Review Article

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# Effectiveness of Ozone against Common Dental Problems: A Literature Review

Dentistry Section

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## ABSTRACT

Oral disease represents a major concern among all populations. Despite great efforts that have been made in the past few decades to overcome these diseases; a large part of the world population still suffers from oral diseases which are considered a major reason for the loss of a tooth. Different bacterial species colonises the oral cavity, some of the bacteria are found to be associated with the cause of one of the most common disease called periodontitis. The infectious nature of periodontopathogens has been studied extensively. Currently, treatment of various oral diseases includes supragingival as well as subgingival debridement, root canal treatment and in severe cases, extraction along with antibiotic therapy to help achieve a pathogen-free environment. Continued research and development in the field of dentistry have brought new approaches in treatment modalities. The use of ozone is one of the latest therapies that has gained the interest of researchers in the past few decades. Ozone is a pale blue colour gas and is the natural constituent of the atmospheric layer of Earth. It is a modern pharmacological approach that is biocompatible and has shown its effectiveness against bacteria (gram-positive and gram-negative bacteria), viruses, and fungi. The beneficial biological effect of ozone has made its usage at all stages of disease propitious. The explication of the mechanism of ozone at the molecular level has proved to be beneficial in different medical and dental treatments. The use of ozone in clinical practice can be advantageous to the patient in terms of pain relief and treatment time. Therefore, the present article briefly reviews the chemical nature of ozone, its therapeutic uses, and the benefits it can provide in the treatment of various oral diseases.

**Keywords:** Chlorhexidine, Immune-stimulating, Ozonator, Periodontopathogens

## INTRODUCTION

Ozone is an allotrope of oxygen that exists naturally in the atmosphere of the Earth. It is a triatomic molecule consisting of three oxygen atoms. It is considered a healthy component of the environment present in the stratosphere and protects the Earth from harmful ultraviolet rays emerging from the sun. Ozone is primarily accompanied by electrical storms [1].

Periodontitis is a common multifactorial inflammatory disease triggered by bacterial microorganisms and antigens that induce a local inflammatory response and trigger innate immune system activation [2]. Dental plaque harbours several bacterial species of which some putative pathogens that were closely associated with the periodontitis are *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis* [3,4]. Even though dentistry is constantly improving, the success of treatment depends upon the elimination and reduction of periodontal pathogens [4]. However, in interproximal areas, root concavities, deep gingival pockets, complete removal of periodontopathic bacteria can be difficult. To overcome this, adjunctive treatment methods like administration of antiseptics, local and systemic antibiotics were introduced which have been found to be effective [4]. However, due to the prevalence of complex periodontal pathogens that require the use of antimicrobial drugs,the development of bacterial resistance to antibiotics has been observed [5]. In the era of antibiotic resistance, the use of ozone therapy as an adjunct treatment modality presents an alternative approach to the management of various oral diseases [6]. The present review article focuses on the properties of ozone and its advancement with time in various dental treatments and also supports its use following non surgical periodontal therapy.

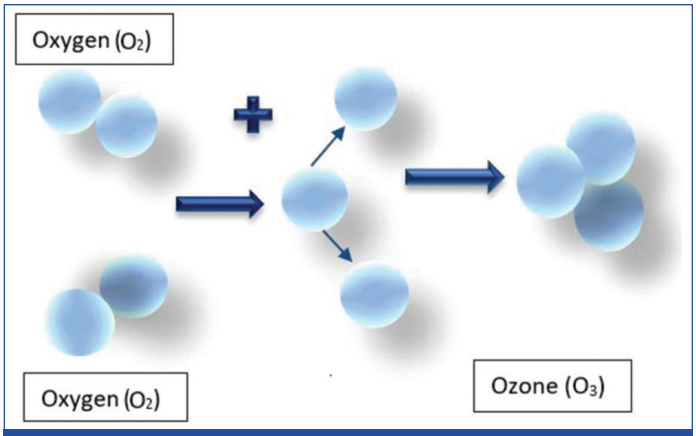
## HISTORY

In 1828, ozone was first identified as the chemical compound by a German Chemist who is also called the father of ozone therapy, Christian Friedrich Schönbein [7]. An electric current was passed through water, and a peculiar smell was created, which he referred to as ozone, derived from the Greek word "Ozein," meaning "odour". He pointed out that, ozone formation is the reaction of white phosphorous with the moist air and is to be called phosphorised oxygen and so the name ozone prevailed [7]. Ozone has a long history of clinical applications and research.

In 1857, a German physicist and physician, Joachim Hansler together with Hans Wolff, who was also a German physicist, created the first ozone generator for the purpose of medical use [7,8]. In 1950, Edward Fisch became the first dentist to make use of ozone [8].

## CHEMISTRY

Ozone is a chemical compound that consists of three atoms of oxygen. The formation of ozone takes place when an electrical discharge breaks a molecule of oxygen into two individual atoms of oxygen. One molecule of oxygen then combines with one individual atom of oxygen and results in Ozone ($O_3$) also called as triatomic oxygen [Table/Fig-1] [7]. Ozone used in medical field is a combination of 95%-99.5% pure $O_2$ and 0.05%-5% pure $O_3$ [9,10]. The molecular weight of ozone is 41.98 g/mol. Ozone has a high oxidation potential




**[Table/Fig-1]:** Formation of Ozone [7].
(Image drawn by Authors)

with a half-life of 40 minutes at 20°C [11]. Thermodynamically, being a highly unstable compound that depends upon temperature and pressure. Due to this property, ozone is prepared immediately prior to use as it canrapidly decompose to pure oxygen.

## OZONE GENERATION

Generation of ozone takes place by the reaction caused when oxygen flows across an electric arc with a potential difference of 10,000 volts [12]. Lightning is then used to induce the reaction giving air its typical smell just like the one experienced after the storm. For medical and dental applications variety of ozone concentrations is required (0.5-80 µg/mL). Transformers are used to vary potential and modify the flow of oxygen across the arc. Ozone being the strongest oxidising agent is capable of oxidising most of the plastic materials except polyethylene, silicone, polypropylene, and teflon and most ferrous material except stainless steel 316 and titanium, therefore all ozone generator modules must withstand oxidation [12]. This medical ozonator was then used to convert 5% of pure oxygen into ozone, generating an oxygen mixture of 95:5. In medical use, the gas produced by medical grade oxygen is administered in precise therapeutic doses, has excellent health benefits in dental caries, significantly reduces blood cholesterol, and is used in the therapeutic option of the hypoxic and ischaemic syndrome [13]. The concentration of ozone generated can be done by the use of a photometer in the ozone generator [14]. Some of the systems available for the generation of ozone developed in the past few decades are:

1. **Ultraviolet system:** This system produces ozone in low concentrations and is typically utilised for esthetics, saunas, and air purification [15].
2. **Cold plasma system:** This system is majorly used for the purification of air and water [15].
3. **Corona discharge system:** This generates high ozone levels. In the medical and dental fields, this system is most widely used, due to its controlled production rate of ozone and easy handling ability [15].

## APPLIANCES PRODUCING OZONE GAS

In dentistry, ozone application has been advocated as a support for many conventional treatments. For this purpose, various appliances have been introduced for use in dentistry.

1. **Heal ozone:** Designed by Cur Ozone USA Inc., is now distributed in Germany by Kavo Dental, Biberch. It is an air-based system with a closed circuit. The application of gas takes place within this closed circuit. The concentration of ozone provided to the tissue is about 2100 ppm [11]. Perfect airtightness is required for the application of ozone ensuring no gaseous escape. It can only be used in areas where air tightness can be achieved.
2. **Ozony tron:** This device uses high frequency and voltage concentration and can adjust current intensity at five levels. It consists of a glass probeformed by a double glass camera and a mix of noble gases emitting electromagnetic energy. Probe tip when comes in contact with the body surface, start emission of energy all around the operation field. Ozone generated in the area of operation is 10 to 100 µg/mL [11]. It is not a closed circuit therefore can be used in areas that are challenging to reach like the gingival pockets.
3. **Prozone:** It consists of plastic attachments (Perio tips and Endo tips) that can be exchanged during different dental procedures, thereby providing a hygienic environment [11,16].
4. **Ozotop:** This ozone delivery system is compact and convenient to use. It utilises a corona discharge system for the generation of ozone and can easily penetrate the periodontal pocket [11,16].
5. **Customised thermo formed dental appliance:** Hard, medium, or soft thermoformed dental appliances can be manufactured that can reach 2-3 mm into the gingival pocket [16].

## MECHANISM OF ACTION

Mechanism of action of ozone are supported by many studies. Some of the studies [17,18] quotes evidence of $O_3$ interacting with fungal cell walls like bacteria. $O_3$ has shown the oxidation of phospholipids and lipoproteins present within the bacterial cell envelope. this results in disruption of bacterial cell envelop. Some of the evidence also demonstrates the ability of $O_3$ to interact with the fungal cell wall. By undermining the integrity of the cytosolic membrane, it can infiltrate the microorganism and cause the oxidation of glycoprotein and block enzymatic function [19]. Ozone oxidises the lipoprotein layer of bacterial cell and disrupts the integrity of the cytosolic membrane. The microorganisms when infiltrated results in oxidisation of glycoproteins, glycolipids, and block enzymatic function [20]. This wide range of microbiologic properties makes it a useful disinfectant.

In lipid enveloped viruses, $O_3$ plays a role in the oxidation of lipoproteins, glycoproteins and result in interference with the reproductive cycles of the virus [20]. Due to multiple causative factors like microorganisms, diet, host response, etc., complete elimination of dental infection has not been very successful. Adaptation of acute infection for longer period coverts to chronic infection. Pathogenic organisms being opportunistic causes damage to the tissues. All pathogenic organisms have weak antioxidant or enzyme systems present in the cell membrane. When ozone is used to treat the infection, it destroys the cell membrane and causes the death of an organism. The pathogenic contents are then exposed to the internal environment, allowing the immunologic system to initiate its physiologic property [20]. Treatment of oral infection involves oral prophylaxis, therapeutic mouth rinses, antibiotics, and sometimes surgical procedure. The use of ozone to treat the dental infection can reduce the use of antibiotics and sometimes the need for surgery [21].

## APPLICATION MODALITIES

### Aqueous Ozone

Ozone can also be administered in the form of water. It is not only a natural disinfectant but also is biocompatible with oral tissues. Therefore, it is not toxic for use and no negative gastrointestinal effects have been found from ingestion. It is also effective against a number of pathogenic bacteria and helps in reducing inflammation. Apart from bacteria, ozonated water is very effective against various, fungi and viruses [11]. Some system that provides a solution up to 4.0 ppm, can be sustained for 30 minutes due to their unstable nature. Even then high levels of aqueous ozone should not be used for long-term repeated use without specific indication. It can be used in the form of nano bubble water that can be retained for six months as aqueous form of ozone [16]. Takahashi M et al., indicated the potential functionality of microbubbles in the form of aqueous application [22]. One of the newly introduced devices called Purecare oral irrigator from Purecare Dental manufacturer has been recently introduced into the market which consists of a patented capsule through which regular water passes and produce ozonated water [23].

### Gaseous Ozone

Ozone used in the form of gas is carried by a device corona discharge ozone generator, which transmits ozone by a suction device that deploys oxygen only when there is negative pressure. If the suction is compromised, ozone deployment is immediately stopped causing a negative secondary effect on respiratory tracts. To avoid this, devices that localise gaseous ozone administration at the target area are used to protect adjacent tissues to the respiratory tract [24].

### Ozonised Oil

Apart from gaseous or the aqueous form, it is possible to administer ozone in the form of oil, commercially available as ozonised olive oil (oleozon) or ozonised sunflower oil (Neozone 4000). Some studies performed using ozonised sunflower oil as an adjunctive treatment have found it to be very effective against microorganisms like *Streptococci*, *Escherichia coli, Pseudomonas*, and *Staphylococci* [25-27].

## THERAPEUTIC ACTION

Ozone in dentistry has a physiochemical property. There are several known actions of ozone. Some of the most important biological action of some known actions of ozone are listed below.

### Antimicrobial Effect

Ozone acts by disrupting the cytoplasmic cell membrane due to dual bond ozonolysis. Due to its substantial antioxidant ability, it does not cause any harm to human body cells. The research application of ozone for few seconds to the bacteria with no immunity can damage the cytoplasmic membrane of the cell and also stops all vital functions of bacteria [26]. Gram-positive bacteria have been found to be more susceptible to ozone exposure than gram-negative bacteria [26].

### Immune-Stimulating Effect

Ozone affects both cellular as well as the humoral immune system. It induces immunocompetent cell proliferation and helps in the synthesis of immunoglobulin. It also enhances the function of macrophages and leads to the production of cytokines. Ozone has also been found to synthesise biologically active substances such as prostaglandins or interleukins that play a significant role in inflammation reduction and facilitate wound healing [26,27].

### Antihypoxic Effect

Ozone by increasing the partial pressure of oxygen in the tissues, promotes the transportation of oxygen in the blood, resulting in alterations in cell metabolism. Ozone changes the configuration of erythrocytes by raising the 2-3 diphosphoglycerate (2,3-DPG) concentration, and allow the return of oxygen to the inflamed tissues [28].

### Biosynthetic Effect

Ozone causes increases in the number of mitochondria and ribosomes and causes activation of protein synthesis in cells and contributes to up-regulation of function and the capacity of tissues for regeneration [29]. It also could attack many biomolecules like cysteine, histidine, methionine, and residue of proteins. Ozone being highly oxidative has a disruptive effect on cariogenic bacteria.

## OZONE IN DENTISTRY

### Effect of Ozone in Endodontics

The success of endodontic treatment depends upon the effectiveness of antimicrobial agents used in treating periapical lesions. A randomised trial done by Kist S et al., in 2017, to assess the efficacy of ozone gas for periapical lesion found to be equally effective as compared to sodium hypochlorite when used as the root canal disinfectant [30]. [Table/Fig-2] provides the summary of studies on the effect of ozone against different bacterial strains [31-34]. While some studies have successfully proved the effectiveness of ozone against bacterial strains [31,33], some in-vitro studies stated, otherwise finding the effect of ozone gas inconsistent [32,34].

### Effect of Ozone in Oral Surgery

Dry socket has been one of the displeasing complications that occur after the extraction. Use of ozone therapy by application of ozone in the intra-alveolar region of the affected area for 12 seconds using a plastic attachment with the help of a device called Prozoneby W and H, has been one great success in preventing dry socket after extraction and reducing the incidence by 3.3% along with improved healing after third molar removal [35]. Application of ozone in the extraction can accelerate the wound healing process [36].

It has also been used in the treatment of osteonecrosis of the jaw in combination with antibiotic therapy. Where, efficacy of a 15-day course of antibiotics, surgery, and ozone therapy in 12 multiple myeloma patients with osteonecrosis of the jaw was evaluated. Treatment results were effectual with eight out of 12 patients having complete resolution [37].

| S. No. | Researcher | Year | Observation |
|---|---|---|---|
| 1 | Hems RS et al.,[31] | 2005 | In an in-vitro study for evaluation of the ability of ozone to kill a strain of *Enterococcus faecalis*, the authorsfound hypochlorite to possess superior cidal activity compared to ozonated water against *E. faecalis* in broth and culture |
| 2 | Estrela C et al.,[32] | 2007 | Evaluated antimicrobial efficacy of ozone gas, water, CHX, and hypochlorite in root canals. Results demonstrated that no solution used as an irritant over a 20-min contact time demonstrated an antimicrobial effect against *E. faecalis* |
| 3 | Huth KC et al.,[33] | 2009 | An in-vitro study evaluated the effect of ozone on enteropathogens in a biofilm and demonstrated that high-concentrated aqueous ozone (20 $\mu g/mL^{-1}$) and Chlorhexidine (CHX) were effective against enteropathogens. |
| 4 | Boch T et al.,[34] | 2019 | In this in-vitro study,it was found thatantimicrobial activity of gaseous ozone on *E. faecalis* in a biofilm anddemonstrated, Ozone reduced *E. faecalis*, even organised in a biofilm, however, lower than NaOCl. No treatment reduced the bacteria. |

**[Table/Fig-2]:** Summary of studies on the effect of ozone against different bacterial strain [31-34].

### Effect of Ozone in Prosthodontics

A common problem that is addressed in denture-wearing patient is denture stomatitis. The causative pathogen that results in denture stomatitis is *Candida albicans*. Immersion of denture in ozonated water was found effective in reducing the number of *Candida albicans* in denture plates when used in 10 ppm of concentration when exposed for 30-60 minutes [38]. A previous study found ozone gas to be more effective against *C.albicans* than its aqueous form [39].

### Ozone in Caries Management

Dental caries is a disease of multifactorial origin. Management of caries ranges from a surgical approach based on “extension for prevention” (Blacks’ philosophy) to the newer concept of minimal intervention. The remineralisation effect of ozone was evaluated by Baysan A and Lynch E in a clinical study with a six month and 12 months follow-up where he exposed root caries with 2100 ppm of gaseous ozone and found ozonated lesion getting rehardened when compared to the control groups [40]. Also, a longitudinal study on management of primary root caries using ozone therapy demonstrated its capability to reverse the carious lesion causing remineralisation and also suggested its use against conventional drilling method [41]. An in-vitro study by Samuel SR et al., also illustrated the remineralisation effect of ozone on the carious toothwhen teeth specimen were subjected to ozone (ozonated water 0.1 mg/L and 10% nano-hydroxyapatite paste, Aclaim™), without ozone (only 10% nano-hydroxyapatite paste, Aclaim™), and control (subjects’ saliva alone). The laser fluorescence recorded greater depth of remineralisation following application of ozonated water and nano-hydroxyapatite were found compared to those of the without ozone and control groups [42,43].

### Effect of Ozone in Biofilm

Ozone gas or ozonated water wa sfound very effective concerning the removal of bacteria as well as a biofilm. With 60 seconds of exposure to the ozonated water or gaseous ozone, microflora like *Lactobacillus casei*, *Streptococcus mutans*, and *Actinomyces naeslundii*, have been found to be inactivated. For reduction of plaque, 0.1 ppm concentration of ozonated water showed positive results [44,45]. When used in a concentration of 0.5-4 mg/dL it can inhibit both gram +ve and gram -ve bacteria and also *Candida albicans* which further prevents the formation of plaque [44].

### Effect of Ozone in Periodontics

Periodontitis is one of the most common chronic disorders which starts with gingivitis and if not treated during this stage causes destruction of supporting tissues, leading to loss of teeth. The severity of disease and its transition depends upon the host response, presence of pathogens and also genetic variance [46]. Principal periodontal pathogens found in the subgingival microbiome are considered an aetiologic factor for periodontal disease. Treatment includes non surgical periodontal therapy (phase I) and in some cases where phase I therapy is found to be ineffective, surgical approach is the treatment of choice. A randomised placebo-controlled clinical trial conducted by Al Habashneh R et al., investigating the effect of scaling and root planning followed by irrigation with ozonated water in 20 lg/mL concentration has expressed significant improvement in terms of plaque index, clinical attachment loss, probing depth, recession [47]. The antibacterial effect of aqueous or gaseous form of ozone, when exposed for 1 minute, was addressed to be beneficial against periodontal pathogens like *Tannerella forsythia Porphyromonas gingivalis*, and *Parvimonas micra* [47].

In the past few decades, ozone has been gaining the interest of many scientific researchers. Various studies have been carried out to evaluate the effectiveness of ozone when used as an adjunctive treatment modality to a periodontal treatment [Table/Fig-3] [48-54].

### Effect of Ozone in Healing of Wounds

When a wound is subjected to oxygen it can help in accelerating the wound healing. A study undertaken to evaluate the effect of Ozone therapy on cutaneous wound healing in the guinea pig model showed a significantly smaller wound size and residual wound area. It also stated that topically applied ozone can affect the granulation tissue formation of the wound healing during the inflammation phase [55].

| S. No. | Researcher | Year | Observation |
|---|---|---|---|
| 1. | Sorokina S and Lukinych L [48] | 1997 | They used ozonated water for subgingival irrigation in their study in combination with oral hygiene measures and found a considerate reduction in dental plaque formation due to its anti-inflammatory effect. However, it is also apparent that just irrigation is not sufficient for better results. |
| 2. | Ebensberger U et al., [49] | 2002 | 2 min irrigation with ozonated water (4 mg/L) leads to mechanical cleansing, root surface decontamination, and no negative effect was seen in the periodontal cell of the remaining tooth surface. |
| 3. | Nagayoshi M et al., [50] | 2004 | Following exposure to distilled water and ozonated water (4 mg/L) for 120 seconds, bacterial cells in dental plaque were analysed. streptococcus mutans in dental plaque treated with distilled water were found alive while that treated with ozonated water reduced remarkably. When tested on the decalcified human tooth in-vitro, they observed inhibition in the formation of dental plaque. |
| 4. | Ramzy MI et al., [51] | 2005 | Stated that quadrants treated with ozonated water along with oral hygiene instructions showed excellent improvement regarding GI (gingival index), PI (plaque index), and bacterial count. |
| 5. | Huth KC et al., [52] | 2007 | Compared gaseous as well as aqueous ozone antimicrobial effects and came to the conclusion that aqueous ozone is biocompatible for oral application and showed less toxicity than gaseous ozone. |
| 6. | Kshitish D and Laxman VK [53] | 2010 | A split mouth study in a period of 18 months was performed using ozonated water and 0.2% CHX. Double blinded method was used regarding irrigation type. Ozonated water was used to irrigate one side of the oral cavity and the other side was irrigated with 0.2% CHX solution. Bacteria (*Porphyromonas gingivalis, Aggregatibacter actinomycetemcomitans, Tannerella forsythensis*), viruses (Herpes simplex virus 1 and 2, Epstein Barr virus, Human cytomegalovirus), and fungi (*Candida albicans*) were examined by means of PCR. Percentile reduction in the concentration of bacteria, viruses, and fungi was observed when irrigated with ozone water in comparison to that with 0.2% CHX solution. In conclusion, amid the CHX substantivity, single irrigation by ozone water was found to be very efficient for microorganisms' inactivation. |
| 7. | Noites R et al., [54] | 2014 | In this in-vitro study, the effect of hypochlorite, CHX, or ozone alone or when used in combination against pathogens like *E. faecalis* and *Candida albicans* were compared and it was found that complete elimination of organism when irrigated for 24s with ozone following use of 2% CHX. This proved that the use of ozone alone is not effective against these organisms. |

**[Table/Fig-3]:** Summary of studies on the effect of ozone in periodontics [48-54].

A chronic wound can significantly affect the health of an individual. A study done by Fitzpatrick E et al., evaluated the response of skin cells when exposed to ozone. It stated that ozone when administered in a controlled dose can help accelerate the cell cycle and also induce the production of growth factors like nuclear factor kappa B, which is a regulatory factor for inflammatory response and wound healing [56].

The injury to tissue elicits many biological processes which promote wound healing. Failure of the wound to heal can lead to severe complications. The immune response plays a very important role in removing the dead cells and helps in preventing further infection [57]. Ozone therapy has proved to be very efficient in the repair of the affected tissue. It can inhibit fungal growth, inactivate bacteria via disrupting their cell envelopes, and can also damage the capsid of the virus. According to a study done by Xiao W et al., on mice, suggested that the treatment of wounds by ozonised oil increases critical genes that increase the production of fibroblast resulting in new tissue formation and wound healing [58].

## OZONE TOXICITY

Given the high oxidative strength of ozone, all components in the contact with ozone gas must be impervious to its effect, some of the material that was found to be resistant to ozone are glass, teflon, and silicone. The maximum ozone concentration in the oral cavity is 0.01 ppm. Up to 0.05 ppm of ozone administered for eight hours does not cause toxicity, but can also be fatal when used in a concentration of 0.3 ppm for 15 minutes or 0.06 ppm, eight hours a day for five days [59]. Ozone therapy-induced complications are uncommon at 0.0007 ppm per application in any form [12]. Some of the reported side effects of ozone over-exposure are: Upper respiratory tract irritation, poor circulation, rhinitis, cough, occasional nausea, vomiting, headache, blood vessel swelling, shortness of breath, heart problems, and epiphora [59,60].

However, in the case of ozone intoxication, the patient must immediately be placed in the supine position, asked to inhale humid oxygen, and take ascorbic acid, vitamin E, and should be treated with n-acetyl cysteine [12,61]. Cytotoxicity of ozone water was considered less when compared to its gaseous form and other

antimicrobial agents when observed its effect on gingival fibroblast and epithelial cells [62].

### Contraindication(S)

Some of the contraindications to be considered before the administration of ozone are Glucose-6-phosphate-dehydrogenase deficiency, severe myasthenia, pregnancy, hyperthyroidism, severe anaemia, recent myocardial infarction, acute alcohol intoxication, haemorrhage was also observed from some organs, allergic to ozone [62].

## CONCLUSION(S)

With the advancement in modern sciences, the face of dentistry has also changed providing a new vision of painless treatment. The present article found ozone therapy to be more advantageous than any other traditional therapeutic modalities. Ozone therapy is a non invasive, conservative, and inexpensive method of treatment that offers a dynamic approach to dental care. Some of the studies have suggested its positive effect in clinical practice. Furthermore, studies are required to prove its effectiveness. Treating patients with ozone therapy has helped minimised recovery time and patient anxiety level with remarkable outcomes following the treatment. Many scientific supports have demonstrated its potential as an adjunct to periodontal therapy. Due to lack of knowledge and evidence use of ozone and its beneficial effect are still not accepted in routine dental practice. However, to allow the use of ozone therapy as a standardised treatment procedure, more clinical research in the dental and medical fields is needed.

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