

# Implications of the use of bisphosphonates in Endodontics

Maria Alice Diniz Pereira,<sup>1</sup> José Leonardo Barbosa Melgaço-Costa<sup>2,3,4</sup>

<sup>1</sup>Graduate Program in Endodontics, Sete Lagoas University (FACSETE), Sete Lagoas, MG, Brazil

<sup>2</sup>Department of Endodontics, School of Dentistry, Sete Lagoas University (FACSETE), Sete Lagoas, MG, Brazil

<sup>3</sup>Department of Endodontics, School of Dentistry, Faculdade de Estudos Administrativos de Minas Gerais (FEAD), Belo Horizonte, MG, Brazil

<sup>4</sup>Dental surgeon of the Military Police of Minas Gerais, Belo Horizonte, MG, Brazil

• **Conflicts of interest:** none declared.

## Dear editor,

This is a brief review about the implication of the use of bisphosphonates in Endodontics. Bisphosphonates are drugs that inhibit osteoclastic bone resorption and prevent the proliferation of tumor cells and angiogenesis.<sup>1</sup> These drugs are used in the treatment of diseases with excessive bone resorption, such as postmenopausal osteoporosis and Paget's disease, and in cases of malignant hypercalcemia or osteolytic bone metastases, common in breast, lung or prostate cancer.<sup>1,2</sup>

These drugs may lead to the development of Bisphosphonate-related osteonecrosis of the jaw (BRONJ).<sup>3</sup> BRONJ is defined by the American Association of Oral & Maxillo Facial Surgeons<sup>4</sup> as: the persistence of exposed bone in the oral cavity in spite of appropriate treatment, for eight weeks, without local evidence of malignancy and no prior radiotherapy on the affected region, in patients who were treated with Bisphosphonates.

BRONJ is more common in women and affects the mandible (65%) more than the maxilla (26%) and may involve both arches (9%). It occurs spontaneously in 40% of cases and the bilateral involvement is more common in the maxilla.<sup>1</sup> Its incidence in patients who use intravenous bisphosphonates is 0.8-12%; cancer patients are the major risk group.<sup>5</sup>

Clinically, intraoral lesions are characterized by exposed areas of petrous bone, yellowish and having smooth or ragged edges.<sup>5</sup> The lesion is painless in one third of the cases and some patients have reported swelling and abscess formation.<sup>4</sup> Radiographically, it appears as a radiolucent image and can be mistakenly diagnosed as a cyst or a periapical lesion.<sup>6</sup> Due to having similar signs and symptoms to endodontic infections, BRONJ may have a late or incorrect diagnosis, thus making a complete anamnesis fundamental. Histologically, it presents necrotic bone fragments, bone sequestration, the presence of inflammatory cells and abundant bacterial colonies.<sup>7</sup>

Bisphosphonates have high affinity to hydroxyapatite, which explains its long retention time in bone tissue, for ten years or more. Such information is valuable and must be

considered during the dental treatment planning.<sup>8</sup>

The patient who will start therapy using Bisphosphonates must undergo a complete oral evaluation. Root remains and nonrestorable teeth must be extracted, including those with mobility, furcation involvement and large periapical lesions, as well as impacted third molars and those associated to odontogenic cysts.<sup>9</sup> The appropriate care during oral surgery must be taken and first intention healing is extremely important,<sup>8</sup> since the risk of getting BRONJ is seven times higher for patients who undergo oral surgeries.<sup>4</sup>

After starting the Bisphosphonates therapy, the patients must be monitored every six months to avoid the appearance of diseases or to identify the necrosis in its early stage.<sup>9</sup> In patients with higher risk of developing BRONJ, i.e., those who used intravenous Bisphosphonates for over three years, dentoalveolar surgery must be avoided.<sup>10</sup> When possible, the endodontic treatment is preferable, because the risk of developing BRONJ after such treatment was associated in 0.8%.<sup>11</sup> Considered as the preferred alternative to extraction, endodontics must be performed with caution, avoiding over instrumentation and the extrusion of microorganisms to periapical tissues.

In apical periodontitis, bone loss is reduced by the use of Bisphosphonates,<sup>12</sup> but it is an inflammatory defense process of the body when facing the infection, and the use of these drugs may harm this defense mechanism, causing the endodontic infection to progress beyond the periapical region.<sup>13</sup>

Regarding the healing process of periapical tissues after the endodontic treatment, the evidence shows that Bisphosphonates do not interfere in this process. The association between the use of Bisphosphonates and the outcome of the endodontic treatment<sup>14</sup> from the analysis of bone remodeling, which is a critical component in the development and healing of periradicular lesions, showed that the overall healing rate was lower (73.5%) for the Bisphosphonate group when compared to the control group (81.6%) and the initial treatment was more successful (81.4%) than retreatments (61.5%).<sup>15</sup>

In traumatized teeth, bisphosphonates can be beneficial in preventing root resorption after the replantation of avulsion tooth. A systematic review,<sup>16</sup> analyzing the anti-reabsorption effect of Bisphosphonates on teeth that underwent avulsion and replantation, showed that the Bisphosphonate applied on the avulsion surface of the root stopped root resorption and failed to trigger BRONJ pictures.

The effect of intracanal Bisphosphonates to inhibit bone resorption in avulsion incisors, when compared to the calcium hydroxide medication, had a significantly worse outcome, probably due to Bisphosphonate's difficulty of spreading over the dentinal tubules.<sup>17</sup>

Suspending the treatment with anti-reabsorptive agents, prior to dental treatment, is defended by some researchers but it is not widely accepted<sup>9</sup>; it does not eliminate the risk of developing BRONJ due to the prolonged retention of the drug on the bone tissue.<sup>18</sup>

Given the lack of evidence about effective measures to treat BRONJ, prevention is still the best option. Evidence shows that, in addition to not being identified as a risk factor for BRONJ, the endodontic treatment is not influenced by the use of Bisphosphonates. However, the professional must prevent damage to the periradicular tissues during treatment, having caution during pre-, trans- and postoperative stages.

## References

1. Woo SB, Hellstein JW, Kalmar JR. Systematic review: bisphosphonates and osteonecrosis of the jaws. *Annals of internal medicine*. 2006;144(10):753-61.
2. Alsalleeh F, Keippel J, Adams L, Bavitz B. Bisphosphonate associated osteonecrosis of jaw reoccurrence after methotrexate therapy: a case report. *J Endod*. 2014;40(9):1505-7.
3. Marx RE. Pamidronate (Aredia) and zoledronate (Zometa) induced avascular necrosis of the jaws: a growing epidemic. *J Oral Maxillofac Surg*. 2003;61(9):1115-7.
4. American Association of Oral and Maxillo Facial Surgeons. American Association of Oral and Maxillo Facial Surgeons position paper on bisphosphonate-related osteonecrosis of the jaws. *J Oral Maxillofacial Surg*. 2007;65(3):369-76.
5. Walter C, Al-Nawas B, Grotz KA, Thomas C, Thuroff JW, Zinser V, et al. Prevalence and risk factors of bisphosphonate-associated osteonecrosis of the jaw in prostate cancer patients with advanced disease treated with zoledronate. *Eur Urol*. 2008;54(5):1066-72.
6. Chiandussi S, Biasotto M, Dore F, Cavalli F, Cova MA, Di Lenarda R. Clinical and diagnostic imaging of bisphosphonate associated osteonecrosis of the jaws. *Dento-maxillofacial Radiology*. 2006;35(4):236-43.
7. Lee SH, Chang SS, Lee M, Chan RC, Lee CC. Risk of osteonecrosis in patients taking bisphosphonates for prevention of osteoporosis: a systematic review and meta-analysis. *Osteoporos Int*. 2014;25(3):1131-9.
8. Russell RG, Watts NB, Ebetino FH, Rogers MJ. Mechanism so faction of bisphosphonates: similarities and differences and their potential influence on clinical efficacy. *Osteoporos Int*. 2008;19(6):733-59.
9. Ruggiero SL, Dodson TB, Assael LA, Landesberg R, Marx RE, Mehrotra B. American Association of Oral and Maxillofacial Surgeons position paper on bisphosphonate related osteonecrosis of the jaws—2009 update. *J Oral Maxillofac Surg*. 2009;67(5 Suppl):2-12.
10. Hellstein JW, Adler RA, Edwards B, Jacobsen PL, Kalmar JR, Koka S, et al. Managing the care of patients receiving antiresorptive therapy for prevention and treatment of osteoporosis: executive summary of recommendations from the American Dental Association Council on Scientific Affairs. *J Am Dent Assoc*. 2011;142(11):1243-51.
11. Marx RE, Sawatari Y, Fortin M, Broumand V. Bisphosphonate induced exposed bone (osteonecrosis/osteopetrosis) of the jaws: risk factors, recognition, prevention, and treatment. *J Oral Maxillofac Surg*. 2005;63(11):1567-75.
12. Xiong H, Wei L, HU Y, Zhang C, Peng B. Effect of alendronate on alveolar bone resorption and angiogenesis in rats with experimental periapical lesions. *Int. Endod. J*. 2010;43(6):485-91.
13. Toussaint ND, Elder GJ, Kerr PG. Bisphosphonates in chronic kidney disease; balancing potential benefits and adverse effects on bone and soft tissue. *Clin J Am Soc Nephrol* 2009;4(1):221-33.
14. Aminoshariae A, Kulild JC, Mickel A, Fouad AF. Association between systemic diseases and endodontic outcome: a systematic review. *J Endod*. 2017;43(4):514-9.
15. Hsiao A, Glickman G, He J. A retrospective clinical and radiographic study on healing of periradicular lesions in patients taking oral bisphosphonates. *J Endod*. 2009;35(11):1525-8.
16. Najeeb S, Siddiqui F, Khurshid Z, Zohaib S, Zafar MS, Ansari SA. Effect of bisphosphonates on root resorption after tooth replantation – a systematic review. *Dental Traumatol*. 2017;33(2):77-83.
17. Thong YL, Messer HH, Zain RB, Saw LH, Yoong LT. Intracanal bisphosphonate does not inhibit replacement resorption associated with delayed replantation of monkey incisors. *Dent Traumatol*. 2009;25(4):386-93.
18. McLeod N, Brennan PA, Ruggiero SL. Bisphosphonate osteonecrosis of the jaw: a historical and contemporary review. *The Surgeon*. 2012;10(1):36-42.

## Mini Curriculum and Author's Contribution

1. Maria Alice Diniz Pereira – DDS. Contribution: writing of the article, review, and final approval.
2. José Leonardo Barbosa Melgaço-Costa – DDS and PhD. Contribution: writing of the article, technical review, and final approval.

Submitted: 06/21/2018 / Accepted for publication: 07/18/2018

### Corresponding Author

**José Leonardo Barbosa Melgaço-Costa**

E-mail: leomelgaco@yahoo.com.br

