

Case Report

Ozone therapy as adjuvant to the treatment of osteoradionecrosis. Case report

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Abstract

Ozone therapy has been shown to be an effective adjunctive therapeutic tool in the treatment of osteoradionecrosis acting directly on the repair. Thus, the objective of this case report was to present the benefits of using ozone therapy as an adjuvant to the treatment of osteoradionecrosis. Female patient, 57 years old, melanoderma, attended the Faculty of São Leopoldo Mandic reporting severe pain throughout her face with difficulty in eating, speaking and a bad taste in her mouth. In the intraoral examination an area of necrosis was found in the region of tooth 38, three months after extraction and 10 years after radiotherapy. Initially, the area was cleaned irrigated with saline and antibiotic therapy associated with 10% hydrogen peroxide as a mouthwash. Then the patient was referred to Ozone therapy Specialized Clinic. Appointments were made fortnightly. The lesion was washed with 250 ml of sterile ozonized bidistilled water at 8 µg/ml and the injection of 20 ml of the oxygen/ozone gas mixture at a concentration of 20 µg/ml, which was bubbled into the lesion through the presence of purulent drainage. Additionally, injections of 1 ml of gaseous ozone were made at 5 points around the lesion. To conclude the ozone therapy protocol ozonated oil was applied into the cavity. After 30 sessions the healed area was observed with no pain. Three-years follow up is displayed. Thus, it was concluded that ozone therapy improved the repair and controlled symptomatology....

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Introduction

Radiotherapy is the preferred treatment for the relief of symptomatology and tumor reduction; however, it destroys healthy adjacent cells and may cause side effects such as xerostomy, periodontitis, mucositis, and osteoradionecrosis (ORN)¹. An ORN diagnosis is defined as bone exposed to radiation which does not heal within 3 months². The lack of an established specific treatment and an often-unfavorable prognosis make prevention a necessary approach in the care of cancer patients³. Nowadays the ORN treatment strategy comprises both local and systemic antibiotics and surgical approachment². The gaseous mixture of oxygen and ozone has been proposed as an effective adjuvant therapeutic tool⁴.

Ozone therapy has shown itself to be an effective complementary method to conventional therapeutic modalities applied to the head and neck area due to its antimicrobial action and ability to stimulate healing and thus modulating the inflammatory response^{5,6,7}. The aim of this case study is to show the benefits of ozone therapy in the treatment of diseases such as osteoradionecrosis when used in conjunction with conventional treatment.

Clinical case report

This case report was approved by Ethical Committee by number On October 5, 2016, patient L.M.C, age 57, female, with melanoderma, was examined at the stomatology clinic of São Leopoldo Mandic College in Brazil to assess a lesion in the left posterior jaw. The chief complaint was pain while chewing, limited mouth opening and an unpleasant taste in the mouth. During the initial assessment and anamnesis, the patient reported having undergone surgery in 2006 to remove a parotid gland tumor, in which both the tumor and the gland were removed. The biopsy confirmed the diagnosis of epidermoid carcinoma. The patient then underwent 22 sessions of radiotherapy.

After 10 years had elapsed, the patient was advised to have tooth 38 extracted, with informed medical consent, since no risk of complication was expected 5 years after radiotherapy. Three months later, the patient reported the onset of severe pain in the entire face, difficulty eating and speaking, and an unpleasant taste in the mouth.

The patient attempted to obtain medical assistance but was unable to solve the problem. During a session with a dental hygienist, an open lesion was detected in the extraction area (Figure 1 and 2). The patient then went to São Leopoldo Mandic College for a clinical examination and x-ray. During the examination, an area of bone necrosis was found in the retromolar trigone. The area was initially prepared and cleaned with saline solution, antibiotic therapy and an application of 10% hydrogen peroxide solution as an oral antiseptic. The patient was then prescribed ozone therapy at the support clinic of São Leopoldo Mandic College.



Fig.1

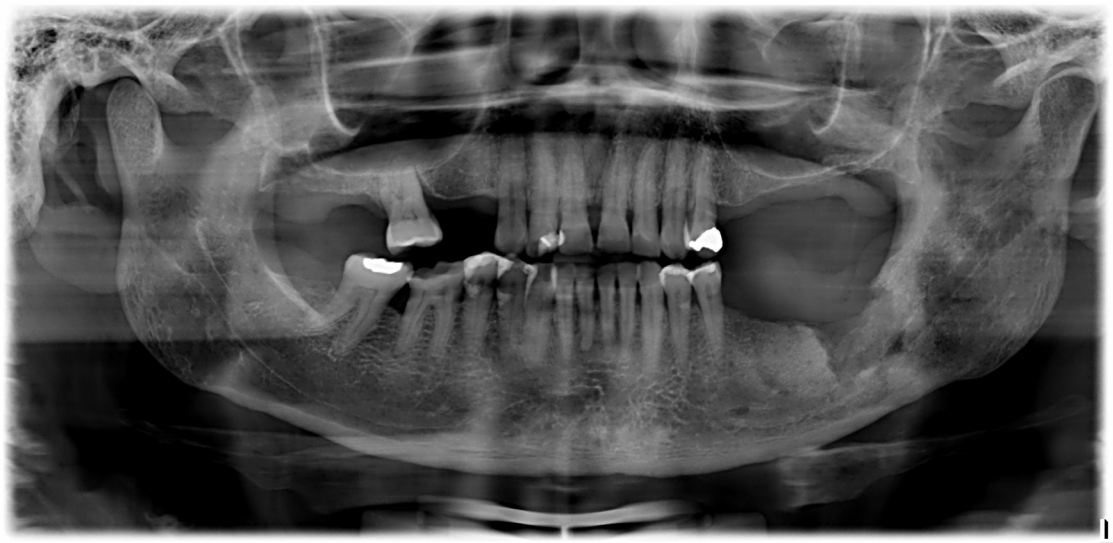


Fig.2

Ozone therapy protocol

Ozone standardization

The ozone was generated *in situ* by an ozone generator (MedPlus, Philozon, Santa Catarina, Brazil). A glass column accessory (Philozon, Santa Catarina, Brazil) was connected to the generator's ozone outlet to produce ozone bubbles in the water. These bubbles were created by a ceramic diffuser operating for 5 min. One liter of cold bidistilled water at 14°C was used for ozonation. The glass column measured 50 cm in height and 6 cm in diameter and received 1 L/min of oxygen/ozone output. The ozone device was calibrated to produce ozone at 40 µg/mL, and the final concentration in the water was 8 µg/mL, as described previously⁸.

The patient underwent the ozone therapy protocol at two-week intervals. The bone cavity was rinsed with 250 mL of ozonated water at 8 µg/mL⁸. Twenty milliliters of the gaseous oxygen/ozone mixture at a concentration of 20 µg/mL were injected into the lesion causing bubbling during the purulent drainage. Five injections were applied around the lesion, each containing 1 ml of the gaseous oxygen/ozone mixture at a concentration of 5 µg/mL - 3 in the vestibule and 2 lingual. To complete the protocol, the cavity was filled with ozonated sunflower oil (Philozon, Santa Catarina, Brazil)^{4,11,12,13}.

Clinical response

The purulent secretion stopped after the first sessions. The patient reported a general improvement, complete absence of unpleasant taste in the mouth, and remission of pain symptoms. In the 15th session, a relapse of the purulent drainage was observed; thus, antibiotic therapy was prescribed with Clindamycin (300 mg) for 7 days.

In the 30th session of ozone therapy, healing was seen at the edge of the gum without any apparent bone defect, complete absence of infection, and without signs of pain. The patient returned for clinical x-ray control 3 months later, at which time it was seen that the treated area remained stable. Thus being, the patient was asked to return 1 year (Figure 3) and 2 years later (Figure 4) for follow-up clinical x-ray control at São Leopoldo Mandic College, and thereafter for annual analyses.



Fig.3



Fig.4

Discussion

Various therapeutic approaches are described for the treatment of cancerous lesions in the head and neck area, for example, surgery, chemotherapy and radiotherapy, often associated. In the treatment of oral cancer, post-operative or pre-operative radiotherapy is the popular option and can be prescribed to improve symptomatology or reduce tumor size. Radiation destroys neoplastic cells but also destroys healthy adjacent cells, which can cause side effects such as xerostomy, periodontitis, mucositis, and osteoradionecrosis (ORN)¹.

An ORN diagnosis is defined as bone exposed to radiation which does not heal within 3 months². Although studies have made strides over the years, this type of disease is not yet fully understood due to its complexity. The greatest concern for professionals treating ORN is the lack of an established specific treatment and an often-unfavorable prognosis, which make prevention the best alternative for patients undergoing radiotherapy³.

Some factors can increase the risk of developing ORN, such as the location of the tumor, radiation dose and the method by which this radiation was applied. Another highly relevant factor is the onset of osteoradionecrosis after molar extractions in the mandibular area². Other habits may also be related to the onset of ORN, such as smoking, drinking, and the patient's nutritional condition⁴. Treatment strategies for mandibular osteonecrosis include administering local antibiotics, systemic antibiotics, and surgical intervention³.

Ozone therapy has emerged as a therapeutic tool with the potential to become a regular part of the clinical arsenal in the search for solutions to these complex cases. The action of ozone on cells produces oxidative stress. During this phase, free radicals are produced that make up reactive oxygen species (ROS). These include hydroxyl radical, superoxide, singlet oxygen, and hydrogen peroxide. The presence of these free radicals induces an antioxidant response to neutralize their toxic effects⁵, in addition to affecting cellular metabolism to increase ATP synthesis^{5,8}. The clinical result of this process is described in medical literature as acceleration in repair and healing^{5,6}. This fact justified the use of the therapeutic protocol based on ozone therapy in the present case report, in which the quality of repair is in alignment with previous studies^{11,13-16,21-22}.

It is important to highlight that the benefits obtained with ozone therapy are described in medical literature^{5,7} and were proven by the present case report. Such effects are linked to therapeutic integration; that is, ozone therapy is a complementary tool in the basic procedures already established^{7,8}. At no time were any basic procedures excluded from the propaedeutic employed in the treatment of osteonecroses⁴.

The ozone therapy protocol used was based on three forms of ozone utilization – gas, water, and oil^{5,6,7}. The ozonated water was produced according to the protocol established in a prior study⁸, and its main purpose was to promote local antiseptics by means of its already proven antimicrobial action^{8,10,13,16-18}, and by local stimulation through increased cell viability^{8,22}. The injection of gas in the area surrounding the lesion at the employed dose aimed to promote local oxidative preconditioning. This procedure drives and optimizes antioxidant defense at the point of application⁵. The local immunological response is thus potentialized and culminates with accelerated repair^{5,6}. The intralesional bubbling of the gas acts directly in decontamination and oxidation of the purulent accumulation, due to ozone reactivity in drainage and ROS formation⁵. It is important to note that hydrogen peroxide, one of the reactive species of the oxygen formed, acts directly as a chemotactic factor for lymphocytes^{5,8}.

The purpose of the ozonated oil is to slowly release ozonides, which are by-products of the reaction of ozone with the oil molecule. These ozonides cause local stimulation which triggers an antioxidant response, thus increasing the release of vascular endothelial growth factor (VEGF) and acting directly on neovascularization²². The current results are in alignment with studies that used ozonated oil associated with antibiotic therapy, vitamin C and 0.2% chlorhexidine as a mouthwash²⁰⁻²².

A consensus has not been reached as to the therapeutic possibilities in respect to pathologies like ORN¹⁻⁴. In this light, ozone therapy presented satisfactory results in the clinical case described by improving the patient's quality of life, especially the pain symptoms, after only one session. It aided in the complete healing of soft and hard tissues, as seen over a three-year follow-up period showing the stability of these tissues.

Consequently, it was possible to conclude that ozone therapy is a viable adjuvant therapeutic alternative in ORN treatment; however, clinical studies with a considerable number of samples are necessary to include this therapy in the clinical arsenal of dentistry.

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