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CASE REPORT

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Use of ozone therapy together to low power laser in osteonecrosis induced bisphosphonates - Clinical case

O uso da ozônio terapia junto ao laser de baixa potência em osteonecrose induzida por bisfosfonatos - Caso clínico

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ABSTRACT

Considering the probable causal association between the use of bisphosphonates and osteonecrosis of the jaw, as well as the high number of prescriptions and use these drugs every year, this paper aims to show different treatment. The combined use of ozone therapy and laser therapy in tissue regeneration and bone repair in patients with osteonecrosis induced by bisphosphonates, held by the discipline of Oral and Maxillofacial Surgery and Traumatology, Paulista State University "Júlio de Mesquita Filho". Female patient, white, 53 years after a breast cancer had an evolution for bone metastases throughout the body, and start the chemotherapy treatment using intra-venous pamidronate 90 mg monthly from 2007 which has been used to the present day, due to disease stabilization. The patient sought the institution complaining of painful symptoms in the mandible and maxilla, and the clinical examination and CT were diagnosed initial sites suggestive of osteonecrosis induced by bisphosphonates. In seeking to reduce the symptoms and clinical signs, to prevent progress in the lesions, we recommend treatment by ozone therapy together to infrared low-power laser, which showed satisfactory reduction in bone necrosis sites. Although there are wide variations and difficulties in treatments for osteonecrosis induced by bisphosphonates, it was possible regression of the lesions through the joint processing applied, and the improvement in life expectancy of the patient.

KEYWORDS

Bisphosphonates; Ozone; Osteonecrosis.

RESUMO

Considerando a associação causal provável entre o uso de bisfosfonatos e osteonecrose da mandíbula, bem como o elevado número de prescrições e dessas drogas todos os anos, este trabalho tem como objetivo mostrar um tratamento diferente. O uso combinado de terapia de ozônio e laser na regeneração de tecidos e reparação óssea em pacientes com osteonecrose induzida por bisfosfonatos, realizada pela disciplina de Cirurgia bucomaxilofacial e Traumatologia da Universidade Estadual Paulista "Júlio de Mesquita Filho". Paciente do sexo feminino, branca, 53 anos, depois de um câncer de mama teve uma evolução de metástases ósseas em todo o corpo, iniciou o tratamento de quimioterapia intravenosa utilizando pamidronato 90 mg mensal a partir de 2007 que tem sido utilizado até os dias atuais, devido à estabilização da doença. A paciente procurou a instituição com sintomatologia dolorosa na mandíbula e maxila, pelo exame clínico e de imagem foram diagnosticados sítios iniciais sugestivos de osteonecrose induzida por bisfosfonatos. Na tentativa de reduzir os sintomas e sinais clínicos, para impedir o avanço das lesões, recomendamos o tratamento por terapia de ozônio junto ao laser infravermelho de baixa potência, que mostrou redução satisfatória dos sítios de necrose óssea. Embora haja variações amplas e dificuldades em tratamento de osteonecrose induzida por bisfosfonatos, foi possível regressão das lesões através das terapias conjuntas aplicadas, bem como a melhoria da expectativa de vida do paciente.

PALAVRAS-CHAVE

Bisfosfonatos; Ozônio; Osteonecrose.

INTRODUCTION

Osteonecrosis of the jaw has been reported in several studies with patients who have used or use of bisphosphonate by oral or intravenous route. The clinical presentation is characterized by gingival ulcers with exposed necrotic bone, intra or extra-oral training sinus tract, and soft tissue swelling. Abscesses, pathological fractures, and nerve disorders are less common. Intense pain is the most frequent complaint and appears radiographically as irregular area of osteolysis, with a presence or absence of bone sequestration portion [1].

Intravenous bisphosphonates are primarily used in the treatment of conditions related to cancer, such as hypercalcemia and bone metastases associated with breast, prostate, lung and multiple myeloma, while oral bisphosphonates are best used in treatments for osteoporosis. [1-3].

Bisphosphonates are absorbed by the skeleton and produce its effect on osteoclasts, reducing its action resorption in bone remodeling, as well as the induction of apoptosis [3]. Osteonecrosis is commonly associated with the use of bisphosphonates considered potent and / or for extended periods of use [3,4] such as intravenous bisphosphonate, pamidronate and zoledronate, in combination with anticancer chemotherapy that they represent the "gold standard" for hypercalcemia treatments, and malignant lesions with bone metastases from multiple myeloma, breast cancer, prostate and lung, as the protocol suggested by the American Society of Clinical Oncology [1].

Considering the ozone when administered in biological systems exert stimulating action on the circulatory, immune, reparative [5,6] and neurological [6-8], it becomes an alternative treatment to reduce symptomatology and stimulate bone repair. Ozone has been effective in diseases related to avascular necrosis as it activates blood circulation, increases red blood cells and hemoglobin concentration [9] improves diapedesis and phagocytosis processes, stimulates the phagocytic mononucleotic system.

Particularly in blood vessels of small caliber, such as those found in the circulation of the maxilla and mandible. These vessels showed rapid filling of hematic components as marked activation of circulation [10]. Ozone can be used in the form of gas, water, and an aqueous carrier, or diluted in oil, and used vegetable oils such as olive and sunflower [9,11].

The ozonated oil is a compound obtained by mixing oil with ozone gas. The ozonated oil by-products form, including peroxides [12] that give the germicidal characteristic, making it useful in the treatment of infected wounds, fistulae local antiseptics and other processes. [9,11,13]. In addition, these peroxides play several functions in the body including: stimulation of various enzymatic systems oxidoreduction, possibly through the influence on the transport of oxygen to tissues and mitochondrial respiratory chain; blocking of viral receptors and death of virus-infected cells; as well as a synergistic effect on the phagocytic capacity [11].

Strategies for the Treatment of osteonecrosis of the jaw include the administration of local and systemic antibiotics and surgical intervention. Recent clinical reports demonstrated that treatment of osteonecrosis with low power laser in combination with antibiotics or surgical treatment improves the healing of tissues and reduces localized pain. The positive effects of low power laser in different cell types have been demonstrated in several studies. However, they were provided only limited information on the effects of laser irradiation on the oral tissues, especially in bone cells exposed in osteonecrosis of injury [14].

Despite the absence of an effective therapeutic protocol, laser therapy may be useful in the management of patients with osteonecrosis [15].

The goals of treatment of patients with osteonecrosis is to eliminate clinical symptoms

such as pain, treat any infection of the soft tissue or bone and minimize the progression of bone necrosis. The main risk factors for osteonecrosis are therapy with bisphosphonates for prolonged intravenous involving high-powered drugs, dento alveolar surgical procedures, ill-fitting dentures and intra-oral trauma. Other factors have also been associated with osteonecrosis are chemotherapy, anti-angiogenic drugs, such as thalidomide, diabetes mellitus, corticosteroids, genetic susceptibility, and poor oral hygiene [3].

The objective is to discuss the treatment of a case of osteonecrosis, with the use of ozone therapy in conjunction laser therapy in tissue regeneration and bone healing in patients with osteonecrosis induced by bisphosphonates held in Maxillofacial Surgery and Traumatology department of the Universidade Estadual Paulista "Julio Mesquita Filho".

CASE REPORT

Female patient, 53 years after a breast cancer had an evolution for bone metastases throughout the body, beginning the chemotherapy treatment using intra-venous pamidronate 90 mg monthly in 2007 which has been used to the present day (2014), due to its effect on the switching of the disease. The patient complained of pain symptoms in the oral cavity, and the clinical examination and CT scan were diagnosed sites in the mandible and maxilla, suggestive of early osteonecrosis induced by bisphosphonate. They were diagnosed two regions suggestive of osteonecrosis, one in the left maxillary premolar region with small bone exposure (Figure 1) and another in right jaw, with purulent discharge in the third molar region, also with small bone exposure (Figure 4). In the mandibular region due to the pus was performed surgical debridement, followed by laser therapy and ozone therapy. In the maxillary by the absence of pus only we perform laser therapy and ozone therapy together. The regions irradiated every 7 days, followed by topical application of ozonated oil after daily oral hygiene together during the first 3 consecutive months (Figures 2 and 5). In seeking to reduce the symptoms and clinical signs, treatment was recommended by ozonated oil (30 mg / ml-Ozone & Life ®) daily concomitant topical use to infrared low-power laser with weekly application. The irradiation was performed using laser diode (Laser DMC, InGaAsP, infrared, 808 nm, 100 mW 200J / cm^2 sec 0:52). This device consists InGaAsP (indium-gallium-arsenide-phosphide) diodes that are positioned to radiate in a standardized way and individually. Necrotic regions were assessed clinically and by imaging tests (cone beam tomography and scintilography). With recommended treatments, we observed the absence of pain, as in the first 2 weeks of treatment, clinical improvement in the first three months of treatment (Figures 2 and 5), and bone repair in the jaws over the months (Figures 3 and 6). But according to maintenance chemotherapy, advocate suspend the ozonated oil after 3 months of treatment and maintain laser therapy for another three months, every two weeks, when we proved by imaging and clinically the absence of bone necrosis of the mandible and maxilla.

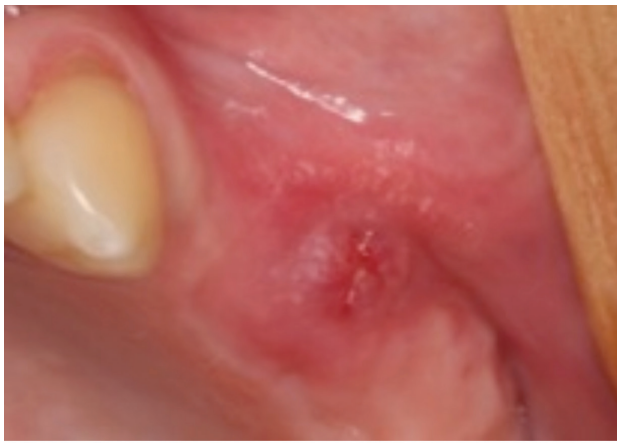

Figure 1 - Left Jaw with erythematous region, painful and exposure bone. February 2014.

Figure 2 - Left jaw, exposed bone. March 2014.

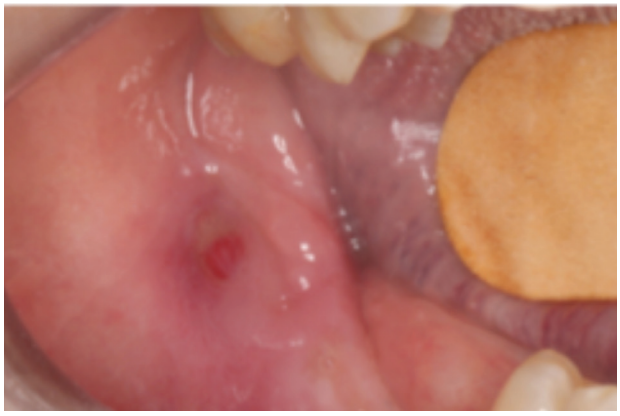

Figure 5 - Mandible right, bone exposure, decreased pus. April 2014.

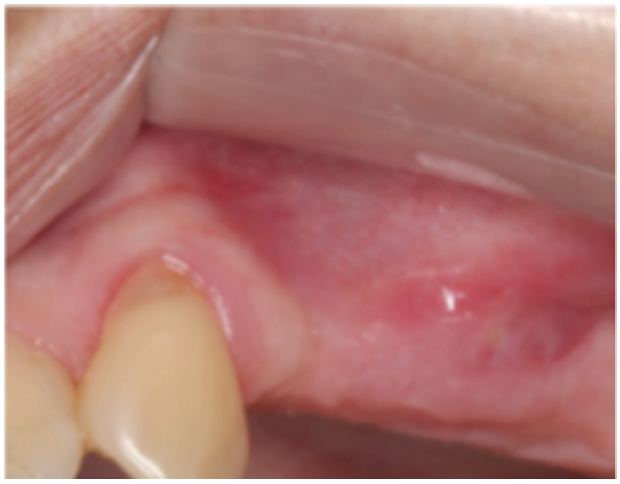

Figure 3 - Left Jaw, scar tissue. August 2014.

Figure 6 - Mandible right after surgical debridement, laser therapy and ozone therapy. August 2014.

Figure 4 - Mandible right, exposed bone and pus. February 2014.

DISCUSSION

This clinical case is undoubtedly further evidence of the potential curative effect of two therapeutic methods for the osteonecrosis lesions induced by the continued use of bisphosphonates. The ozonated oil (30 mg / Ozone & Life ® ml-) was applied daily complemented by weekly radiation of low power laser (Laser DMC, GaAlAs, infrared) that together provided site byostimulation with reparative power. The technique employed could be complemented by other technical alternatives described in

the literature, such as use of autologous serum sanguine enriched with platelets, application of low doses of parathyroid hormone and ascorbic acid administration [16]. However, in this study, the association only of ozone therapy and laser therapy proved to be competent enough to halt the necrotic process. Evaluated in 2012 the methods described in this paper with the addition of antifungal therapy, vitamin C and daily mouthwash with chlorhexidine 0.2%. In this way significant improvement was obtained in 94 patients within 6 months and through Their results were 60% of the complete resolution of the lesion and a reduction of symptoms; 30% of resolutions marked with improvements symptoms in only 10% were partial cure of symptoms and without considerable signs of injury improvements. Moreover, the cited order of pain complaint in 100% of the 94 treated patients [10]. Thus, considered as a "new therapeutic protocol" the use of amoxicillin with clavulanate potassium every 12 h; an antiviral and antifungal for 20 days.

Also making use of ozone therapy in 2011, [17] proved contrary to surgical debridement of the injury, but in favor of the use of antibiotics in concurrent time the ozonated oil applications, as was done in this case. Thus, we chose Administration of antibiotics (azithromycin 500 mg / day) before the application of ozonated oil by keeping it gelled less than 4 °C (10 applications per day on 3 days). Nevertheless, he declined to submit any patient to surgery and this technique has been very successful. According [10,17] obtained good developments in the frames of their patients, with 54% of them with complete wound healing after ozone therapy combined with other available pharmacological methods such as antibiotic therapy, administration of vitamin C and use of chlorhexidine 0, 2% as a mouthwash.

In the ideal therapy [10] stressed the importance of an accurate and detailed clinical examination, which is essential to avoid future inconvenience to the oral health of a patient who makes use of bisphosphonates, be it by cancer or reasons for the treatment of rheumatoid arthritis. This step must be taken before the start of administration of the drug in order to avoid aggressive interventions in the future, which can substantially facilitate the process of necrosis. Next to that, the cancer monitoring, hematology and should be avoided as much as possible the intake of pyrophosphate should be done and was done with the treated patient. When there is a need for a surgical debridement of the lesion, as was done in the case discussed, [18] advocated the use of conservative techniques in order to grant again, the epithelial integrity and preserve bone tissue underlying, preventing its subsequent degeneration and necrosis associated with local infections. In the case studied, the procedure was done under local anesthesia, unlike that established [19], who submitted their patients to general anesthesia before surgery.

Unlike as was done in the clinical case described, using platelet-rich plasma, associated with antibiotics and mouthwash with chlorhexidine 0.2% yielded very significant results in the regression of osteonecrosis by use of bisphosphonates. [16] showed complete healing in 12 of 14 patients undergoing treatment, while one had partial response to the trial and only 1 did not get meaningful answers.

Although the clinical use of laser emission made in the clinical case described is not consistently reported and proven in the literature, his reparative capacity through biostimulation in irradiated sites has been well reported by those who use this technique, [16] have provided improvements in clinical status of patients with lesions similar to those of this case, with stage III osteonecrosis, according [15] with epithelial disruption, bone exposure, pain, local infection with pus. The authors submitted their patients to laser radiation emission, InGaAlP; 660 nm; 40 mW; 0,24 J / cm^2; 6 s, and obtained regression of necrotic process. So we have to use a viable and applicable method.

Given the above, the treatment prescribed for the patient promoted the stimulation

of vascular smaller vessels and the local biostimulation of connective and bone tissue. So we got healing and end the destructive process. Also, the germicidal characteristic of ozone was of great importance, since it inhibited the local infections. Therefore, the two methods were able to relate the initial goal: to end the necrotic progression in the jaws, to be a relativily afforable therapeutic method and to improve the quality of life of patients.

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