



REVIEW ARTICLE

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## PERI-IMPLANTITE FROM THE USE OF BISPHOSPHATES: A REVIEW

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### ABSTRACT

Nowadays, it is increasingly common to have dental implants rehabilitated, which has the function of playing the same role as the root of a lost tooth, returning a more aesthetic and reliable smile to the patient. It is a piece of biocompatible titanium that will be attached to the bone to replace one or more teeth. When evaluating a patient who will be submitted to the placement of implants, we must take into account the systemic health, hygiene and some medications used by it, especially the bisphosphonates (BP). The objective of this study was to evaluate, through a literature review, the occurrence of peri-implantite due to the use of bisphosphonates. Bisphosphonates (BP) are inhibitory drugs of bone resorption, capable of modifying bone remodeling, acting directly on osteoblasts (bone reconstruction) and osteoclasts (bone resorption), thus generating a bone tissue with little blood supply and discharge density. It was concluded that the prior knowledge of the professional about the undesirable effects of this substance and the correct management in patients who use bisphosphonates is of paramount importance.

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## INTRODUCTION

Dental implants have long revolutionized the possibilities of rehabilitation for both partially edentulous and fully edentulous patients, raising self-esteem due to improved smile aesthetics (Matos, 2010). Rehabilitation is considered a reliable and safe method, and although many studies report the high success rate, there is still a growing number of patients with peri-implant diseases, such as peri-implant mucositis, which is nothing more than inflammation and ulceration of the soft tissues around the implant (Matos, 2010 and Polo, 2011). Early diagnosis of peri-implant mucositis is critical to successful treatment, as the disease progresses naturally to peri-implantitis, thus initiating a consequent loss of bone structure, and the greater the tissue destruction, the more complex and difficult it will be. the treatment, resulting in an irreversible process of loss of fixation and the inevitable removal of the implant (Junior, 2007).

Another very important complication occurs in patients who use drugs of the bisphosphonate class, medications that are capable of modifying bone remodeling, and that have the function of modifying the bone matrix, making the bone more resistant to fractures, but, due to the excess of this bone the nutrition of the same is compromised, causing in loss of the dental implants and other complications (Caldas, 2016). The onset of clinical use of BP occurred in 1994, and in 2004 a series of reports were published alerting its adverse effects, especially when it was administered intravenously (Barrantes, 2016). After the start of administration of this drug, the patient should be evaluated and kept on maintaining his oral health, under the constant guidance of the dental surgeon, where he will inform in detail about the benefits and risks of certain dental treatments. It is of paramount importance the prior knowledge of the professional about the undesired effects of such substance and the correct management in patients who use bisphosphonates (Bejar, 2017). Implant therapy should be carefully and carefully planned preoperatively, intraoperatively and postoperatively in order to avoid treatment failure (Oliveira, 2014).

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Table 1. Characteristics of Bisphosphonates available in the Brazilian market

Generic	Commercial	Nitrogenated	Indications	Dose	Potency	Via
Etidronate	Didronel	No	Paget	5mg/kg/day 400mg/day	1x	IV
Tiludronate	Skelid	No	Paget	400mg/dia	10x	Oral
Clodronate	Bonefos	No	Neoplasias	300mg/day IV	10x	IV/Oral
Pamidronate	Aredia	Yes	Paget/Neoplasias	60mg	100x	IV
Alendronate	Fosama, Alendil, Recalfe, Endrox, Cleveron, Osteoral, Osteoform, Osteonan, Osteotrat, Osteofar, Bonalen, Endronax, Minusorb	Yes	Osteoporose/Paget	Osteoporose 70mg/week or 10mg/day. Paget 40mg/dayper 6 months	500x	Oral
Ibandronato	BondronatBoniva	Yes	Osteoporose	150mg/month	1.000x	IV/Oral
Risedronato	Actonel	Yes	Osteoporose	35mg/week ou 5mg/day	2.000x	Oral
Zoledronato	ZometAclasta	Yes	Paget/Neoplasias	5mg single Dose	10.000x	IV

Therefore, the objective of this study was to review the literature showing the occurrence of peri-implantitis due to the use of bisphosphonate.

## MATERIALS AND METHODS

**Eligibility and Study Design:** A total of 28 articles were found involving Bisfosfonato, Odontologia and Peri-implantite. Initially, it was held the exclusion existing title and duplications following the interest described this work. After this process, the summaries were evaluated, and a new exclusion was held, 12 articles were included and discussed in this study. Experimental and clinical studies were included (case reports, retrospective, prospective, randomized trials and systematic review and meta-analysis) with qualitative and/or quantitative analysis. Initially, the keywords were determined by searching the DeCS tool (Descriptors in Health Sciences, BIREME base) and later verified and validated by MeSh system (Medical Subject Headings, the US National Library of Medicine) in order to achieve consistent search.

## LITERATURE REVIEW AND DISCUSSION

Bisphosphonate (BP) is an analogous synthetic drug of inorganic pyrophosphate, being endogenous regulators of bone mineralization. Its chemical structure presents PO<sub>3</sub> phosphate bound to a central carbon and the union of chains called R1 and R2, chains of extreme importance for the efficacy of these drugs (Matos, 2010 and Polo, 2011). The R1 chain is short and also responsible for having pharmacokinetic and chemical properties of BP (Junior, 2007). However, the R2 chain is long and determinant in relation to the mechanism of action and the anti-resorptive power, presenting non-nitrogenous BP and nitrogenous structures, which are incorporated by osteoclasts into the bone resorption, resulting in apoptosis cell death (Caldas, 2008). In the chemical structure of BP, which are not nitrogenous, when they are metabolized by osteoclasts, they will be substrates for the synthesis of cytotoxic ATP analogs, where cell death will occur (Barrantes, 2016; Polo, 2018; Bejar, 2017 and Oliveira, 2014). However, the nitrogenates after being reabsorbed by the osteoclasts act in the interruption of the mevalonate pathway, which is responsible for controlling the synthesis of cholesterol. This interruption will compromise intracellular vesicular transport, causing cell death, impairing bone resorption (Perez, 2013). Bone resorption is made by osteoclasts, which consists of bone mineral dissolution, leading to cavity formation and the release of bone matrix elements; already in the bone deposition occurs osteoblast matrix synthesis, leading to primary mineralization

and an extensive sequence of secondary mineralization (Bernal, 2010). In addition to resorption, bone production is also limited by a decrease in the neoformation surface. This decrease in bone formation occurs secondarily to reduced reabsorption. The newly formed bones will have a lower chance of being neoformed, due to the reduced volume of remodeling, generating a longer time for complete mineralization (Sampaio, 2011 and Andrade, 2014).

## Conclusion

The prior knowledge of the dental surgeon about the side effects of bisphosphonate medications is of paramount importance, as well as a correct planning, management, clinical protocol, prevention and rehabilitation of recurrent alterations of the use of this medicine. It is up to the professional to perform previous clinical evaluations and constant monitoring of oral health conditions in patients subject to the use of these substances, in order to take the best measures, both preventive and curative for each case.

**Conflict of interests:** There is no conflict of interest between authors.

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