

## DENTAL MANAGEMENT OF PATIENTS TREATED WITH INTRAVENOUS BISPHOSPHONATES. A CASE REPORT

### *TRATAMENTO ODONTOLÓGICO DE PACIENTES EM USO DE BISFOSFONATOS INTRAVENOSOS. RELATO DE CASO*

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#### ABSTRACT

Bisphosphonates are drugs used for the inhibition of osteoclastic bone resorption. Their therapeutic use is indicated for Paget's disease, hypercalcemia of cancer, bone metastases, and osteoporosis. The main side effect of these drugs is osteonecrosis of the jaw, which is difficult to control. The aim of the present study was to report a patient, who was referred to the Special Needs Clinics of the Ribeirão Preto Dental School, University of São Paulo, for dental treatment. His medical history revealed a diagnosis of multiple myeloma with bone marrow transplantation in November 2007. Since then, he has been using zometa every 3 months. After physical examination and complementary exams, a diagnosis of angular cheilitis, erythematous candidiasis, caries, localized chronic periodontitis, pulp necrosis and partial edentulousness was established. The treatment plan was based on control of angular cheilitis candidiasis, basic periodontal therapy, supportive periodontal therapy, endodontic treatment, and partial mandibular and maxillary dentures. All invasive procedures were performed with antibiotic prophylaxis. The patient is under treatment and care is being taken to avoid osteonecrosis of the jaws. The authors highlight the need for knowledge of the side effects of bisphosphonates to prevent such effects and to maintain the oral health of the patients.

**DESCRIPTORS:** Bisphosphonates • Osteonecrosis • Dental care • Mouth rehabilitation.

#### RESUMO

Os bisfosfonatos são drogas empregadas para inibição da reabsorção osteoclástica. Seu uso terapêutico está indicado na doença de Paget, hipercalcemia, metástases ósseas e osteoporose. Dentre os efeitos colaterais dessas drogas destaca-se a osteonecrose dos maxilares; lesões de difícil controle. Apresenta-se um caso de paciente que foi encaminhado ao serviço de atendimento odontológico a pacientes com necessidades especiais (DAPE) da Faculdade de Odontologia de Ribeirão Preto - USP para tratamento odontológico. A história médica revelou mieloma múltiplo submetido a transplante de medula óssea em novembro de 2007, e desde então usando zometa a cada 3 meses e carbonato de cálcio (CaCO<sub>3</sub>). Após exame físico e exames complementares estabeleceu-se o diagnóstico de: queilite angular, candidíase eritematosa, cárie, periodontite localizada, necrose pulpar, desdentamento parcial. Como plano de tratamento foi proposto: controle da queilite angular e candidíase, terapia periodontal, tratamento endodôntico e confecção de prótese parcial removível superior e inferior. Todos os procedimentos invasivos foram feitos sob antibióticoprofilaxia. O paciente encontra-se em tratamento, e cuidados estão sendo tomados para evitar a ocorrência de osteonecrose. Os autores destacam a necessidade do conhecimento dos efeitos colaterais dos bisfosfonatos, no intuito de prevenir tais efeitos e manter a saúde oral de seus pacientes.

**DESCRIPTORIOS:** Bisfosfonatos • Osteonecrose • Assistência odontológica • Reabilitação bucal

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## INTRODUCTION

Bisphosphonates (BPs) are inhibitors of bone resorption and angiogenesis which are used for the treatment of diseases that affect bone metabolism, since they directly or indirectly inhibit osteoclastic bone resorption. Their therapeutic use is indicated for Paget's disease, hypercalcemia of cancer, bone metastases, and secondary osteoporosis due to menopause and to the chronic use of corticosteroids<sup>1,2</sup>. The most important side effect of these drugs is osteonecrosis of jaw (ONJ), lesions which are difficult to control and cause high morbidity<sup>3,4</sup>.

ONJ is diagnosed based on clinical and imaging findings<sup>3,5</sup>. These lesions are characterized by necrotic exposure of jaw bones, without clinical evidence of healing for at least 8 weeks in patients using BPs, without exposure to head and neck radiotherapy<sup>3,4</sup>. They are usually asymptomatic, but may be associated with pain, purulent secretion, swelling, tooth mobility, and paresthesia<sup>3</sup>.

The radiographic examination is usually nonspecific and inconclusive in the early stages of bone necrosis, but magnetic resonance is the best technique for the early detection of osteonecrosis and for the establishment of the differential diagnoses with other bone diseases such as osteomyelitis, hematologic malignancies, bone tumors and abscesses<sup>5</sup>.

ONJ can occur after any invasive procedure involving alveolar bone, especially in the posterior mandible site<sup>3,6,7</sup>. Dentoalveolar surgery is the main cause of these alterations<sup>8,9,10</sup>. However, other invasive procedures have been reported to cause osteonecrosis, such as invasive periodon-

tal surgery, dental implants, and the presence of advanced periodontitis<sup>9,10</sup>.

Currently, there is no definitive therapy for ONJ and the relationship between physicians, dentist and other specialists involved in the care of the patient is fundamental for a correct management of these conditions<sup>11,12</sup>. Some authors recommend curettage of bone sequestration associated with systemic antibiotics<sup>13</sup>, while others suggest conservative therapy because of the possibility of dissemination following manipulation of the necrotic bone<sup>4</sup>. In fact, the most important approach is prevention<sup>11</sup>. However, in order to reduce the risk for ONJ, the interruption of oral BP 3 months before and after the dental surgery should be considered, in case either low risk of fracture or stable systemic condition of the patient<sup>10</sup>.

The aim of the present study was to describe the dental management of a patient taking BPs and to warn about the necessary precautions to be taken during the care of this group of patients.

## CASE REPORT

A 70-year-old male patient was referred to the Special Needs Clinics of the Ribeirão Preto Dental School, University of São Paulo, for dental treatment. His medical history revealed a diagnosis of multiple myeloma and a bone marrow transplant in November 2007. Since then, he has been using zoledronic acid (Zometa, Novartis) every 3 months and  $\text{CaCO}_3$ ; he has arterial hypertension controlled with captopril 50 mg daily, and asthma controlled with the continuous use of formoterol/budesonide 12/400 every 12 hours. After physical examination and complementary exams, a diagnosis of angular cheilitis, erythema-

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Figure 1. Clinical presentation at the first visit (a and b)



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Figure 2. Clinical presentation during prosthodontic treatment (a), and after positioning of the dental prosthesis (b)



Figure 3. Clinical presentation after prosthodontic treatment (b) comparing with clinical presentation of the patient 40 years ago (a)

tous candidiasis, caries, localized chronic periodontitis, pulp necrosis and partial edentulousness was established (Figure 1). The treatment plan was based on control of angular cheilitis candidiasis, basic periodontal therapy, supportive periodontal therapy, endodontic treatment and crowns in teeth<sup>11,21</sup> and<sup>22</sup>, and mandibular and maxillary partial dentures (Figure 2). All invasive procedures were performed with antibiotic prophylaxis (amoxicillin 1g, in a single dose 1 hour before the procedure). The patient is currently under treatment and care is being taken to avoid ONJ (Figure 3).

#### DISCUSSION

The present report emphasizes the

importance of knowledge about the side effects of BPs affecting the jaws, since the occurrence of ONJ has a negative influence on quality of life and promotes significant morbidity in affected patients<sup>13</sup>.

The ONJ associated with the use of BPs was first described by Marx<sup>14</sup> (2003) in his report of 36 cases using intravenous zoledronate or pamidronate, as described in the present patient, who is being treated with zoledronic acid every 3 months for the control of hypercalcemia related to multiple myeloma. Since this initial report an increasing number of literature reports have suggested that BPs may be associated with ONJ<sup>3,13,15</sup>.

The pathogenesis of ONJ and the pre-







dominant occurrence of these lesions in the jaws are not yet well understood. BPs are a group of synthetic analogues of inorganic pyrophosphate with a high affinity for calcium<sup>1</sup>. These drugs are deposited in the mineralized bone matrix during long periods of time, and their mechanism of action is based on their effect on hydroxyapatite, resulting in impaired osteoclastic bone resorption<sup>2</sup>. In addition, BPs reduce the release of bone calcium induced by stimulating factors released by tumor cells<sup>1,16</sup>. Some BPs, particularly zoledronic acid, incorporate nitrogen in their molecule, showing an inhibitory effect on cell proliferation and tumor angiogenesis. All this can contribute to the inhibition of bone resorption leading to an increase in bone mass<sup>17</sup>.

Most of the studies about the adverse effects of BPs on the jaws are related in particular to those given intravenously (IV)<sup>9,13,14</sup>. However, patients receiving oral BPs are also at risk for developing ONJ. In general, these patients seem to have less severe manifestations of necrosis and respond more readily to stage-specific treatment regimens than patients receiving BPs IV<sup>15,18</sup>.

The dental treatment for this group of patients aims to minimize the risk of developing ONJ<sup>11</sup>. Thus, it is recommended that, if the systemic conditions of the patient permit, the initiation of BP therapy should be delayed until dental health is optimized<sup>7,19,20</sup>. This decision must be made in conjunction with the treating physician, dentist and other specialists involved in the care of the patient. All of non-restorable teeth with a poor prognosis should be extracted, and any other necessary dentoalveolar surgeries should also be completed at this time<sup>11</sup>.

Patients receiving BPs IV who present non-restorable teeth due to endodontic involvement may be treated by removal of the crown and by endodontic treatment of

the remaining roots<sup>21</sup>. Patients presenting alveolar bone loss attributable to chronic periodontal disease should also be treated since periodontal disease itself is a risk factor to developing of ONJ<sup>9</sup>. In both the above situations, we recommend antibiotic prophylaxis. The rationale for this is the possibility of bone being infected with microorganisms from the mouth, since the bone of patients receiving oral BPs becomes avascular.

Basic and supportive periodontal treatment, caries control and conservative restorative dentistry are critical to maintaining functionally sound teeth, as shown in the present patient. This level of care must be continued indefinitely, and the intervals between visits should be established based on each case<sup>10</sup>. Full or partial dentures must be planned with minimal trauma to the mucosa and these patients should be examined for areas of mucosal trauma, especially along the lingual flange region. In addition, it is very important that this group of patients be advised about the importance of dental hygiene and regular dental evaluations, and specifically instructed to report any alterations in their mouth<sup>11</sup>.

This paper demonstrated that it is possible to do dental treatment in patients using bisphosphonates without causing ONJ as long as the treating professional takes care to avoid these effects. Thus, the authors highlight the need for knowledge of the side effects of bisphosphonates in order to prevent such effects and to maintain the oral health of the patients.

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#### *Conflict of interest*

The authors have no conflict of interest in the present study.

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