The use of ozone in dentistry and maxillofacial surgery: A review

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Ozone has been successfully used in medicine because of its microbiologic properties for more than 100 years. Its bactericide, virucide, and fungicide effects are based on its strong oxidation effect with the formation of free radicals as well as its direct destruction of almost all microorganisms. In addition, ozone has a therapeutic effect that facilitates wound healing and improves the supply of blood. For medical purposes, ozone may be applied as a gas or dissolved in water. Despite the advantages that the therapeutic use of ozone offers, reservations remain in terms of its application in the oral and maxillofacial area. Particularly, the gaseous application of ozone is critically evaluated because of its possible side effects on the respiratory system. The objective of this article is to provide an overview of the current applications of ozone in dentistry and oral surgery. Research was based on peer-reviewed sources found through a Medline/PubMed search and other textbooks, reviews, and journals. *(Quintessence Int 2006;37:353–359)*

Key words: caries, dentistry, disinfection, germs, microbiologic effect, oxidation, ozone, soft tissue, surgery

Ozone (O_3, molecular weight of 47.98 g/mol) is a triatomic, endothermic, and thermodynamically highly instable oxygen compound that, dependent on system conditions like temperature and pressure, decomposes to pure oxygen with a short half-life. The decomposition produces, apart from molecular oxygen, atomic oxygen,[1] which is highly reactive; oxidizes all nonnoble metals immediately; and attacks numerous organic compounds as a radical.[2] This makes ozone, apart from fluorine, one of the strongest oxidants.[3] Its oxidation effect ranges clearly above that of molecular oxygen. Therefore, materials used in ozone production or processing must be ozone-resistant.

Dissolved in water, ozone is relatively instable. Its decomposition rate, which may

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range from seconds to hours,[4,5] is essentially dependent on the quality of water (purity of water) and system conditions (temperature, mechanical movement of the water, vessel material).[6] During the decomposition in water, hydroxyl (OH) is formed as a second oxidant accelerating the decomposition process of ozone.[7]

At room temperature, ozone is a blue gas with a characteristic smell that can still be noticed in air at a concentration of 2 ppm. Gaseous pure ozone passes the mucous membrane of the upper respiratory tracts essentially without absorption and can therefore reach the unprotected bronchioli and alveoli directly.[8] Ozone oxidizes parts from sulfhydryl groups of enzymes, peptides, and proteins of certain lipoproteins on cell membranes, which causes an accumulation of toxic intermediate products like free radicals and peroxides. These can lead to vascular-inflammatory damage of the bronchioli and alveoli walls, forming fibrinous coats and destroying the surfactant.[9] Particularly, the oxidative reactions of ozone with unsaturated fatty acids and phospholipids on membrane surfaces and erythrocytes have been described several times.[10,11] Long-time exposure to high ozone concentrations can cause an acute collapse of the alveoli and bronchioli and potentially irreversible damage of the alveoli function.[12,13]

However, pure ozone is not used for medical purposes; a mixture of ozone and oxygen or a solution of ozone in distilled and demineralized water is used. The ozone-oxygen mixture is very tissue-friendly, revealing a positive effect on the flow properties of blood. It is based on a structural modification of the erythrocyte membrane that causes an inhibition of the surface Na^+-K^+ adenosinetriphosphatase (ATPase).[14] The effect of ozone on the erythrocytes changes the proteins of the cytoskeleton and increases the elastic molding properties of the membrane in dependence on the concentration.[15] This prevents adhesions between erythrocytes; their improved elasticity facilitates their passage through fine capillaries.

Apart from stimulating the blood flow, ozone also has strong bactericide, virucide, and fungicide effects,[16,17] making it a possible therapeutic agent in inflammatory and infectious diseases.[18,19] Intraorally it can be used for the treatment of chronic periodontitis, caries, infections after tooth extractions, chronic wound-healing impairments after radiotherapy, aphthae, mycoses, or root canal disinfection.[20–22] The current use of ozone for oral soft and hard tissue application is summarized in this article. For gathering the vitally important information for this article a Medline/Pubmed search was performed, setting the emphasis on peer-reviewed dental and medical journals containing the terms *ozone, surgery, caries, dentin, microbiological effect,* and *oral*. Additionally, common textbooks, reviews, and open source journals were scrutinized.

CLINICAL APPLICATION

Molecular level effects of ozone

Ozone was first investigated in 1933 by the Zürich dentist Fisch for the treatment of infected wound cavities and chronic periodontal infections.[23] Ozone has a broad antimicrobiologic spectrum[24] and a strong disinfecting effect[25] superior to that of chlorinated water.[26] Ozone dissolves better in water than does oxygen, even if the solubility quotient is stated differently.[27] However, ozone does not have the same strength on all germs, and there is a difference in action between applications involving individual bacteria and complete bacterial strains.[28] For example, enteroviruses and rotaviruses,[29] hepatitis A,[30] and human immunodeficiency viruses[31,32] are more ozone-sensitive than poliomyelitis and coxackieviruses.[33] The main antiviral actions of ozone are the change of the capsid and the irreversible destruction of viral DNA.[34] In bacterial cultures, *Escherichia coli* and *Candida albicans* are by far more ozone-sensitive than staphylococci.[35] Apart from an inhibition of their metabolic activity, the cell walls of bacteria are primarily damaged.[36] Current results have shown that bacteria can be completely destroyed by ozone-produced antibodies.[37] A study on human pathogenic germs showed the effectiveness of local ozone gas

application in bone surgery.[38] By the formation of peroxides on the surface of the mucous membrane, ozone is stimulating gluthation peroxidase, catalase, and superoxide dismutase.[39] This leads to enhanced phagocytosis.[40]

These antimicrobial properties make ozone an effective therapeutic agent for gingivitis or periodonitis.[41] The application of ozonated water in the peridontal ligament has revealed good results.[42] But, despite the promising results, no further clinical or experimental studies concerning ozone and periodontitis are currently known in the English literature.

Effects of ozone on bone and soft tissues

In oral surgery ozonated water is suitable for prophylactic applications against infections after osteotomies. In a prospective study involving 250 patients, the application of ozonated water during surgery as a cooling and rinsing medium in the osteotomy of third molars reduced the occurrence of infectious complications after the operation.[43,44] In another prospective study, the positive effect of ozone water in oral soft tissue healing could be demonstrated clinically and histologically.[45] Apart from the microbiologic effect, a therapeutic one must also be assumed. Several experimental studies on blood treated with ozone showed that the contact with ozone led to an increased release of interferons (IFN-α, -β, -γ), interleukins (IL-1β, IL-2, IL-6, IL-8), tumor necrosis factor (TNF-α), as well as transforming growth factor (TGF-β1).[46–50] In addition, ozone improves the rheologic properties of erythrocytes and facilitates oxygen release in tissue,[51] which can be attributed to the stimulation of 2.3-diphosphoglycerate and adenosine triphosphate (ATP) production in the erythrocyte metabolism.[52,53] In addition, it was possible to show in reinfused ozonated serum that an increased nitosyl reduction results in human endothelial cells, leading to a vasodilatation of vessels with an improved supply of blood to ischemic zones or to a reduction of a hypoxia.[54]

Particularly after radiotherapy in the maxilla or mandible, oxygen supply may be considerably reduced in the affected area: Apart from numerous intraoral side effects like xerostomia, mucositis, or loss of the sense of taste,[55] the obliteration of intraosseous vessels is caused, resulting in a deficient vascular supply of the spongy medullary spaces. The consequences are fibrosing and aseptic osteonecrosis. Such compromised bone as that after surgical interventions like tooth extractions[56] or implant dentistry[57] heals later than does healthy bone with a good blood supply. Also, surface wounds, eg, caused by denture pressure, frequently heal much later. Such cases always carry the risk of a persisting osteoradionecrosis.[58,59] Ozone might possibly be successfully used to treat such wound-healing impairments after radiotherapy. A clinical survey involving 11 radiotherapy patients demonstrated the local effectiveness of ozone in intraoral infected wounds after high-dose radiotherapy.[60] The wound areas of about 1 to 3 cm^2 were covered by necrotic tissue and superinfected. For 4 days, an ozone-oxygen mixture (3%) with an ozone concentration of 59 μg/mL was applied daily for 15 minutes under vacuum (1.5 bar) via a custom-made suction cup with respective feed and discharge tubes. Subsequently, the mixture was reduced to 30 μg/mL (1.5%) until the wound had completely healed. Prior to the therapy the wounds were curetted and cleaned. The result was significant hyperemia in the wound area as well as complete healing in nine patients.

The literature also contains varying results in relation to ozone application for the treatment of wound-healing impairments or severe skin reactions after radiotherapy outside of the oral cavity. While some authors report good results after ozone application,[61,62] a study group basing its findings on the evaluation of statements of the nursing staff and the treated patients could not recognize any properties of ozone promoting wound healing.[63] The patients of the same study reported, however, a pain-alleviating effect of ozone, which had been described earlier.[64] It should be mentioned, however, that simultaneously with the ozone therapy a drug therapy was performed so that it was not possible to evaluate the single action of ozone.

Apart from osteoradionecrosis, chronic and refractory osteomyelitis in the head-neck area can also be difficult to treat.[65,66] Also in this case, diffusion hypoxia results with reduced vascular blood supply and subsequent destruction of bone tissue. Several gram-positive and gram-negative germs are involved in an acute or chronic osteomyelitis[67] in which *staphylococcus aureus* is considered problematic and methicillin-resistant.[68] It could be shown that ozone has a good microbiological effect on methicillin-resistant strains of *Staphylococcus aureus*.[69] This potentially could make ozone an alternative to hyperbaric oxygen therapy after the removal of the bone sequestra.[70] Its action is based, on the one hand, on the enormous oxidation strength and, on the other hand, on the fact that bacteria can be more easily recognized and destroyed by granulocytes and the complement system after contact with ozone,[71,72] as well as on an increased phagocytosis performance of polymorphonuclear cells.[73]

Application of ozone in endodontics, treatment of dental caries, and prosthodontics

The oral application of ozone, however, is not limited to surgery. It is also applied in endodontics and prosthodontics.[74,75] Apart from the well-examined water disinfection of dental units,[76,77] gaseous ozone is particularly suited for caries therapy.[78,79] An in vitro survey showed the bactericide effect of ozone on *Streptococcus mutans* and *Streptococcus sobrinus*.[80] In comparison to a control group, a blood agar demonstrated a significant reduction of the 2 germs responsible for caries after 10 seconds of ozone gas application. Furthermore, it was shown that the microorganisms were reduced to less than 1% in 40 freshly extracted teeth with a slight incidence of root caries after 10 or 20 seconds of ozone water application as compared with a control group. These results correspond to the positive findings of other study groups[81]: In a study involving 89 patients with primary root caries, ozone application led to a complete arrest or hardening of caries in the sense of remineralization after ozone application of 18 months. A control group showed a deterioration of the original caries lesions. These results raise the hope for a new approach to caries therapy, facilitating, particularly in pediatric dentistry, a treatment free of anxiety and stress.[82] Controlled long-term studies in caries therapy with ozone are, however, still not available.

Another area of ozone use in dentistry would be the decontamination of root surfaces of teeth avulsed in accidents prior to replantation. A study on 23 extracted third molars showed immunohistochemically that the proliferation rate of cementoblasts and periodontal fibroblasts were not affected by the rinsing of the root surface with ozonated water for 1 minute as compared with sterile isotonic natrium solution.[83] Moreover, a slight increase in the proliferation rate was noted under ozone influence. This could have been observed on the epithelium, too, as confirmed by the results of other study groups[84]: Nonisotonic ozone water does not have any negative effect on the cells of the root surface at an exposure time of less than 2 minutes. These results raise the hope of future application of ozone in tooth transplantation or replantation and regenerative periodontal therapy.

In implant dentistry, the use of ozone is currently being investigated for the decontamination of the implant surface in periimplant therapy (not as the sole therapy, but only for the removal of microorganisms).[85]

Furthermore, the disinfecting action of ozone is used to clean dentures.[86] The action of ozone on the typical oral germs of *S mutans* (strain IID 973), *Sta aureus* (strain 209-P), and *C albicans* (strain LAM 14322), which are also found on dentures, have been investigated.[87] Apparently gaseous ozone revealed a more effective antimicrobial action than ozonated water and thus is more recommendable for denture cleaning. Similar results have been reported about denture-cleaning solutions enriched with ozone (concentration 10 ppm) against methicillin-resistant *Sta aureus* and *E coli* T1 phage strains.[88] All available studies show the effective bactericide, virucide, and fungicide action of ozone.

CONCLUDING REMARKS

1. Despite the positive properties of ozone gas or ozonated water—not only in waste water and pool water treatment but also in many fields of medicine—the use of ozone in oral and maxillofacial surgery is considered rather limited to date. This might be due, on the one hand, to the described possible side effects of ozone gas on the upper respiratory system during intraoral applications and, on the other hand, to the few long-term studies in the English literature.
2. The intraoral use of ozone must be performed by preventing ozone from getting into the respiratory air of the patient. This may be achieved by suction cups or vacuum caps.
3. The information related to proper ozone therapeutic dosage is controversial.
4. Initial data indicates promising potential of ozone usage for the treatment of certain carious lesions.
5. Additional clinical trials are needed to validate the feasibility and safety of routine usage of ozone in dentistry and oral and maxillofacial surgery.

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