bone regeneration.[4,9,12,14,21,22,24,26,27]

Ozone in Prosthodontics - Ozonated oil is helpful in curing denture stomatitis which occurs mainly due to C. albicans and is found in full denture wearers. Topical application of ozonated oil is preferred over the tissue surface and over denture surface. Ozone is also used toclean denture due to its disinfecting action. The patient is asked to soak dentures in ozonated water for at least10 minutes after removal and rinse them before inserting into mouth.[4,9,12,14,21,22,24,26,27]

Ozone in Oral Surgery - After extraction or any surgical procedure, the area is immediately irrigated with ozone, which promotes faster healing of the wound without complications Ozone therapy is essential for the treatment of the refractory osteomyelitis in the head and neck in addition to treatment with antibiotics, surgery,and hyperbaric oxygen.[4,9,12,14,21,22,24,26,27]

Ozone in Pedodontics - Abu Naba'a*et al.*[28] found that ozone treatment provoked the least state of anxiety in children comparing to traditional dentistry.

Ozone in Orthodontics -During orthodontic treatment ozonized olive oil gel is helpful in reducing enamel demineralization around orthodontic bracket as enamel-bracket interface is the most susceptible area for white spot lesion formation, microleakage can invade beneath the bracket area.[14]

CONTRAINDICATIONS OF OZONE THERAPY

Ozone therapy is contraindicated in pregnancy , glucose 6 phosphate dehydrogenase deficiency, hyperthyroidism ,severe anemia, thrombocytopenia, autoimmune disorders, severe myasthenia , acute alcohol intoxication ,recent myocardial infarction, haemorrhage from any organ ,ozone allergy . Prolonged inhalation of ozone can be deleterious to the lungs and other organs but well calibrated doses can be therapeutically used in various conditions without any toxicity or side effects.[29]

ADVANTAGES OF OZONE THERAPY

Advantages of topical ozone therapy- Antibiotics can lead to development of resistance and pathogens on the other hand, cannot overcome oxidative challenges of ozone. In addition, there is evidence that ozone directly inactivates bacterial toxins, while antibiotics do not. [26]

As a whole ozone treatment is simple, less invasive, painless, time efficient, completely safe and possess no hazard for the environment, person treating and most important for the patient when used in correct dosage and method. It reduces the anxiety associated with drilling and filling techniques and in order to improve the treatment quality it can be the sole mode of treatment or may be combined with minimally invasive techniques. Ozone therapy is quite economical; it will markedly reduce both medical cost and invalidity in contrast with traditional medicine modalities such as antibiotics and disinfectants. [20]

DISADVANTAGE OF OZONE THERAPY - OZONE TOXICITY

The respiratory tract lining fluid is constituted by a very thin, watery film containing a minimal amount of antioxidants that makes mucosal cells extremely vulnerable to oxidation. Thereby, inhalation of ozone can be toxic to the pulmonary system and other organs. European cooperation of Medical Ozone Societies prohibited the intravenous injections of Ozone gas due to risk of air embolism. Complications caused by ozone therapy are infrequent at 0.0007 per application. Epiphora, upper respiratory irritation, rhinitis, cough, headache, occasional nausea, vomiting, shortness of breath, blood vessel swelling, poor circulation and heart problems are known side-effects of ozone therapy.[5] **Cure**- the event of ozone intoxication, the patient must be placed in the supine position, inhale humid oxygen, and take ascorbic acid, Vitamin E and n-acetylcysteine. Further, because of its high oxidative power, all materials that come in contact with the gas must be ozone resistant such as glass, silicon andTeflon.[26,31]

OZONE- A RECENT ADVANCEMENT IN DENTISTRY- Recently, in dentistry, ozone has got its role in various dental treatment modalities. Interest in ozone usage in dentistry developed due to the infectious diseases associated with the oral cavity and traumatic painful procedures associated with conventional therapy in treating them. Thereby, ozone therapy being atraumatic, painless and less invasive bought a ray of hope when used as a support for conventional treatments[21]and hence, considered breakthrough that is expected to be a cornerstone of dental care in the near future.[1]

OZONE THERAPY AS A POSSIBLE OPTION IN COVID-19 MANAGEMENT

Ozone therapy has recently been suggested as a possible economic and accessible option for Sars-CoV-2 due to its immunomodulatory, anti-inflammatory and biocide action and to the nitric oxide associated and dependent antiplatelet eff ect. About the relationship between ozone and Sars-CoV-2 is also worth noting the “triangle” existing among human angiotensin-converting enzyme 2 (ACE2), that both is a receptor facilitating virus entry and, as fundamental component of renin-angiotensin system, also protects from acute lung injury, and Nrf2 pathway modulation, influencing ACE2 activity and being in turn influenced by ozone. Interestingly, the virus has also been found in substrates other than respiratory secretions, such as fecal swabs and blood, suggesting a possible interaction with the virus in case ozone is in the blood.[32-34]

Currently, there are divergences in the developed studies regarding ozone therapy action. Therefore, the studies available in the literature must be reviewed in order to estimate the effectiveness of ozone therapy. [3] Further research is needed to regulate indications and treatment procedures of ozone therapy.

VI. CONCLUSION

Ozone therapy has a wide range of applications in almost every field of dentistry because of its unique properties such as immunostimulant, analgesic, antihypnotic, detoxicating, antimicrobial, bioenergetic and biosynthetic actions. It is considered as an ideal treatment of choice because of its atraumatic, painless, non invasive nature and relative absence of discomfort increase patient's acceptability and compliance. Despite these advantages, therapeutic ozone's application in dentistry is limited because of its possible side effects. Hence, dental practitioners need to know the proper usage of ozone therapy that can provide better patient care and considerably cut down the time and cost of the treatment. Further studies should be conducted to review the exposition of molecular mechanisms of ozone hence, benefitting practical function in dentistry.

Conflicts of interest – None

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