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DENTAL IMPLANTS IN PATIENTS UNDER BISPHOSPHONATE THERAPY AND THE RISK OF OSTEONECROSIS

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Abstract: Oral rehabilitation with dental implants has shown a high success rate reported in the literature and with that, implantology presents itself as a safe technique, widely accepted and used. However, the implant is subject to complications from several factors at any stage of treatment, the most common being the risk of developing osteonecrosis of the jaws in patients using antiresorptive and/or antiangiogenic drugs. Bisphosphonate is a drug used in the treatment of diseases such as osteoporosis, bone metastasis from cancer, among others. It is capable of interfering with osteoclastic and osteoblastic activity, inhibit osseointegration or even delay the healing of bone tissue and consequently can negatively interact with the installation of the dental implant that needs to have osseointegration for its fixation. Even in the face of this drug interaction, although implant rehabilitation is very complex for these patients, it is not a contraindication to this treatment. It is necessary to evaluate all risks, other comorbidities, systemic diseases, deleterious habits and patient hygiene. Those who perform the installation of implants using these drugs must be monitored by the dental surgeon for possible signs of bone infection and avoid triggering bone necrosis. If this occurs, despite all precautions.
Keywords: Dental implant; bisphosphonate; osteonecrosis; osseointegration.

INTRODUCTION

Implant dentistry is an area of dentistry that has gained great visibility due to its high success rates. It allows a rehabilitation treatment by which it is possible to replace lost natural teeth with a titanium or zirconia screw called a dental implant. The most modern ones described are the morse taper models by which their designer allows a better fixation of the implant in the bone and even though they present treated surfaces in order to improve the primary and secondary stability. This fixation occurs through osseointegration, that is, a direct connection between the bone and the implant surface, providing stability to the implant (MENDES; DAVIES, 2016). Rehabilitative treatment with implants in patients using antiresorptive and/or antiangiogenic medications is conflicting, has an uncertain prognosis and must be avoided despite not being an absolute contraindication (GIOVANNACCI et al., 2016). Medicines such as bisphosphonates (BFs) have a synthetic compound similar to pyrophosphate, a natural inhibitor of bone resorption present in the body, and its differentiation occurs through the exchange of the carbon atom for oxygen. These drugs come in two compositions that can be nitrogenous or non-nitrogenous with two ways of being administered, orally (VO) or intravenously (EV). They are able to bind to hydroxyapatite crystals, depositing themselves in the bone matrix mainly in regions of great bone remodeling for long periods. They also have antiresorptive and antiangiogenic characteristics, which can trigger avascular bone necrosis (STRAMANDINOLIZANICOTTI et al., 2018). Gelazius et al. (2018) highlighted many risk factors for drug-induced osteonecrosis of the jaw (ONMIM) such as invasive dental procedures, periodontal surgery, extractions, chronic trauma from ill-fitting dentures, implant placement, systemic diseases, age, alcohol consumption and smoking. Coléte et al. (2019) highlights the contemporary existence of many reports of recent or late dental implant failures due to different etiologies, one of which is the use of bisphosphonates. BFs have been used since the 1960s for the treatment of several diseases such as multiple myeloma, Paget's disease, osteoporosis, malignant hypercalcemia, bone metastasis from breast, prostate and lung cancer, among others (SALES; CONCEIÇÃO, 2020). (2018)

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LITERATURE REVIEW

Osseointegration of implants Osseointegration is the bone growth around the implant, providing it with stability to withstand masticatory loads. This stability occurs in two stages, the primary one being

obtained at the time of surgery, measured in Newtons and decreasing over time due to the action of osteoclasts that reabsorb the traumatized bone tissue during the milling of the implant placement. Secondary stability initially occurs together with primary stability and increases over time, due to the action of osteoblasts that deposit bone matrix around the implant, gradually increasing the stability of the implant. In these two stages, several biological events occur for the success of implant anchorage. During bone remodeling, angiogenic action is perceived, that is, neoformation of blood vessels to lead to the remodeling portion osteogenic cells that migrate to the implant surface, undergo cell differentiation and deposit bone matrix directly on this surface. The type of surface can also interfere with the adhesion of the bone to the implant, since treated surfaces that present micro-cracks in their topography have greater deposition of bone matrix and, consequently, greater resistance to the dental implant (MENDES; DAVIES, 2016).

There are a variety of local and systemic factors that can affect osseointegration and result in implant failure such as bone type, implant length and diameter, cortical layer rupture, absence of keratinized tissue, periodontal disease, poor hygiene, smoking, osteoporosis, epidermolysis bullosa and lichen planus. Osteoporosis is a pathology characterized by the deterioration of microparticles of the skeletal structure, leaving the bone tissue fragile. The most common treatment for this and some other diseases that affect bone tissue is a medication based on bisphosphonates (ALI et al., 2016).

The action of bisphosphonates can interfere with osteoclastic and osteoblastic activity, inhibit osseointegration or delay the healing of bone tissue (THIRUNAVUKARASU; PINTO; SEYMOUR, 2015).

Mendes et al. (2019) reported that these drugs act negatively on implants as they directly inhibit bone turnover and discussed a hypothesis that such a condition predisposes to the development of osteonecrosis of the maxilla and mandible. The author reports that there are many contemporary studies against this hypothesis and that suggest that bisphosphonate has an important role in osseointegration through its local use, enabling the biomodulation of bone remodeling. Javed and Almas (2010) analyzed 12 studies described in the literature and which were carried out in universities or medical centers, with 7 case reports and 5 retrospective analyses. In 10 of them, oral BPs from 6 months to 10 years were used. And in the other 2 intravenous Bfs were used for more than two years. In 10 studies used BFs with nitrogen and in 2 BFs without nitrogen. Of all the studies analyzed, only one showed a negative interaction of BFs on the osseointegration of the implant and six case reports demonstrated that the implants had successful osseointegration and functionality. The authors also highlight another study carried out by Brooks et al that describes a 90% success rate of osseointegrated implants.

For Mozzati et al. (2015) it is possible to improve the osseointegration of implants using a protocol by which the implant is incorporated into liquid Plasma Rich in Growth Factor (PRGF) to bioactivate its surface and uses a small part of this PRGF clot as a covering membrane before closing. the retail. When a bone graft was needed in the maxillary sinus region, Bio-Oss (Geistlich Pharma, Wolhusen, Switzerland) mixed with PRGF was used, enriching its cohesive properties, facilitating its handling and application, as well as the immediate positioning of the implants. When analyzing some studies, it is clear that there is an interrelationship between the failed implant and the use of BFs. However, despite little evidence on the subject,

MECHANISM OF ACTION OF DRUGS

Bisphosphonates represent a class of drugs capable of inhibiting the differentiation and maturation of osteoclastic cells and also inducing apoptosis of these cells, causing an imbalance in bone remodeling, decreasing its resorption (CUNHA et al., 2019). Because they have these characteristics, they are used in endocrinology, oncology, orthopedics and dentistry to prevent and combat resorption bone pathologies. Due to their three-dimensional molecular structure, they are able to bind metal ions such as CA^{2}+ present in the skeleton. Despite their preference for osteoclasts, they can also interfere with keratinocytes and vascular endothelial growth factor (VEGF) (SANTOS et al., 2015). The molecular mechanism of action depends on the presence or absence of nitrogen in the chain. Those containing nitrogen stimulate osteoblasts to produce a signal that inhibits osteoclastic action, decreasing resorption synthesis and also bind to osteoclasts, breaking their cytoskeletal integrity, inhibiting their differentiation and causing cell apoptosis, directly affecting bone resorption and predisposing the patient to makes its use more likely to trigger bisphosphonate-induced osteonecrosis of the jaws. Non-nitrogenous BFs are metabolized intracellularly and produce non-hydrolyzable cytotoxic substrates of adenosine triphosphate (ATP) that cause osteoclast cell death (CASTILHO et al., 2013; BROZOSKI et al., 2012). In its molecular composition, BPs present oxygen (PCP) as a central atom, making this drug more resistant to the natural enzymatic degradation of the human body and consequently increasing its metabolic bioavailability. Examples of nitrogenous BFs include Zoledronic Acid or Zoledronate - administered intravenously, being indicated mainly for the treatment of osteoporosis, malignant hypercalcemia, multiple myeloma and bone metastases; Pamidronate - administered intravenously and is mainly indicated in cases of malignant hypercalcemia, multiple myeloma and bone metastases from breast, lung and prostate cancer.; Aledronate, Ibandronate and Rizedronate - are all administered orally and have as main indication the treatment of osteoporosis. As for the non-nitrogenous compounds, we have Clodronate and Etidronate (CHAVES et al., 2018). Bfs have a high affinity for hydroxyapatite crystals, can bind to them and deposit themselves in the mineralized bone matrix, remaining in cell 7 for long periods of time. This action is due to the fact that these drugs have a half-life of several years and provide residual power to the drug, which can remain in the skeleton for up to 10 years after treatment (FEDE et al., 2018). BFs administered orally are metabolized by the gastrointestinal tract and have a low absorption rate, with 10 to 50% of the substance being incorporated into the bone. Due to this concentration of unabsorbed substance, some patients may experience irritation of this mucosa and a consequent symptomatology such as epigastric pain, dyspepsia, nausea and vomiting. When these patients present a picture of ONMIB, the suspension of the drug is indicated as long as it does not harm their general health, it is evaluated and authorized by the doctor. The most used BFs are those containing nitrogen such as Zoledronic Acid and Pamidronate being administered EV, they are more potent and therefore more used in cancer patients. It is also reported that zoledronate has a risk of osteonecrosis 9.5 times greater when compared to pamidronate (CHIANESI; MONTEIRO, 2018). Non-nitrogen compounds are metabolized faster, decreasing their action potential, which makes them a less potent drug than nitrogen compounds (CARVALHO et al., 2010). A data survey was carried out by the AAOMS comparing patients who use BPs orally to

those who use the intravenous route and analyzing the risk of developing osteonecrosis after performing dental procedures. It was observed that after periodontal procedures, osseointegrated implants, extractions and endodontic treatments had approximately the same rate at risk of developing osteonecrosis, being 0.5% for patients with VO treatment and from 1.6% to 14.8% for VE patients. (CHIANESI; MONTEIRO, 2018). There is another new drug described by some scholars which is called denosumab. It has an action on bone metabolism and despite having a slightly different mechanism of action from BPs, it can also be associated with the development of osteonecrosis of the jaws, as observed by Carvalho (2018, p. 51): Denosumab is a human monoclonal antibody that blocks RANKL, a member of the tumor necrosis factor (TNF) superfamily that plays a key role in resorption regulation. RANKL is secreted by 8 activated osteoblasts in response to circulating cytokines (interleukins) and hormones (glucocorticoids) and triggers an intracellular signaling cascade that results in osteoclast maturation and proliferation. Unlike BPs, which tend to accumulate and persist in bone for several years after therapy is discontinued, denosumab can remain in the body for a limited period of time due to a lack of affinity for hydroxyapatite. The irreversible deactivation of osteoclasts promoted by denosumab persists only until cell death. As new osteoclasts are formed daily, if a new osteoclast is formed after one administration of the drug and before the next administration, this osteoclast will be fully functional. Thus, its effects are expected to dissipate after 6 months. For all these reasons, the author believes that this drug is a possible alternative treatment to the use of BPs and that, due to its shorter half-life, it would present a lower risk to the patient of developing osteonecrosis after therapy with this drug. However, further randomized research is needed to obtain concrete data on such speculation. Denosumab is administered subcutaneously and reaches its maximum concentration in 10 days, which allows its rapid elimination from the blood system, establishing a reversible inhibition of RANKL. Even so, there are cases reported in the literature associating its use with the appearance of osteonecrosis of the jaws. As an example of denosumab drugs, we have Prolia and Xgeva, both administered intravenously and mainly indicated for the treatment of osteoporosis, malignant hypercalcemia, multiple myeloma and bone metastases (CHAVES et al., 2018).

Other widely used drugs are antiangiogenics, used for the therapy of malignant neoplasms since angiogenesis is a crucial part of the evolution of tumors. They are divided into two categories, the first of which is when it binds directly to VEGE and neutralizes its biological activity. The second are tyrosine kinase inhibitors (TKI) that act on macrophages and thus block VEGE receptors and signaling and consequently inhibit the development of osteoclasts (CARVALHO et al., 2018).

Chaves et al. (2018) presents sunitinib, sorafenib and bevacizumab as examples of antiangiogenic drugs and states that both have cases of progression of osteonecrosis in the jaws.

RISK OF BISPHOSPHONATE-ASSOCIATED OSTEONECROSIS

ONMIB was first referred to by Marx in 2003 as painful bone exposure in the mandible and/or maxilla that did not respond to standard treatment in patients undergoing therapy with BPs such as pamidronate and zolendronic acid. Subsequently, this bone alteration was also identified related to the use of other drugs such as antiresorptives and antiangiogenics, being then suggested

by the American Association of Oral and Maxillofacial Surgeons (AAOMS) to be called drug-induced osteonecrosis of the jaw (ONMIM). This association defined osteonecrosis of the jaws as exposed bone in the maxillofacial region, which may have an intraoral or extraoral fistula, persistent for more than 8 weeks in patients undergoing therapy with antiresorptives and/or antiangiogenics without a report of radiotherapy incidence in the head and neck region (CARVALHO et al., 2010). The continuous use of drugs based on BFs is related to several adverse reactions such as kidney problems, gastrointestinal problems, fever, chills, myalgia, arthralgia, atrial fibrillation, eye inflammation, esophageal cancer and since 2003 through the study of Marx it is also associated with osteonecrosis. of the jaws. Cases of ONMIM are reported both by medication administered intravenously and orally, with its highest incidence in intravenous BPs. The patients most likely to develop ONMIM are women over 60 years of age on this therapy for more than three years, those on hemodialysis, who have a low hemoglobin level, who use immunosuppressants, who have obesity, diabetes and who use tobacco (CASTILHO et al., 2013). ONMIB has a different incidence in its drugs due to the type of BFs (if they are nitrogenous or not); potency (lower in oral BPs); the route of administration (intravenous or oral); to the treatment period (short or long) and cumulative dose of the drug (COLÉTE et al., 2019). According to Chianesi and Monteiro (2018), the bones of the maxillomandibular complex are more susceptible to developing avascular osteonecrosis because they are regions with greater blood supply compared to other bones in the body, with rapid remodeling when compared to teeth and therefore would lead to a higher concentration of BFs in its skeletal structure. It also states that 10 invasive dental procedures with bone exposure, poor hygiene, The high possibility of endodontic and/or periodontal infections favor microbial contamination of the oral environment and consequently lead to osteonecrosis. It is observed that extraction and dental implant are surgical procedures with bone involvement considered to have the same level of risk to develop this pathology. However, they present different healing processes, which may imply different rates for the development of ONMIM. The extractions promote surgical wounds that can be closed at the edges, preventing their contamination, being free from infection and consequently increasing tissue neoformation. Implants, in turn, traumatize bone tissue and it is not possible to close the surgical wound, leaving it exposed to oral microorganisms,

Although its etiopathogenesis is still unknown, it is known to be multifactorial, including genetic factors, drug-related factors, local and systemic factors. In addition, the mechanism of action of this drug is known and researchers believe that this can explain much of the development of the pathology (CASTILHO et al., 2013; CARVALHO et al., 2018).

DENTAL MANAGEMENT FOR PATIENTS ON BISPHOSPHONATE THERAPY

The relationship between the development of osteonecrosis of both the maxilla and the mandible with bloody dental procedures is undeniable. That is why it is so necessary to recommend that these patients undergo, whenever possible, dental treatment before undergoing therapy with antiresorptive and antiangiogenic drugs, carry out a periodic clinical-dental follow-up so that the dental surgeon can provide them with a planning of rehabilitation, always looking for the best health prognosis, not only for oral health, but also for general health, talking to the patient,

presenting all the treatment possibilities, from the conservative to the surgical phase, clarify all your doubts and make it very clear the risks to which the patient is being subjected through the interaction of their medications with the result of the treatment accomplished. All documents and information must be attached to the patient's medical record so that the dental surgeon can protect himself in case the patient is dissatisfied or wants to accuse him of medical malpractice and still sue him on such accusation. It is known that prevention is the most effective way to reduce the incidence of ONMIM and that those patients who underwent all necessary oral rehabilitation prior to drug therapy had a 50% reduction in the risk of developing this pathology (CARVALHO et al., 2018). Chianesi and Monteiro (2018) highlight the dental treatments recommended for patients already under drug therapy with BPs according to each specialty. For dentistry and orthodontics, no evidence was found about the relationship of their procedures with osteonecrosis. For endodontics, canal 12 obturator treatment is recommended as long as it does not go beyond the apex of the root. Periodontics must prevent infectious foci and disease progression in the least invasive way possible. Prostheses can be performed whenever necessary, normally with adequate adjustments and well-adapted marginal edges so as not to traumatize the mucosal tissue. For surgery, it is recommended that they be performed only in essential cases and that the surgical wound be closed with the principle of first intention. When suturing is not possible, a semipermeable membrane must be placed over the wound to prevent contamination, and a mouthwash twice a day with 0.12% chlorhexidine must be prescribed before and after surgery for a period of 4 to 8 weeks. In implantology, however, there are many reports of the risk of osteonecrosis for patients undergoing intravenous BP therapy, and therefore, osseointegrated implants are not indicated for these people. However, patients undergoing therapy with oral BPs and who do not have risk factors can be fitted with implants taking all forms of precaution. Those who use the drug for more than three years are recommended, when possible, to discontinue the drug three months before surgery.

According to Freitas et al. (2016), the evolution of ONMIB in dental implants presents a higher rate when the patient is using the drug or after completion of treatment. Osteonecrosis is clinically visible with bone exposure in the maxilla and/or mandible, and may remain asymptomatic for months or even years. When this is symptomatic, localized pain, tooth mobility, fistulas that do not heal, drainage of pus and edema in soft tissues may be reported. This pathology primarily affects the alveolar bone and may extend to the lower border or ramus of the mandible, the zygomatic portion or wall of the maxillary sinus. In complementary imaging tests, radiographs show radiolucent areas and decreased bone density (CHIANESI; MONTEIRO, 2018).

The researchers CHAVES et al. (2018), CHIANESI; MONTEIRO (2018), FREITAS et al. (2016), SALES; CONCEIÇÃO (2020) and SANTOS et al. (2015) demonstrate in their articles another test used to assess the risk and help the dental surgeon choose the best period for a surgical intervention, which is type I collagen cross-linked carboxytelopeptide (CTX). However, this test cannot be considered decisive for the diagnosis due to the few evidenced data, requiring further research on its effectiveness. Those who believe in this exam follow table 2 to verify the risk and outline an adequate surgical plan.

Even with all the precautionary measures taken prior to surgery through examinations, thorough analysis of the case, oral hygiene instruction, control of periodontal diseases and antibiotic prophylaxis, antiresorptives

can trigger the osteonecrosis process. Despite being a difficult-to-treat pathology and still not having a standard protocol developed to be followed, the majority of scholars believe that the treatment consists of eliminating pain, controlling infection and progression of the necrotic lesion. CARVALHO et al. (2018) brings in their study data presented by the AAOMS that, together with a commission, classified the ONMIM in stages and determined guidelines for the treatment of lesions, from conservative to surgical/ invasive in order to assist dental surgeons in the treatment of this pathology.

It is known that it is very important that all patients diagnosed with a disease whose treatment involves therapy with antiresorptive and antiangiogenic drugs are immediately referred to a dental surgeon in order to carry out a thorough anamnesis and perform all dental procedures prior to drug therapy. Prevention of osteonecrosis aims to eliminate all foci of infection and/or inflammation, identify teeth that need restoration and those that cannot be restored, the necessary surgeries such as extractions, bone grafts, removal of torus/exostoses and installation of dental implants, periapical pathologies and in case the patient wears prostheses, check their retention and reline them or even change them if they are poorly adapted. This first consultation is essential for the dentist to be able to solve all the patient's doubts regarding the disease, explain how it occurs, what care is taken to prevent osteonecrosis and especially how its early manifestation in the oral environment. The dentist must recommend that the necessary invasive procedures be performed three weeks before the treatment with BPs, with extra care to avoid the presence of bone spicules and thus have the healing of the surgical lesion. the 17 patient must receive guidance on how hygiene is important in combating this disease and how it must be performed. (CARVALHO et al., 2018; SALES; CONCEIÇÃO, 2020). what care must be taken to prevent osteonecrosis and especially how its early manifestation in the oral environment. The dentist must recommend that the necessary invasive procedures be performed three weeks before the treatment with BPs, with extra care to avoid the presence of bone spicules and thus have the healing of the surgical lesion. the 17 patient must receive guidance on how hygiene is important in combating this disease and how it must be performed. (CARVALHO et al., 2018; SALES; CONCEIÇÃO, 2020). what care must be taken to prevent osteonecrosis and especially how its early manifestation in the oral environment. The dentist must recommend that the necessary invasive procedures be performed three weeks before the treatment with BPs, with extra care to avoid the presence of bone spicules and thus have the healing of the surgical lesion. the 17 patient must receive guidance on how hygiene is important in combating this disease and how it must be performed. (CARVALHO et al., 2018; SALES; CONCEIÇÃO, 2020). the 17 patient must receive guidance on how hygiene is important in combating this disease and how it must be performed. (CARVALHO et al., 2018; SALES; CONCEIÇÃO, 2020). the 17 patient must receive guidance on how hygiene is important in combating this disease and how it must be performed. (CARVALHO et al., 2018; SALES; CONCEIÇÃO, 2020).

There are in the literature some joint treatments for osteonecrosis of the jaws that researchers believe to improve the healing capacity of the necrotic lesion, such as hyperbaric oxygen therapy (with the number of sessions decided individually for each patient), ozone therapy, laser therapy (with low intensity), use of platelet-rich plasma, bone morphogenetic protein and parathyroid hormone (PTH) in order to

biostimulate bone regeneration (BROZOSKI et al., 2012; CHIANESI; MONTEIRO, 2018; SALES; CONCEIÇÃO, 2020; STRAMANDINOLIZANICOTTI et al.., 2018).

Regarding the use of antiangiogenics and denosumabs, there is little evidence about their action on metabolism and relationship with drug-induced osteonecrosis of the jaws, leading dentists to follow the same recommendations made for bisphosphonates (CARVALHO et al., 2018).

DISCUSSION

The risk of developing osteonecrosis in the placement of dental implants in patients undergoing bisphosphonate therapy is real and is greater when the drug is used intravenously (CHIANESI; MONTEIRO, 2018). BPs have a mechanism of action capable of inhibiting the biomodulation of osteoclastic cells and inducing the death of these cells, generating an imbalance between bone absorption and deposition (STRAMANDINOLI-ZANICOTTI et al., 2018). The installation of implants is an invasive rehabilitation treatment before its surgical phase. Its indication for those users of bisphosphonates is complex, but it is not contraindicated because the maxillary/mandibular bone is able to perform the necessary osseointegration, taking a little longer to heal. The dental surgeon is supported by contemporary literature to perform these procedures cautiously and always attentive to the first signs of osteonecrosis to intervene as soon as possible. In some of these articles, it was highlighted that BPs, when used at the implant installation site, would be able to help bone remodeling in a beneficial way, accelerating its healing precisely because of the decrease in osteoclastic cells. Among these, Guimarães et al. (2017) states that the local use of BFs seems to favor the osseointegration of titanium implants in humans. For Marques et al. (2019), when analyzing the occurrence of osteonecrosis and the installation of the implant, a greater risk of the emergence of ONMIM is perceived when dental treatment is performed during or after the beginning of the use of BFs. In addition to antiresorptive and antiangiogenic drugs, there are other etiological factors capable of increasing the chances of ONMIM treated in the studies by Castilho et al.(2013), Carvalho et al.(2018) and Marques et al. (2019). These factors can be local (bone density, oral diseases such as periodontitis), systemic (diabetes, obesity, being on hemodialysis and chemotherapy), genetic (predisposition to osteoporosis and polymorphisms) or deleterious habits (smoking). BFs are long-life drugs capable of staying in the bone for a long period of time and accumulating with use. This accumulation is capable of inhibiting bone tissue repair after trauma (physiological or induced), decreasing blood flow, cell apoptosis and consequently bone necrosis, which can be identified clinically (CHIANESI; MONTEIRO, 2018; FERREIRA et al. 2020). There are controversial reports that the CTx test that measures the serum concentration of CTx in the blood can be used as a parameter to assess the risk of osteonecrosis, and authors such as Santos et al. (2015) and Ferreira et al. (2020) that describe the possibility of its use in dentistry. Researchers such as Brozoski et al. (2012); Carvalho et al. (2010); Chianesi and Monteiro (2018); Coléte et al. (2019); Cunha et al. (2019); Grant et al.(2008); Mozzati et al. (2015); Santos et al. (2015); Thirunavukarasu; Chick; Seymour (2015); Viela-Carvalho et al. (2018) highlighted that for both the American Dental Association (ADA) and the AAOMS, those patients undergoing therapy with oral BPs for more than three years can undergo rehabilitation with implants together with discontinuation of the medication (with medical authorization) for 3 months before

and 3 months after the procedure to reduce the bioavailability of BFs and consequently reduce the risk of osteonecrosis. Most of these scholars also state that if the patient needs to undergo invasive procedures in more than one tooth, it is necessary to wait until the injured bone has completely healed. Although there is no gold standard for treating osteonecrosis, some researchers such as Zamora et al. (2021) and Carvalho et al.

There are also reports of joint treatments that can be used for healing and regeneration of necrotic bone, such as hyperbaric oxygen therapy, ozone therapy, laser therapy, platelet-rich plasma, bone morphogenetic protein and parathyroid hormone (BROZOSKI et al., 2012; CHIANESI; MONTEIRO, 2018; SALES; CONCEIÇÃO, 2020; STRAMANDINOLI-ZANICOTTI et al., 2018).

CONCLUSION

It is undeniable that there is an influence of drugs such as bisphosphonates and denosumab before, during or even after dental rehabilitation therapies with dental implants, which can trigger osteonecrosis of the jaws. That is why it is important for the dental surgeon to have prior knowledge about this interaction so that he can safely indicate this procedure, with the development of a multidisciplinary plan, aware of the risks and seeking to minimize the chances of developing drug-induced osteonecrosis of the jaws and, if this occurs.

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