Review paper

Do topical ozone therapy procedures cause side effects during the treatment of chronic wounds? Our own experience

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Abstract

Ozone therapy is an innovative therapeutic method that has been used and applied in many areas of medicine, where it has been valued primarily for its viral, bacterial and fungicidal effects. In the case of ozone therapy treatments, ozone can be administered to the body in various ways. Ozone therapy may take the form of a dry bath in an oxygen-ozone mixture, dressings made of ozone water or oil treated with ozone, and in the form of intra-articular or intravenous (so-called autohemotransfusion) administration of ozonated fluids. Ozone is an allotropic form of oxygen. It is an unstable, non-flammable compound that dissolves well in water. Thanks to its beneficial properties and versatile effects, ozone therapy has been getting more and more popular as a supportive therapy for various diseases and ailments, with therapeutic effectiveness confirmed in clinical trials. In high concentrations, ozone is a gas poisonous to humans. The documented research is more scarce as regards the potential for ozone to cause adverse side effects during treatments, depending on the duration of exposure and the concentration of ozone applied in air or other media, such as water or oil. In the present article, the authors present their own observations aimed at determining possible side effects when performing local ozone therapy treatments with the use of oxygen-ozone gaseous mixture for difficult-to-heal wounds.

Key words: chronic wound healing, ozone therapy procedures, treatment, side effects.

Introduction

In recent years, there has been increasing interest in the therapeutic use of ozone in various fields of medicine. Ozone therapy is considered to be one of the most effective methods of treating infections, having a very wide range of applications. Due to its strong oxidizing and disinfecting properties, ozone is used all over the world in the treatment of many diseases as a method supporting conventional medicine, as well as in aesthetic medicine [1, 2].

Currently, the vast majority of the biological mechanisms of ozone action have been explained, showing that they fall within the area of orthodox biochemistry, physiology, and pharmacology. The results of research conducted so far and presented in literature reviews confirm that ozone therapy is particularly useful in cardiovascular disorders and tissue ischemia of various etiologies (venous and arterial leg ulcers, diabetic foot syndrome, post-traumatic wounds or post-operative wounds), especially those complicated by bacterial infections, and although, as in the case of chronic viral infections, ozone therapy cannot eliminate them completely, it proves to be helpful in stimulating the immune system [1, 3, 4].

Ozone (O_3) is a gas that is a high-energy, allotropic form of oxygen, highly soluble in water, whose specific smell is noticeable even at a dilution of 1 : 600 [5].

Ozone is a gas that is present naturally in the environment. It is formed in a natural way during strong lightning discharges, it is also formed in the upper layers of the atmosphere as a result of the decomposition of molecular oxygen under the influence of ultraviolet radiation (when O_2 combines with atomic oxygen made

by the splitting of O_2 by ultraviolet radiation). Although ozone therapy, as most authors emphasize, is used in medicine as an alternative treatment method, for over forty years it has met with skepticism, if not complete opposition, from mainstream medicine. This prejudice is not unfounded, because ozone therapy treatments were often performed by unqualified personnel without authorizations in this field and no proper supervision, without rational basis and compliance with safety rules [5, 6].

Ozone is a strong oxidant that easily enters into chemical reactions. Depending on the concentration, it may have therapeutically beneficial aseptic or toxic properties which, however, if the appropriate concentration and dosage levels are observed, do not seem to have a significant negative impact on the safety of the therapy applied [5, 7].

With the advent of modern ozone generators enabling monitoring of the dosage of treatments, it is now possible to more precisely assess the mechanisms of action of ozone and the potential toxicity of treatments [5, 8].

According to literature data, ozone poisoning occurs in situations where the ozone concentration exceeds the recommended standards. Ozone is detectable in the air at a concentration of 0.02–0.05 ppm, and due to its characteristic smell, its presence in the air is easily spotted. The first unfavorable symptoms can be noticed when the concentration reaches the level of approximately 0.2 mg/m^3. When the concentration of ozone in the ambient air increases to 9–20 mg/m^3, it becomes a serious threat to human life, leading to death due to pulmonary edema and a sharp increase in blood pressure [8, 9].

Ozone therapy was first applied in 1873. Since then, it has consolidated its position in medicine for the period of over 130 years, and recently ozone has been increasingly used as part of local ozone therapy treatments, most often in the form of a gaseous oxygen-ozone mixture (5% ozone and 95% oxygen), in which the ozone content does not exceed permissible safety levels [10, 11].

In the case of treatments applying ozone therapy, the main route of accidental exposure of the patient to the absorption of ozone into the human body is *via* the respiratory system. Symptoms depend primarily on the concentration and time of exposure to ozone. When normal breathing occurs, approximately 75% of inhaled ozone is absorbed by the upper respiratory tract and bronchi, which may cause throat irritation, rapid breathing or coughing. There are other ailments that may also occur temporarily, such as drowsiness, fatigue, headache, itching of the eyes or lower blood pressure [4, 10, 12]. Since the absorption of ozone through the upper respiratory tract is lower when breathing through the mouth than through the nose, the penetration of ozone into the lungs is greater during intense physical exercise, which is not observed in the case of topical ozone therapy treatments. Also, the size and surface area of the respiratory tract walls is important for ozone absorption, making it greater in children and women. The mucus covering the bronchial mucosa prevents direct exposure of the epithelium to ozone, but oxidation products of some mucus components can damage epithelial cells and cause inflammation. The level of ozone absorption may also be influenced by the amount of antioxidants present in the mucus (such as vitamin E), depending on the nutritional status. Also, coexisting respiratory diseases are important, such as asthma, chronic bronchitis or emphysema, which may cause airflow disturbances and the resulting uneven exposure of various sections of the respiratory tract to inhaled ozone, increasing the susceptibility of patients to its harmful effects [10, 12].

With chronic exposure to ozone, the patient may experience irritation of the conjunctiva of the eyes, dizziness, nausea, or decreased concentration levels. With repeated exposure to ozone, the protective reactions of the respiratory system weaken, but the induced inflammatory reactions, especially in the bronchioles, may persist. Longer exposure to ozone causes structural changes in the lungs, such as: mucosal hyperplasia, bronchiolar narrowing, and alveolar fibrosis [4, 10, 12].

So far, our experience in topical ozone therapy is based only on the treatment of cases of chronic limb ischemia, chronic skin ulcers caused by ischemia and diabetes, and difficult-to-heal wounds. In those cases, ozone was applied to the lesions localized on the skin surface of the lower or upper limb in the form of a gaseous oxygen-ozone mixture (5% ozone and 95% oxygen) with a concentration of 40 µg/ml, using the polyethylene bag, the so-called "ozone shoe" or "ozone sleeve", which was tightly sealed to the skin surface of the treated limb. The duration of a single procedure was 30 minutes. Treatments were performed daily for 30 days in two series of 15 treatment procedures (except for Saturdays and Sundays). The interval between two series of ozone therapy treatments was 4 weeks, applied in order to counteract the potential risk of exposing patients to the negative effects of long-term application of ozone on the skin around the ulcers and deeper tissues. Considering that topical ozone therapy was applied to the wound with a plastic bag creating a tight closed space around the ulcer, it was practically impossible for the patient to inhale ozone, and thus the harmful effects of ozone entering the body through the lungs were prevented. After the end of each procedure, Allevyn Adhesive Ag dressing (Smith & Nephew) was applied to the wound, in order to maintain proper humidity of the wound, and allowed for an antibacterial effect and enhancement of wound cleanliness.

Such procedure of topical ozone therapy enabled, unlike other forms of ozone therapy (ozone bath, ozone autohemotherapy, intramuscular injections, ozone preparations and others), a significant reduction of the release of ozone that was introduced into the shoe or sleeve leaking outside those plastic bags, and that is why we did not observe either acute or chronic general side effects reported by patients in the course of the therapy.

It should be emphasized that local ozone therapy treatments last approximately 30–45 minutes each. Since the decomposition of ozone occurs relatively quickly, in most cases after about 30 minutes, the ozone present in the room decomposes spontaneously, and the smell lingering in the air is a completely natural phenomenon accompanying the ozonation carried out. Therefore, a short-term exposure of the patient to air with a low ozone concentration does not show any side effects. After ozonation, it is recommended to ventilate the room for some 20 minutes, which helps to get rid of the chemical compounds formed as a result of the impact of ozone, and to reduce the concentration of this gas to a safe level of 0.1 ppm.

Our observations, especially regarding the treatment of difficult-to-heal wounds, indicate that local ozone treatments have a negative effect only on the drying of the treated wound beds. Current guidelines for the treatment of difficult-to-heal wounds recommend maintaining a moist environment around the wound as a standard. Therefore, drying of the treated wound bed should be considered a local side effect of ozone therapy treatments, which has a negative impact on the healing process, as drying out of the wound may carry the risk of wound dehydration or necrosis. In order to eliminate or significantly reduce this side effect, it is advisable to use specialized dressings between subsequent treatments to maintain the appropriate moisture level in the wound area.

Conclusions

The results of current experimental and clinical research concerning the impact of ozone on human health confirm the therapeutic effectiveness of ozone therapy and may result in a significant increase in the use of this method in clinical practice in the near future. A clear assessment of possible side effects of these treatments based on good-quality multicenter research on large groups of randomized patients will enable confirmation of the safety of ozone therapy. The current experience of our center shows that the use of local ozone therapy treatments using an ozone-oxygen mixture applied in the recommended concentration, in the form of an ozone shoe or sleeve, does not cause systemic side effects, and the only noted local side effect of this method is drying of the bed of treated wounds, which can be eliminated by using specialized dressings in the period between subsequent treatments, applied to maintain the appropriate moisture level in the wound area.

Disclosures

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