OZONE AND ITS APPLICATIONS IN DENTISTRY

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Introduction

Dental carries is a chronic disease of childhood, Rules for dentistry, in 1800 **G.V.Black** mentioned "extension for prevention", Paradigm shift shows clinicians practice → conservative & preventive methods

"Prevention of extension" "constriction with conservation"

Term 'Minimal Intervention Dentistry' & 'Minimal Invasive Dentistry' used, *Minimal Intervention dentistry* → cause & not just the symptom, prevention & control, *Minimal invasive dentistry* → operative restorative procedures, Ultraconservative & Microdentistry

HISTORY

1. Ancient greeks – ozein
2. American indians – predictor for good outcomes in fishing.
3. In 1785, Van Marum – electrifier.
4. In 1801, Cruickshank – water electrolysis.
5. In 1840, Christian Friedrich Schoenbein discovered an "electric and pungent smell" - voltaic pile in the presence of oxygen.
6. Oxidant but also a disinfectant.
7. First medical application is by Dr.C.Lender – blood in test tubes.
8. In 1930 Dr.E.A.Fisch used ozone in dental practice.

What is ozone?

Ozone is a naturally occuring molecule. Exists in the form of a gas in the stratosphere in the layer known as the 'ozone layer.' It is a simple molecule of three oxygen atoms in an unstable, highly reactive, cyclic tri-atomic configuration. 1 and 10 ppm in the stratosphere. 90% of the ozone - in the stratosphere. 10% of the ozone - in the troposphere. It is indicated for 260 different pathologies in medicine & dentistry.

Without ozone layer, UV-C and UV-B rays damage DNA, would slowly destroy life on the planet. Wang et al. (1993), Ozone is also a greenhouse gas so it plays a role in keeping the planet warm.

DELIVERY SYSTEMS:

In 21st Century the first ever ozone generators came into existence by which controlled amount and controlled concentration of ozone could be produced. Joachim Hansler and Hans Wolff (German physicians) developed this ozone generator for medical use. Today's ozone generator reflects the same basic design that was given by them. Hot Spark (corona discharge) - in medical/dental fields. Cold Plasma - therapeutic work & air and water purification. Ultraviolet light - therapeutic work – when smaller, steady trickle of ozone is needed. Now a day's hot spark (corona discharge) production is commonly used for generation of high concentration of ozone (most common system used).The other two (Ultraviolet and cold plasma) are most commonly used in therapeutic work. In comparison to ultraviolet method, Cold plasma produces greater quantities of ozone in a given time span hence, commonly used for air and water purification.

Corona Discharge:-

Oxygen is passed through a tube containing a hot cathode surrounded by a screen anode. This system tends to have a limited life time due of the effect of ozone on the hot plates, and as the heat from these plates heats the gas, a proportion of the ozone formed reverts to oxygen. This in turn causes further damage to the anode and cathode.

Cold Plasma:-

The cold plasma generator, originally invented by Nikola Tesla in the 1920s, is still in use today. This is a similar design to the corona discharge tube, but the anode and cathode are encased in glass rods filled with a noble gas.

Ultra-violet light:-

The production of ozone from oxygen is carried out as the stream of oxygen moves through a tube illuminated with a narrow frequency bandwidth of ultraviolet light.

FORMS OF OZONE:-

Ozone gas is difficult to manage. ozone dissolved in pure water or in oils such as olive oil, groundnut oil, sunflower oil can be handled much more easily. Using ozone in the

aqueous phase makes it suitable for topical applications, as a soaking solution to disinfected dental instruments, or as a solution to disinfect medical and dental tubing and parts. There are three basic forms of ozone application.

1) ozone gas - half life of about 5-30 min.

2) ozonated water - 10hrs.

3) ozonated oil - 15 yrs or more.

Garcia EJ et.al in 2012 reported a study on the influence of ozone gas and ozonated water application to prepared cavity and bonded interfaces on the resin/dentin bond strength of two-step etch-and-rinse adhesive systems (Adper Single Bond 2 [SB2] and XP-Bond [XP]). Ozone gas and ozonated water used before the bonding procedure or on resin/dentin bonded interfaces have no deleterious effects on the bond strengths and interfaces. Various studies have shown that all the forms of ozone have a great impact but if precisely used gases ozone has a upper hand.

1. Ozone Gas: Some of the commercially available Ozone Units for medical use are:

- HealOzone TEC 3 (Curozone, USA).
- Prozone (W&H)
- O3 ozicure ozone device.

Millar and Hodson compared the safety of two ozone generating systems. The Ozicure device (which is no longer available and is not licensed for use in Europe) HealOzone developed by CurOzone USA Inc., now distributed by KaVo Dental, Biberach, Germany, for use in dentistry. The two were compared based on the amount of ozone that escaped during gas application. The investigators found the Ozi-cure device, when used without adequate suction, allowed ozone to reach concentrations above the permitted levels and, therefore, should not be used.

HEALOZONE:-

The HealOzone procedure consists of :-

1. The application of ozone gas.
2. The use of remineralizing agents.
3. A patient kit.
4. Information on oral hygiene.

The HealOzone device comprises

1. An air filter

2. A vacuum pump
3. An ozone generator
4. A handpiece fitted with a sealing silicone cup and a flexible hose.

The generated Ozone is applied to patient through hand piece which gets adapted to teeth through a silicon cup and is exposed. The used ozone is passed through a reducing agent to convert back to oxygen and then led back to the generator. Immediately after ozone application the tooth surface is treated with a remineralising solution (reductant) containing fluoride, calcium, zinc, phosphate and xylitol dispensed from a 2-ml ampule Patients are also supplied with a patient kit, which consists of toothpaste, oral rinse and oral spray, all containing fluoride, calcium, zinc, phosphate and xylitol, and aims to enhance the remineralization process.

2. Ozone aqueous Solution:-

a. Useful for disinfection and sterilization.
b. As hemostatic agent in cases of hemorrhage.
c. To accelerate wound healing as it improves oxygen supply and supports metabolic processes.

2a.Ozone Oil:-

Ozonated olive oil (Oxaktiv) is pure olive oil that has undergone ozonization using a steady flow of ozone–oxygen mixture in the ratio of 5:95% until olive oil transforms from the greenish-colored liquid status to the whitish gel status. useful for external application.

2b.Ozonated water:

Studies have shown that ozonated water increased metabolic activity of fibroblast cells and improved lipopolysaccharide induced inflammatory response. It also had strong bactericidal activity against plaque biofilm.

INDICATIONS:-

1. Reversal of incipient caries
2. Prevention of pulpal infection in deep caries.
3. Disinfection during RCT
4. Disinfection of cavity preparations prior to

   restoration
5. Treatment of cervical sensitivity

6. Prior to all fissure sealant placement

7. Bleaching

8. Combined with other approaches to manage

   caries, such as ART.

9. Aphthous ulcer and Herpes simplex lesions.

CONTRAINDICATIONS:-

a. In favism a hemolytic disease G6PD enzyme is deficient . G6PD is responsible for abolishing excessive oxidation and intensive haemolysis
b. In pregnancy due to mutagenic risk – unlikely.
c. Hyperthyroidism, cardiovascular instability, thrombocytopenia.
d. Allergy - ??? Seen in asthmatic patients due to hypersensitivity because of breathing polluted air with ozone.

MECHANISM OF ACTION:-

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.

Nagayoshi et al. 2004, Arita et al. 2005

More ozone can then penetrate into the cell, and this causes further destruction and cell death.By oxidizing the biomolecules featured in dental diseases, ozone has a severely disrupted effect on cariogenic bacteria, resulting in their elimination.

Anti-microbial (bactericidal, viricidal, and fungicidal):-

a. Damages cytoplasmic membrane due to ozonolysis of dual bonds.

b. It does not damage healthy human body cells - superoxide dismutase, catalase, hydrolase and antioxidant nutrients like vitamin C, E, beta-carotene, selenium, methionine, glutathione.

c. Ozone is very efficient in antibiotic resistant strains.

d. In viral infections, ozone action lies in the intolerance of infected cells to peroxides and change of activity of reverse transcriptase, which takes part in synthesis of viral proteins.

e. Herpes, Hepatitis, Epstein Barr, Cytomegalovirus and other lipid envelope viruses are readily destroyed by ozone.

Immunomodulation:-

a. Ozone stimulates and modulates immune system particularly lymphocytes producing interleukins.

b. Also activates the function of macrophages and increases sensitivity of microorganisms to phagocytosis.

c. So the application of medical ozone is extremely useful for immune activation of patients especially with a low immune status &/or immune deficit.

Anti-Inflammatory Agent:-

a. Helps in synthesis of interleukins, leukotrienes and prostaglandins.

b. Inhibits inflammatory cytokines like NF-κB system.

Severe oxidative stress activates nuclear transcriptional factor kappa B (NF-κB), resulting in an inflammatory response and tissue injury via the production of COX2, PGE2, and cytokines. Moderate oxidative stress activates another nuclear transcriptional factor, nuclear factor-erythroid 2-related factor 2 (Nrf2). Nrf2 then induces the transcription of antioxidant response elements (ARE). Transcription of ARE results in the production of numerous antioxidant enzymes, such as SOD, GPx, glutathione-s-transferase(GSTr), catalase (CAT), heme-oxygenase-1 (HO-1), NADPH-quinone oxidoreductase (NQO-1), phase II enzymes of drug metabolism and heat shock proteins (HSP). Both free antioxidants and anti-oxidative enzymes not only protect cells from oxidation and inflammation but they may be able to reverse the chronic oxidative stress.

Anti-hypoxic :-

a. Ozone acts as a super-oxygenator, bringing oxygen to tissues, assisting body in its natural healing process.

b. Increases oxygen saturation of haemoglobin.

c. Shifts the oxygen-saturation curve towards the right side, so that more oxygen is released to peripheral tissues.

Bioenergetics:-

a. Activates protein synthesis.

b. increases amount of ribosomes and mitochondria in cells, elevating functional activity and regeneration potential of tissues and organs.

c. Enhaced cell metabolism. (ribosome,mitochondria).

Biosynthetic:-

a. Activates metabolism of carbohydrates, proteins, lipids etc.

DOSE CALCULATIONS:-

a. How much ozone to use in the treatment of oral tissues is key.

b. The ozone concentration used may vary between 1 and 100gm/ml (0.05-5%) according to the medical/dental indication and the patient's condition**.**

APPLICATIONS IN DENTISTRY:-

ENAMEL PROPERTIES:-

Celiberti P, Pazera P, Lussi A in 2006 reported a study on the effects of ozone on sound enamel physical properties and its effects on sealing ability.

a. Prepared fissures exhibited no unfilled areas and a statistically significantly lower microleakage compared to intact fissures.

b. Ozone was shown to dehydrate enamel and consequently enhance its micro hardness, which was reversible.

Caries Severity Index	Diagnodent Reading	Clinical diagnosis	Radiographic interpretation	Treatment plan
1	<10	May be a sound tooth	Normal	10 Sec O_3/Seal Fissures if indicated with GIC or flowable composite
2	10-16	White spot lesions	Normal (lesion not seen on x-rays)	40 sec O3 and remineralisation therapy Air abrasion and/or seal fissures
3	20-24	Carious lesion at EDJ	May not be visible on x-rays	Air abrasion/etch/40 sec O_3 therapy and restoration with GIC/composite
4	25-29	Caries involving 1-2mm of dentin	May/may not be visible on X-rays	Remove infected dentin, leave affected dentin. Etching – 60 sec O_3 therapy and restore with GIC/composite/Light cure GIC
5	>30	Caries involving >2mm of dentin	Mostly visible on X-Rays	Remove infected dentin to leave affected dentin, ozone exposure for 60 sec. depending on remaining dentin thickness liner/base and restoration.
6	>99	Deep carious lesion, may/may not involve pulp.	Visible on x-rays and assessing pulp vitality	If vital, indirect pulp capping is advised. Expose O_3 for 120 sec and seal with GIC. After 1 month, reassess and If remineralisation is evident, it can be restored with a permanent restoration.
Recommended ozone concentration (O_3): 3.5-5 g/ml& flow Rate: 0.5-1 L/min.				

Ozone treatment either alone or combined with a remineralizing solution was found to be effective for remineralization of initial fissure caries lesions.Ozone can decarboxylate pyruvic acid, a potent caries producing bacterial acid, into acetic acid, a much less potent cariogenic acid (Abu Naba 2004).Results in the elimination of bacteria. This treatment is an alternative therapy to conventional cavity preparation for non cavitated deciduous carious lesion. The infusion of Ozone into noncarious dentin prevented biofilm formation in vitro from S. mutans and Lactobacillus acidophilus over a 4 week period. Dahnhardt JE, Jaeggi T, Lussi A 2006 reported a study on whether the treatment of dental caries with ozone was possible in apprehensive children and to ascertain whether ozone reverses caries in open single-surface lesions. 94% of the children were treatable and 93% lost their dental anxiety. Some studies have demonstrated that 40s application of Ozone is sufficient to kill different concentrations of S. mutans and application of 60s has almost completely eliminated S. mutans, L. casei and A. naeslundii. But randomized double blind standardized clinical studies are still required to establish Ozone therapy in the treatment of dental caries. It can be used in conjunction to the conventional treatment modalities.

EXTENSIVE CARIES:-

It must be stressed that larger lesions are not those to be treated with ozone alone. Most will require a combined approach of traditional therapy, as well as ozone. The aim is to allow natural remineralization to take place on a predictable basis, without destruction of tooth tissue. Where the lesion extends deep into the dentine, the action of ozone will take a longer time period of treatment, or may require several treatment periods over time. The basic protocol is the same, the soft debris is removed along with any unsupported enamel. If

possible, denatured dentine is removed to the leathery layer. Ozone is applied for 40 seconds or longer. Some practitioners are using 2 to 3minutes for large deep lesions that extend on x-ray almost to the pulp chamber. Then, the remineralizing wash is applied.

I option:--

The lesion is left as self cleansing, and the patient is instructed with modified oral hygiene instructions. After routine brushing and rinsing, they are asked to place a small amount of the paste directly into the cavity. Then they spray two puffs of the remineralizing solution directly into their mouths. This is repeated at least 3 times each day.

II option:-

The lesion is restored using a mineral-releasing glass ionomer, such as FujiVII or a resin-bonded composite. This will allow remineralization to occur, without the possibility of ingress of food debris and re-colonization of the cavity.

ROOT CANAL THERAPY:-

Ozone was found to be effective against endodontic pathogenic microorganisms like E.Faecalis, Candida albicans, Peptostreptococcus micros and Pseudomonas aeruginosa disinfecting of root canals and dentinal tubules.Ozone also eliminates the distinctive anaerobic odor associated with some chronically infected teeth.

The following steps should be added before the final fill of the canals -

a. The files are coated with ozonated olive oil for lubrication & disinfection.

b. The canals are prepared & then irrigated with ozonated water and dried.

c. Before filling, a slow insufflation (45-60sec) into each canal with moderate/high concentration of ozone gas.

d. Insufflation of ozone electrochemically travel into the lateral canals and dentinal tubules killing the microbes.

e. Ozone will also penetrate through the apical foramen and enter into the surrounding and supportive bone tissue, encouraging healing & regeneration of bone

A Japanese study published in 2004 demonstrated the antimicrobial activity of Ozone in root canal treatment without any tissue toxicity. The study also shown that there was high metabolic activity of the associated fibroblasts indicated an increase in the healing process. But it was found that even after 20 minute of contact time of Ozonated water, gaseous Ozone and antiseptic agents did not have antibacterial effect on Enterococcus Faecalis. Estrela C et.al in 2007 reported a study on to determine the antimicrobial efficacy of ozonated water, gaseous ozone, sodium hypochlorite and chlorhexidine in human root canals infected by Enterococcus faecalis.No solution used as an irrigant over a 20-min contact time demonstrated an antimicrobial effect against E. faecalis.The 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. Rita Noites et.al in 2014 reported a study on whether irrigation with sodium hypochlorite, chlorhexidine, and ozone gas, alone or in combination, were effective against E. faecalis and Candida albicans. The 5% NaOCl combined with ozone, even in the maximum time (180 s), did not show significant differences from the isolated treatments.

Application of gaseous ozone during short periods (24 and 60 seconds) was not sufficient to eliminate neither C.albicans nor E. faecalis. Great antimicrobial activity with 2% CHX followed by gaseous ozone even only for 24 s, with a complete elimination of both C. albicans and E. faecalis.

Nagayoshi and colleagues, found nearly the same antimicrobial activity (against E. faecalis and Streptococcus mutans) and a lower level of cytotoxicity of ozonated water as compared with 2.5% NaOCl. They stated, Ozone is known to act as a strong antimicrobial agent against bacteria, fungi, and viruses.

S.P.Chandra, R. Chandrasekhar et.al in 2014 reported a study on success rate of mixture of ozonated oil and zinc oxide as a primary teeth root filling material. Clinical and radiographic evaluation suggested that teeth obturated with ozonated oil-zinc oxide demonstrated good success rate (93.3 %) as compared to zinc oxide eugenol (63.3 %).

BLEACHING:-

Bleaching can be done using ozone gas due to its strong oxidising properties. After removing the root canal filler material from the pulp chamber, the canal is sealed tight at the level of cementoenamel junction. Now a bleaching paste or a cotton pellet moistened in bleaching solution is packed in the chamber and sealed with GIC.Then the crown is irradiated with ozone for minimum of 3-4min. For bleaching of entire dentition, tray technique can be used. This ozone treatment bleaches the teeth within minutes.

HYPERSENSITIVITY:-

Smear layer present over the tooth surface prevents the penetration of ionic calcium and fluoride deep into the dentinal tubules. Ozone removes the smear layer, opens up the dentinal tubules, broadens their diameter and allows calcium and fluoride ions flow into tubules easily, deeply and effectively to plug dentinal tubules, preventing the fluid exchange through these tubules. Quick and prompt relief from root sensitivity has been documented after ozone spray for 60sec followed by mineral wash on to the exposed dentine in a repetitive manner.

Dahnhardt JE, Gygax M, Martignoni B, Suter P, Lussi A in 2008 reported a study on whether the treatment of hypersensitive teeth with gaseous ozone (Healozone, KaVo 1600 ppm) for 60 seconds reduces pain immediately after treatment and in the longer term. Found no statistically significant results.

DECONTAMINATION OF AVULSED TEETH:-

A high level of biocompatibility of aqueous ozone on human oral epithelial cells, gingival fibroblast cells, and periodontal cells has been found. Two-minute irrigation of the avulsed teeth with non isotonic ozonated water not only provides mechanical cleansing, but also decontaminate the root surface, with no negative effect on periodontal cells remaining on the tooth surface before replantation.

HALITOSIS:-

It oxidizes the volatile sulphur compounds to its corresponding negative sulphoxide.

CONC. & EFFECT ON MICROBES:-

Ozone is an effective anti-microbial agent capable of killing bacteria, fungi, protozoa, and viruses as well. It acts well on gram -ve Anaerobes (like Porphyromonas endodontalis and Porphyromonas gingivalis) and gram +ve bacteria (oral streptococci).Concentrations up to 1 μg ml^{-1} can eliminate E. coli, Pseudomonas aeruginosa, and Serratia marcescens, as well as Candida albicans. Staphylococcae are killed with 3–5 μg ml^{-1}. Concentrations over 5 μg ml^{-1} will eradicate most microorganisms in a few seconds.

WOUND HEALING:-

The influence of ozonized water on the epithelial wound healing process in the oral cavity was observed by Filippi . It was found that ozonized water applied on the daily basis can accelerate the healing rate in oral mucosa. Reduces the post extraction healing time by forming a pseudo membrane over the socket and protecting it from any physical and mechanical insults.

SOFT TISSUE LESIONS:-

Soft tissue lesions like herpes, aphthae, denture stomatitis,cheilitis, candidiasis, cysts and traumatic wounds can be treated with either Ozonated water or oils. The disinfectant and healing properties help in the healing of these lesions.

DISINFECTING DENTURES:-

Arita et al in 2006 reported that application of ozonated water may be useful in reducing the number of C.albicans on denture plates. The heat-cured acrylic resins were cultured with C.albicans. After treatment of flowing ozonated water, the number of attached C.albicans was counted. Significantly reduced count.

IN DENTAL UNIT WATER LINES:-

Wirthlin et al(2003) concluded that controlling DUWL biofilm would have beneficial effects on nosocomial infections. According to Montebugnoli et al(2004) DUWL's are ideal environment for the growth of microorganisms entering dental units from the municipal water supply and from previously treated patients. In model dental unit water lines, Ozone achieved 57% reduction in biofilms and 65% reduction in viable bacteria inspite of being used in a very low dose and with a short time of application

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.

CURE FOR OZONE INTOXICATION:-

The patient must be placed in the supine position. The patient should inhale the humid oxygen and treated with Vitamin E, ascorbic acid and n-acetylcysteines.

CONCLUSION

Inconsistent use…epiphora, URTI, rhinitis, cough, headache, shortness of breath, heart problems, stroke, High oxidative power…..ozone resistant – glass, silicone, Teflon Intoxication – supine, Vit E, n-acetylcysteine, Effectiveness of Ozone with or without the Additional Use of Remineralizing Solution on Non-Cavitated Fissure Carious Lesions in Permanent Molars

40 children….9-12 yrs…non-cavitated fissure caries, Group 1 – ozone applied….40 sec, Group 2 – ozone + remineralising agent, Assessment…imm., 1,2,3,6 mon…No statistically significant difference

Author name:

Dr. Gayathri, Senior Lecturer

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