


# Medication-Related Osteonecrosis of the Jaw Treated by Ozonized Oil: A Case Report

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## Abstract:

Ozone is an atmospheric gas well-known for its excellent medicinal properties, including antimicrobial activity, immunostimulant and antioxidative. Ozone therapy has been used in dental medicine for treatment of herpetic infection, periodontitis, endodontic infection, acute abscesses and medication-related osteonecrosis of the jaw. This study aims to report the protocol and results of the local use of ozonized oil in the management of patient with medication-related osteonecrosis of the jaw. 81-year-old white female, with exposed bone in the jaw, on left side, and a history of sodium alendronate used to treat osteoporosis. The treatment consisted of ozone therapy with ozonized oil, according to the following protocol: previous mouthwash chlorhexidine 0.12%, Periogard®, for one minute; local application of ozonized oil, Philozon®, with a 5ml syringe no needle, for 10 minutes, re-appliance every two minutes; 10 sessions, once a week each. Between the eighth and ninth treatment week, we observed spontaneous bone sequestration and after six months of follow up, we found local tissue regeneration.

**Keywords:** Medication-related osteonecrosis of the jaw; Ozone therapy; Alendronate.

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## INTRODUCTION

Ozone (O<sub>3</sub>) is a natural gas founded in the Earth's stratosphere. It is a highly energetic and oxidative molecule. Ozone therapy is an excellent, minimally invasive and conservative approach that has been showing therapeutic properties on the treatment of bone lesions, including antimicrobial action, wound healing, circulatory system stimulation with increased tissue oxygenation, promotion of angiogenesis and fibroblast formation. It was first applied in dentistry by Edward Fisch in 1950 and since then, this technique has been applied to fight herpetic infections, periodontitis, acute abscesses, intracanal route for the reduction of the infecting microbiota and in medication-related osteonecrosis of the jaw.<sup>1,2,3,4</sup>

Medication-related osteonecrosis of the jaw (MRONJ) is a rare condition defined as necrotic bone exposed or bone probed through an intraoral or extraoral fistula(e) in maxillofacial region that has persisted for more than eight weeks in patients current or previous treatment with antiresorptive or antiangiogenic agents and has no history of head and neck radiation. Osteonecrosis occurs in patients who use oral or intravenous drugs like bisphosphonates, denosumab and angiogenesis inhibitors to treatments of bone prevent skeletal-related events such as osteoporosis, osteopenia, Paget's disease and in oncological patients with multiple myeloma and bone metastasis.<sup>5,6</sup>

The incidence of osteonecrosis in oncology patients treated with high doses of these medications (1% to 15%) are bigger than in patients that used low doses to treat osteoporosis (0,001% to 0,01%). MRONJ etiology is unknown, but there is evidence that the combination of several factors may increase the risk of developing MRONJ, such as prior use of bisphosphonate or denosumab, poor oral hygiene, periodontitis, smoking and other medical conditions (cancer, anemia, diabetes mellitus, immunological disorders)<sup>7,8</sup>

In 2014 American Association of Oral and Maxillofacial Surgeons created a staging system to guide managements decisions about MRONJ. The treatment is determined according each stage. Refer to dental specialist, follow up every 8 weeks, communication between dentistry and physician, patient education and reduction of modifiable risk factors is indicated to all stages. In advanced stages of lesion, antibacterial mouth rises, pain and infection control, surgical debridement or resection are needed.<sup>5</sup>

Ozone therapy can stimulate the oxy-reduction equilibrium and when in contact with fluids induces

formation of reactive oxygen molecules which may be beneficial systemic and local effects. Specifically, in bone injuries causes sequestrum formation, reduces infection of adjacent tissues, promotes osteogenesis in consequence of enhanced vascularization and the re-epithelialization of oral mucosa.<sup>3,4,9,10</sup>

This study aims to report the protocol and the results of topical application of ozonized oil in the treatment of medication-related osteonecrosis of the jaw in an Oral Medicine clinic.

## CASE REPORT

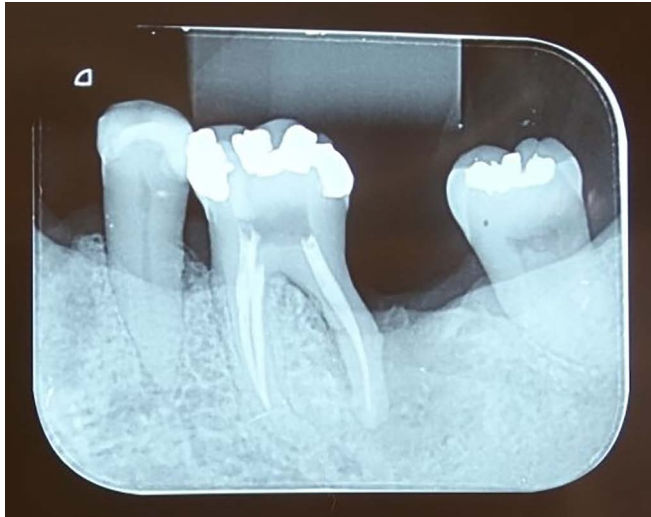
An 81-year-old white female was referred to a private dental clinic to the Oral Medicine clinic with the main reporting "I visited my dentist and she told me that the bone was necrotic".

The patient used sodium alendronate, Fosamax®, to treat osteoporosis. She denied having bad habits like smoking and drinking. No history of trauma was reported by the patient. She noted a purulent secretion after having extraction surgery and she was in pain for over a year.

No change was observed in the extraoral examination. However, in the intraoral exam an exposed bone in the jaw, on the left side, associated with the distal root of tooth 36 and in the region of absent 37 was observed, with no pain and no purulent secretion (Figure 1). Panoramic and periapical radiographs revealed an osteolytic lesion close to these teeth (Figure 2 and 3). The diagnostic of medication-related osteonecrosis of the jaw was clinically established.



**Figure 1.** Intraoral appearance of necrotic exposed bone in jaw, on left side, associated with distal root of tooth 36 and in the region of absent 37.



**Figure 2.** The initial periapical radiograph showing an osteolytic lesion associated with the distal root of tooth 36.



**Figure 3.** The initial panoramic radiograph showing an osteolytic lesion in the jaw, on the left side.

The treatment consisted in ozone therapy with ozonized oil (Figure 4), following this protocol: previous mouthwash chlorhexidine 0,12%, Periogard®, for one minute; topical application of ozonized oil, Philozon®, with a 5ml syringe no needle, for 10 minutes, with reapplication every two minutes; in 10 sessions with a weekly break. The ozonized oil was stored in a refrigerator.

Application was performed by a trained professional, under absolute isolation and assistance of a sucker. The oil was poured into a sterile vat to be captured by the syringe. At the end of the session, the excess ozonized oil was removed with sterile gauze.

After the end of the protocol, a monthly clinical follow up was set for the next 5 months following the last application.

The result was successful, the spontaneous bone sequestration between the eighth and ninth week of treatment (Figure 5 and 6). After six months of follow-up, we observed an improvement in gingival health, local tissue regeneration and no recurrence of bone injury (Figure 7).



**Figure 4.** Ozonized oil.



**Figure 5.** Clinical appearance after spontaneous bone sequestration during treatment.





**Figure 6.** Periapical radiograph showing no necrotic bone.



**Figure 7.** A 6-months clinical follow-up showing a good healing, without signs of infection and local tissue regeneration.

## DISCUSSION

Ozone therapy was introduced in the list of approaches to treat MRONJ. AGRILLO et al., 2012 performed sequestrectomy and ozone therapy in all patients who presented exposed bone (94 patients) diagnosed with BRONJ. They suggest a protocol based upon minimally invasive surgery removal of bone sequestrum, antibiotic and anti-mycotic therapy including ozone therapy, three minutes of exposition twice a week. 90% of the cases treated with this protocol confirmed it, with total healing or reduction of the lesion and improvement on the signs and symptoms. Ozone therapy was considered a powerful antimicrobial adjuvant procedure capable of stimulating granulation tissues formation [4].

In a previous study, RIPAMONTI et al, 2012 with 24 patients already treated with zoledronic acid and diagnosed with osteonecrosis of the jaw were observed

and treated with azithromycin 500 mg for ten days before insufflation ozone medical gas. The results showed that in six patients occurred spontaneous or not traumatic sequestrum of the necrotic bone, after a range of 4-27 insufflation. Surgical intervention was needed for 12 patients to remove the sequestrum of necrotic bone, after 10 a 38 insufflation. In all cases, they noted healing of the gum mucosa and re-epithelization. No cases of toxicity of intolerance to the ozone have been reported and not relapse was observed after a follow-up of 18 months. [3] In our study, a spontaneous sequestrum occurred between the eighth and ninth week of treatment and an improvement gingival healing.

Our study showed that before the tenth session the necrotic bone was spontaneously expelled as well as in the study of RIPAMONTI et al, 2011. Ten patients with single lesions ( $\leq 2,5$  cm) of osteonecrosis of the jaw were treated with antibiotic for ten days before 10 topical application of medical  $O_3$  delivered in an oil suspension for 10 min. All patients had complete clinical resolution with no surgical intervention. 70% of patients developed spontaneous expulsion of necrotic bone before the last session [6].

The therapeutics effects of ozone are explained by the diversity of mechanism of action in the organism, due to the capable to stimulate human cells such as interleukins, prostaglandins and leukotrienes reducing the inflammation effects, induces the function of macrophages to phagocytize microorganisms, synthesis of immunoglobulins and act on cellular and humoral system. Several studies have shown the effectiveness of ozone over microorganisms in order to inactivate them. The mechanism of action can work in distinct ways: it can either attack immediately cell walls and afterwards destroy DNA, or it can cause direct injury over the DNA. It is showed that bacteria, viruses and yeasts are vulnerable to oxidizing power of ozone.<sup>1,2,11</sup>

## CONCLUSION

Ozone therapy has low cost, is easily applied for properly and able professional, no side effects and is a promising coadjuvant therapy and minimally invasive for medication-related osteonecrosis of the jaw, due to its ability to cause necrotic bone sequestration and stimulate bone and gingival tissue regeneration. Moreover, several studies showed that ozone can be applied as additional treatment in oncological patients to support the effects from conventional treatment. However, other clinical and experimental trials are required to improve the efficacy and safety of ozone therapy.

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