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RESEARCH ARTICLE

OZONE - A BOON TO DENTISTRY AND MANKIND.

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Manuscript Info	Abstract
Manuscript History:	Ozone is a triatomic molecule of oxygen with powerful oxidative potential
Received: 12 May 2016 Final Accepted: 22 June 2016 Published Online: July 2016	which makes it a potent antimicrobial, antihypoxic, immunostimulating, analgesic, bioenergetic and biosynthetic agent ,offering a wide range of therapeutic benefits ,in various fields of medicine and dentistry. The current article attempts to summerize the advances pertinent to ozone
<i>Key words:</i> Ozone,Dentistry.	therapy in dentistry, over the years.
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Introduction:-

Oral health is essentially the window to general health and quality of life. Reason for tooth decay is considered to be a metabolic imbalance that results in demineralization².

In the early 1900's, dental caries was believed to be "gangrene" of the teeth, which called for nothing but extraction. This was replaced by Dr. G V Black's extension for prevention restorative concept throughout the twentieth century, as the microbiological model of dental disease took hold known as macro-dentistry which implies on the complete removal of carious tooth structure¹³.

Over time, modern dentistry has evolved to a minimally invasive approach, in which caries is managed as an infectious disease, deferring operative intervention for as long as possible; the focus being maximum conservation of demineralised, noncavitated enamel and dentin³⁰.

In the current era of antibiotic resistance²⁴, Ozone a naturally occurring energized form of oxygen, presents solid potential for an atraumatic, biologically-based treatment,³² that follow a minimally invasive and conservative approach to various clinical conditions encountered in dental practice⁹; facilitated by emerging technologies for early diagnosis, prevention and treatment known as "Minimally invasive dentistry"¹⁷.

History^{1,39,40}:-

Ozone (O_3) gas discovered in the mid-nineteenth century is a dynamically unstable molecule consisting of three atoms of oxygen owing to the presence of mesomeric forms.

In 1785, Van Marum noticed that air near his electrostatic machine acquired a characteristic odour when electric sparks were passed. In 1801, Cruickshank observed the same odour at the anode during electrolysis of water. The early production of ozone for medical use was generated, when a German chemist Christian Friedrich Schonbein (known as the Father of ozone therapy, 1840) passed an electric discharge through water, and a strange smell was produced, which he named Ozone (Derived from Greek word-Ozein i.e. odour).

Numerous researchers since then have worked to elucidate the nature and actions of ozone. Mariniak and Delarive showed that it is an allotropic form of oxygen, and Mulliken and Dewar clarified its molecular structure.

In 1901 Wiesbaden, Germany became the first city that used ozonation for purifying drinking water. A Wolff, during First World War, treated putrescent wounds, suppurating bone fractures, fulminating infections and abscesses with ozone therapy.

Dr. E.A. Fisch, in 1950 of Switzerland was the first dentist to use the ozone as a treatment modality in his practice. He treated Ernst Payr, a renowned Austrian surgeon, who later became an ozone enthusiast and began a line of research dedicated to use of ozone in healthcare.

In 1958 Hansler presented his first reliable model of medical ozone generator. Together with H.Wolff, they introduced ozone therapy as we know it today.

Biological actions of ozone^{21,22,40}:-

Anti-microbial Action:- Ozone damages the cytoplasmic membrane, and oxidises intracellular components non specifically in bacteria, virus and fungi by ozonolysis of dual bonds in them. Human cells, due to their high antioxidative potential are resistant to the detrimental effects of ozone. In viral infections, ozone activity also lies in the intolerance of infected cells to peroxides and alteration of reverse transcriptase activity. However, gram-positive bacteria have been found to be more sensitive to ozone than gram-negative bacteria. Ozone therapy has been proved effective in both acute as well as chronic microbial infections.

Immunomodulation and Anti-oxidative Action:- Ozone help synthesize immunoglobulins. It has inhibitory effects on TNF- α production, preserves cell redox state. Continuous low concentration exposure of ozone (0.2ppm) results in increased Glutathione(GSH) peroxidase levels in cells.. Therefore, ozone is immune-stimulating in low concentration but immuno-depressive in high concentration

Hypoxia Abatement/Anti-hypoxic Action:- Enhances oxygen saturation of haemoglobin thereby helps in revitalizing organic functions. Also reduces local inflammatory process by changing blood cell elasticity.

Anti-inflammatory Action: Aids in synthesis of interleukins, prostaglandins and leukotrienes. Also helps in inhibiting inflammatory cytokines.

Detoxicating Action: - Activation of aerobic process (Kreb's cycle, glycolysis and oxidation of fatty acids)

Bioenergetic Action:- Acivates protein synthesis, and enhances cell metabolism

Biosynthetic Action:- Enhances metabolism of carbohydrates, proteins, lipids etc. Secretion of vasodilators like nitrous oxide (NO) is increased by ozone resulting in dilatation of arterioles and venules.

Studies revealed that this allotropic form of oxygen²⁷ takes only 10 sec for ozone to kill 99% of bacteria, fungi and viruses³⁶. Thus ozone rapidly kills otherwise hard to kill microorganisms²⁶. Ozone is organic in nature and it disinfects the tissues treated and leaves no chemical trail like chlorinated products following its application^{16,38}. Thus Ozone has numerous applications in day to day life ranging from purification of air we breathe to the water we drink.

Forms of ozone:- The three basic forms of application of ozone, to attain therapeutic benefits are ozonated water, ozonated olive oil, and oxygen/ozone gas 5,35,40 . These forms can be used singly or in combination to treat different dental pathologies²⁸.

Routes of Ozone administration⁶:-

Parenteral:- Intravenous, intra-arterial, intramuscular, subcutaneous, intraperitoneal, intrapleural, intra-articular, periarticular, myofascial, intradiscal, intraforaminal, intralesional

Topical or locoregional:- Nasal, tubal, auricular, oral, vaginal, urethral and intrabladder, rectal, cutaneous, dental.

Systems of ozone generation^{2,5,22}:-

a)Ultraviolet radiation system b) Cold plasma system c) Corona discharge system and d) Electromagnetic system.

The ozone unit for dental use was first developed by CurOzone Inc. (Canada) and subsequently manufactured under license and distributed by KaVo Dental GmbH and Co. (Germany) under the name "HealOzone"²⁴. It delivers 2,100ppm (parts per million) ozone at a flow rate of 615cc per minute that has been proven safe²⁶. Other appliances used for ozone production in dentistry includes: Ozony Tron by MYMED GmbH, and Prozone(W&H)^{22,36}.

Role of Ozone in Various Disciplines of Dentistry:-

Sterilization and ozone:-

Ozone assures complete sterilization of all instruments and handpieces without heat build up in just 5 sec in any operatory. These instruments can be removed totally dry and ready to use¹⁸.

Ozone in operative and aesthetic dentistry:-

Treatment of deciduous teeth lesions:-

Most child patients show fear and anxiety towards dental treatment, though treatment in these patients will have a long lasting effect. Ozone therapy using the Heal ozone unit for 30 sec and fluoride releasing glass ionomers, following the application of Curozone remineralizing wash was found effective in such patients with good cooperation and significant anxiety reduction^{18,41}.

Treatment of permanent teeth initial/early carious lesions:-

The application of ozone gas for a period of 10 sec was capable of reducing the number of *S. mutans* and *S. sobrinus invitro*. In addition, ozone treatment has been demonstrated to produce significant remineralization in fissure caries of permanent teeth regardless of lesion type or location⁸.

Ozone application to carious lesions is considerd an alternative to conventional drilling and filling. It reduces the bacterial count in active carious lesions and therefore, may temporarily arrest the progression of caries, resulting in prevention or delaying the need for tooth restorations^{3,37}.

Ozone gas applied prior to etching and the placement of sealant proved to have no negative impact on sound enamel physical properties. The longer the exposure to ozone gas, stronger will be the bactericidal effect on microorganisms within the dentinal tubules of deep cavities, increasing the clinical success rate of restorations^{3.}

Treatment of larger carious lesions:-

In cases of severe tooth breakdown, after initial ozone application for remineralisation, a suitable restorative material must be used to restore the cavity.

Polydorou *et al* stated that an 80 sec application of ozone in deep cavities shall eliminate residual microorganisms effectively, thereby increasing the success rate of restorations considerably²³.

Ozone and Root caries:-

Baysan et al, reported 10 or 20 sec ozone application was found effective to kill the great majority of microorganisms in primary root carious lesions (PRCLs) in vitro and this application for a period of 10 sec was also capable of reducing the numbers of *S. mutans* and *S. sobrinus* in vitro. Therefore ozone therapy is considered as an alternate treatment strategy for the management of root caries⁴.

Over 90% of all root caries lesions were reported with either partial or complete reversal, following ozone therapy¹⁵.

Bleaching:-

In previously root canal treated teeth, crown discoloration is a major aesthetic problem, especially in anterior teeth. Conventional walking bleaching when used in conjunction with ozone readily enhances the whitening effect¹⁸.

Desensitization and ozone:-

Delivering ozone spray for 60 sec followed by mineral wash onto the exposed dentine produce quick relief from root sensitivity, with a lasting effect. Smear layer present over the exposed root surface prevents deeper penetration of ionic Calcium and Fluorine into the dentinal tubules. Ozone removes this smear layer, opens up the dentinal tubules, broadens their diameter and then Calcium and Fluoride ions flow into the tubules easily, deeply and effectively to plug the dentinal tubules, thereby preventing the fluid exchange through these tubules. Thus, ozone can effectively terminate the root sensitivity than using conventional methods²⁷.

Cracked tooth and ozone:- After crack detection, prognosis of tooth in question is assessed, then exposed to ozone for 60 - 120 sec and sealed with an intermediate restoration like GIC. The tooth needs to be periodically assessed and restored³⁶.

Ozone therapy in Endodontics:-

Huth *et al* declared higher concentrations of gaseous and aqueous ozone to be dose, strain and time-dependently effective against *E. faecalis, C. albicans, P. micros and P. aeruginosa* in suspension and biofilm test model¹⁹. Another study conducted by Estrela *et al* concluded, irrigation with ozonated water, 2.5% Sodium hypochlorite, and 2% Chlorhexidine for 20 min was not sufficient to inactivate *E. faecalis* present in infected human root canals¹¹. According to Hems *et al*, ozone in solution for 240 s showed antibacterial efficacy against planktonic *E. faecalis* but was not found effective against *E. faecalis* cells within a biofilm until they were agitated into the surrounding medium¹⁴.Cardoso and colleagues concluded the use of ozonated water as irrigant, caused significant reduction in the number of *C. albicans and E. faecalis* in human root canals. Also Virtej and collagues found Healozone to have equivalent efficacy towards mixed bacterial infections of root canals as that of 3% Sodium hypochlorite. Sequeira *et al* stated ozonated oil to be most effective against bacterial species associated with etiology of periradicular diseases²⁶.

Nagayoshi *et al* confirmed marked decrease in the viability of *E. faecalis* and *S. mutans* invading dentinal tubules following irrigation with ozonated water thereby improving the outcome of endodontic therapy³¹.

Ozone therapy in Prosthodontics:-

Denture plaque control is essential for the prevention of denture stomatitis. Four known studies reported ozone gas to be an efficient denture cleanser as compared to ozonated water, with little impact on the quality of alloy in terms of reflectance, surface roughness, and weight³. The application of ozonated water may be useful in reducing the number of *C. albicans* on denture bases³³. Ozone application to cavity and crown preparations prior placement of restoration significantly reduces post operative pain symptoms by preventing bacteria from reinfecting dentin thereby avoiding the need for endodontic procedures¹⁸.

Ozone therapy in Periodontics:-

Ozone application is found efficacious in removal of oral malodour¹⁶ as well aids to cleanse tooth brush bristle microflora³⁵.

An audit by Iliadis *et al* revealed significant depth reduction of pockets in patients with periodontal disease following gaseous ozone therapy within three months after initial application²⁰ Use of ozonated water, ozonated oil and ozone gas insufflations was reported to reduce and eliminate pathogenic load within the sulcus and pocket areas²⁹. In addition, the tissue subjected responds with increased perfusion and immunologic activity, allowing enhanced healing³⁴.

Also aqueous ozone maintains high biocompatibility levels with human oral epithelial, gingival fibroblast and periodontal cells²⁵.

Ozone in Oral surgery and Implantology:-

Dry socket is a common complication following extractions. With the use of ozone faster healing of wounds⁴² is accomplished, with little or no complications even in osteonecrotic lesions and prevents the need for systemic antibiotics^{18,38}.

In dental surgery, ozonated water was used to promote haemostasis, enhance local oxygen supply, and inhibit bacterial proliferation. Ozone therapy was found to be beneficial for the treatment of the refractory osteomyelitis in the head and neck region as an adjunct to treatment with antibiotics, surgery and hyperbaric oxygen.

Also use of aqueous ozone along with amino alcohol is advocated for decontamination of implant surfaces³. In addition, sterile ozonated water can be used as a coolant for burs and to rinse wounds in dental surgery^{12.}

Matsamura K *et al* found periodontal cell regeneration similar to that around natural teeth in ozone treated implants. Implant site is bubbled with ozone prior placement in order to prevent infections and enhance bone regeneration 41 . Yet another application of ozonated water is the mechanical cleansing and decontamination of avulsed teeth before attempting replantation^{10,35}.

Ozone in oral medicine:-

Ozonated oil neutralizes herpes virions by inhibiting bactericidal supra infections and stimulate tissue healing via circulatory prompting when applied on herpes lesions³³.

Ozone treatment demonstrated rapid resolution of painful apthous ulcers when delivered for about 40 sec to the lesion using a large cup that seal the ulcer. A dramatic decrease in symptoms were reported in all cases within 24 hours while three cases reported with complete healing within 48 hours¹⁸.Neuralgias and soft tissue lesions like chelitis and candidiasis can also be effectively treated with ozonated water or oils³⁵.

In addition, ozone infusion into temporomandibular joint and jaw bones have been advocated for the treatment of pain and inflammation²¹.

Ozone in orthodontics:-

Prophylactic ozone pretreatment of enamel showed a higher shear bond strength of orthodontic brackets bonded with total or self-etch adhesive systems as compared to a self-etch adhesive used alone.

In various clinical situations ozone pretreatment before bracket bonding resulted in less residual adhesives after debonding 8 .

Ozone treatment if repeated at 8-14 week intervals may prevent possible demineralization surrounding orthodontic brackets during the routine treatment regime¹⁸.

Dhingra *et al* proposed that ozone irrigation will reduce subgingival inflammation caused by plaque retentive orthodontic appliances²².

Dental unit water lines and ozone:-

Ozone application showed almost 57% biofilm reduction and 65% reduction in viable bacterial count in model dental unit water lines despite the low dose and short time of application²⁵. Increased number of unrevealed high risk patients (HIV, Hepatitis etc.)highlight the importance of effective infection control; In this respect ozone can be used for purification of dental unit water lines to minimize cross infections in the dental operatory⁴¹.

Ozone in stomatology:-

Sechi *et al* evaluated the effect of ozonized sunflower oil on different bacterial species isolated from different sites. Ozone proved to be effective against all bacteria when tested, while mycobacteria were shown to be the most susceptible to the oil.

It was found that ozonated water applied on the daily basis can accelerate the healing rate of oral mucosa due to its anti inflammatory and immune modulatory capacities²⁷.

Ozone toxicity:-

Reported incidence of ozone toxicity is extremely rare (0.0007 per application) if administered with proper precautions⁴⁰. Bronchopulmonary system and other vital organs are reported to be very sensitive to ozone gas inhalation beyond tolerated limit⁷. Known signs of ozone toxicity includes epiphora, cough, rhinitis, headache vomiting, occasional nausea, swelling of blood vessel, difficulty in breathing, poor circulation and related cardiovascular problems²⁸.

Numerous intraoral side effects like xerostomia, mucositis, or loss of taste sensation may be encountered if ozone administration is not done with precision and accuracy, as instructed by the manufacturer^{41,42}. The European

Cooperation of Medical Ozone Societies warns that direct intravenous injections of ozone/oxygen gas should not be practiced due to the possible risk of air embolism¹⁰.

All the materials that come in contact with ozone must be resistant to its oxidative property, such as Teflon, glass and silicone. However, if intoxication occur, the patient should be kept in supine position and given moist oxygen inhalation, and also administered vitamin E and N-acetylcysteine²⁸.

Contraindications^{5,28} :-

Contraindications of ozone therapy include systemic conditions like Glucose-6-phosphate-dehydrogenase deficiency (favism), internal haemorrhage, recent myocardial infarction severe anaemia, severe myasthenia and hyperthyroidism. Ozone allergy, even though rare, is an absolute contraindication. It is also contraindicated in pregnancy and acute alcohol intoxication.

Conclusion:-

Ozone therapy has been proved to be a safe and efficient treatment modality to patients of all ages with minimal and preventable side effects¹ and low cost making it more affordable compared to the traditional treatment protocols¹⁸. It not only reduces the treatment time but also offers painless procedures thereby enhancing patient compliance²³. Therefore, it is definite that ozone will play a pivotal role in the future of dentistry.

Further studies are to be conducted to standardize indications and treatment protocols of ozone therapy for the benefit of mankind³⁹.

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