Ozone Therapy: Healing Properties of the Blue Gas

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Abstract
Ozone is a medically versatile gas with a high oxidation potential. Ozone due to its antibacterial and antiviral action is used in the field of general medicine and dentistry. There are various industrial applications of ozone owing to its antioxidant property. This review of literature is an attempt to summarize the different modalities of ozone applications; especially in dentistry, highlighting its advantages, disadvantages, indications and contraindications.

Key Words: Antioxidant, Healing properties of ozone, Ozone, Dentistry

Introduction
The term ozone comes from the Greek word “ozein” meaning odorant. It is an allotropic form of oxygen, also known as triatomic oxygen or trioxygen. It can be found in ambient air at levels exceeding the national air quality of 0.12 ppm averaged over a period of one hour. It is produced naturally during thunderstorms and by the action of UV rays on atmospheric oxygen. Medical versatile oxidative therapy is a mixture of purest form of oxygen and ozone that is electrically activated. This blue gas is one of the most potent oxidant known to mankind. It is a bactericide, virucide and fungicide owing to its strong oxidation effect and formation of free radicals. Thus it is an effective antimicrobial agent that can be used to disinfect equipments, purify water and reduce microbial load. It is a toxic, reactive and an unstable compound that needs to be incorporated into other substances. For medical purposes, ozone may be applied as a gas or dissolved in water.

Historical Flashback
Ozone, discovered by Schonbein in 1840, is an allotropic variation of oxygen. During the First World War it was used as a heroic therapy for gangrene. Wolff invented the simple technique of exposing blood directly to a gaseous mixture of oxygen and ozone. Thus, was born the Ozonated Autohemotherapy (O3-AHT) procedure which is widely used. Ozone was used in a vapor-phase test as early as 1942 in an effort to reduce airborne bacterial infections. It has been used as a disinfectant in France since several years. It is widely suggested to be a good available alternative to present chlorination practice for treatment of domestic water.

Chemical Structure
Ozone, containing three oxygen atoms has a cyclic chemical structure. It is 1.6 times denser and 10 times more soluble in water than oxygen (49.0 mL in 100 mL water at 0 degree celsius). Although ozone is not a radical molecule, it is the third most potent oxidant after fluorine and persulfate. Ozone being an unstable gas, cannot be stored and hence needs to be used at once. It has a half-life of 40 min at 20 degree celsius. Ozone being thermodynamically unstable, is dependent on system conditions like temperature and pressure. It decomposes with short half time into pure oxygen. When pure oxygen is passed through a high voltage gradient (5–13 mV) medical ozone is generated. Thus, we collect mixture of more than 95% oxygen and not less than 5% ozone. Ozone generators are made of chemically resistant materials like stainless steel, eutal glass and Teflon.
Table 1: Routes of administration

<table>
<thead>
<tr>
<th>Parenteral</th>
<th>Rectal/vaginal insufflations</th>
<th>Topical or locoregional</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intravenous</td>
<td>Humidified ozone is administered by catheter.</td>
<td>Nasal</td>
</tr>
<tr>
<td>Intra-arterial</td>
<td></td>
<td>Tubal</td>
</tr>
<tr>
<td>Intramuscular</td>
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<td>Auricular</td>
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<tr>
<td>Subcutaneous</td>
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<td>Oral</td>
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<tr>
<td>Intraperitoneal</td>
<td></td>
<td>Vaginal</td>
</tr>
<tr>
<td>Intrapleural</td>
<td></td>
<td>Urethral and intrabladder</td>
</tr>
<tr>
<td>Intra-articular</td>
<td></td>
<td>Rectal</td>
</tr>
<tr>
<td>Periarticular</td>
<td></td>
<td>Cutaneous</td>
</tr>
<tr>
<td>Myofascial</td>
<td></td>
<td>Dental</td>
</tr>
<tr>
<td>Intradiscal</td>
<td></td>
<td></td>
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<tr>
<td>Intraforaminal</td>
<td></td>
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<tr>
<td>Intralesional</td>
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</tr>
</tbody>
</table>

Mechanism of action

1. Inactivation of bacteria, fungi, virus, yeast and protozoa
2. Stimulation of oxygen metabolism
3. Activation of immune system

Applications in general

1. Prevention of Indoor Air Pollution: Ventilation and Air Cleaners
2. To Prevent Nosocomial Infections
3. In Food and Beverage Industries
4. To Prevent and Control Animal Diseases
5. To clean invasive Medical Devises and Rooms
6. In Water Safety, Contamination, Recycling Issues
7. In Prevention and Control of Infectious Disease by Travelers

Applications in medical field

1. Treatment for rheumatoid arthritis and as additive therapy for geriatric carcinoma patients
2. Indicated for treatment of acne, allergies and furunculosis
3. It is also useful in treatment of hepatitis A, B and C
4. Bacterial, viral and fungal disinfection
5. Enhance healing ability of tissue by oxygenation
6. Balance of various metabolic reactions
7. Production of adenoside triphosphate by stimulating KREB’s cycle thus increasing cell energy
8. Increase in elasticity of erythrocytes and blood flow
9. Helps in treating Arteriosclerosis and Artherosclerosis by clearing arterial plaque

Application in Dentistry

1. Use in Endodontics and Conservative dentistry
   Dental caries: Upcoming atraumatic dental practice is ozone therapy. When ozone gas was applied to carious lesion for 10-20 sec, there was reduction of about 99% of microorganisms. Thus ozone therapy is introduced as conservative line of treatment. Studies reveal, reduction in microorganisms from small carious lesion was more than large lesion and lesion close to gingiva.

Root canals: Endodontic treatment of tooth is used for long standing infections within the tooth. It includes disinfecting the canals and filling it with biocompatible materials. Disinfection is carried out using sodium hypochloride, saline and calcium hydroxide. Thus aim of the procedure is to make tooth and surrounding bone sterile. Lateral canals provide opportunity to obligate anaerobes like bacteria, viruses and fungi to cross the root canal and communicate with periodontal tissues. Ozonated water is as good an antimicrobial as 2.5%
sodium hypochloride\textsuperscript{18}. According to studies, healing of periapical tissue is enhanced after use of ozonated water due to high metabolic activity of fibroblasts. Literature suggests that ozonated oil is much more effective than calcium hydroxide as an intra canal medicament. Infected area has negative charge due to anaerobic bacteria and their acidic nature\textsuperscript{19}, while ozone too has negative charge which helps in disinfecting canals and dentinal tubules\textsuperscript{20}.

2. Uses in Periodontics
Periodontal disease is a multifactorial condition treated with traditional and conservative treatments like root planning and scaling, surgical intervention with a scalpel or LASER therapy (with the Periolase, Nd: YAG LASER)\textsuperscript{21}. Ozonated water is used to irrigate sulci and pockets during scaling and surgical procedure thus reducing preoperative bacterial load\textsuperscript{22}. Each pocket and sulcus is insulflated with ozone gas after treatment. Due to direct contact of gas with crevicular fluid and tissue pathogenic load is reduced. For LASER therapy with the Periolase, ozonated water is to be used during ultrasonic debridement. A silicone tray isolation technique can be used in certain cases and multiple visits are required. Routine minor recall treatment cases, such as gingivitis, utilize pretreatment rinsing with ozonated water, irrigation of the periodontium and insufflation of any periodontal pockets\textsuperscript{23}. Topical application of ozonated olive oil jar is provided to patients for application at home. This continuous dose of ozone will decrease infection and percentage of recurrence.

3. Uses in Prosthodontics
According to a study, few oral microorganisms and no viable \textit{C. albicans} were detected after exposing the denture to flowing ozonated water (2 or 4 mg/L) for 1 min. Thus, the application of ozonated water is effective in reducing number of \textit{c.albicans} in denture base\textsuperscript{24}.

Comparison between microbicidal effect between gaseous ozone and ozonated water on dentures were carried out and found that direct exposure to gaseous ozone was more effective. Ozone is found effective against methicillin-resistant \textit{S. aureus} and viruses, thus is a potential denture cleaner\textsuperscript{25}.

4. Adjunct therapy for extractions, other surgical procedures and bisphosphonate osteonecrosis
Ozone is so versatile that it can be used for almost any type of dental procedure. After a tooth is extracted or any basic surgical procedure it is recommended post-surgically to irrigate and insufflate the area. This reduces the positive electric potential of the wound and potential scar with the negatively charged gas or water. Healing of the wound is generally much faster and with less or no complications\textsuperscript{26}. Bisphosphonate necrosis has been extremely difficult to treat medically and surgically. There has been some success with ozone utilizing the foundational protocols along with intraosseous injections and intraoral silicone tray treatment of the osteonecrotic lesion\textsuperscript{16}. The patient is always sent home with a jar of ozonated olive oil as a postoperative dressing for the wound.

5. Uses in Oral medicine
Good anti microbial power and capacity of stimulating circulatory system along with ability to modify immune system helps to treat hepatitis, herpes simplex, herpes zoster, ANUG and aphthous ulcers\textsuperscript{15}.

From a pilot study it was discussed that ozone therapy accelerate healing compared to conventional approach to treat aphthous stomatitis due to its properties like immunomodulating, analgesic, antimicrobial and capacity to promote blood circulation\textsuperscript{27}.

6. Implant cases
During placement of implants, ozone gas is bubbled into prepared socket and implant is placed. This reduces percentage of infection in implant cases. Ozone therapy can also be used in perimplantitis cases.

7. Other uses
Many studies are being conducted owing to ozone’s anti-immunological and anti-inflammatory properties. Ozone therapy can also be used in oral premalignant conditions like oral lichen planus. It is used to desensitize teeth and to clean avulsed tooth before placement and in many pediatric treatments as minimally invasive line of treatment.

**Dosages**
The dosage of ozone used in therapy is reported as gammas. The conversion for gammas to more familiar units is as follows:
1 $\mu$g/ml = 1 mg/l = 1 g/m3 = 1 gamma

The dosage range reported varied from .00001 gammas (Ionozone therapy)\textsuperscript{26,27} to 100 gammas (autohemotherapy)\textsuperscript{9}. Total dose = ozone concentration and gas volume.

| Table 2: Ozone doses (μg/ml per gram of blood)\textsuperscript{9} |
|-------------------------|---------|---------|
|                        | Initial | Final   |
| Vascular disease       | 20      | 40      |
| Degenerative disease   | 20      | 40      |
| Infectious disease     | 25      | 70      |
| Respiratory disease    | 20      | 40      |
| Autoimmune disease     | 20      | 40      |
| Metastatic cancer      | 25      | 80      |

**Contraindications**\textsuperscript{28}
1. Pregnancy
2. Hyperthyroidism
3. Severe anemia
4. Severe myasthenia gravis
5. Active haemorrhage
6. G6PD deficiency

Side Effects
1. Direct intravenous injection of ozone increases risk of embolism.
2. Burning sensation to eyes
3. Difficulty to breathe
4. Ozone was reported to cause certain side effects like rhinitis, occasional nausea, vomiting, blood vessel swelling, poor circulation, heart problems, respiratory tract irritation and at times stroke.

Conclusion
Ozone is a versatile blue gas. It has applications all over the world in various fields and we have touched many aspects of ozone in this article. In dentistry it is proved to be minimally invasive and cost effective choice of treatment. On the other side, there are some contraindications and side effects of the ozone therapy, as mentioned above. It is a boon to cure numerous pathologies and thus improve the quality of treatment. Along with dentistry, it has given positive and remarkable effects in the field of medicine and other industries.

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References