The American Academy of Oral Medicine clinical practice statement: dental care for the patient on antiresorptive drug therapy

Juan M. Bugueno, DDS, MS, ABOM, Assist Prof[a] and
Cesar A. Migliorati, DDS, MS, PhD, Prof[b]

(Oral Surg Oral Med Oral Pathol Oral Radiol 2019;127:136−139)

The American Academy of Oral Medicine (AAOM) affirms that medication-related osteonecrosis of the jaw (MRONJ) is defined as a condition of exposed bone or bone that can be probed through an intraoral or extraoral fistula in the maxillofacial region and that has persisted for more than 8 weeks in patients who are with current or have had previous exposure to antiresorptive or antiangiogenic agents and have no history of radiation therapy of the jaws. The AAOM also affirms that over the years, important information has emerged and can help providers make treatment decisions and minimize the risk for MRONJ. However, there still is limited clinical trial−related evidence to support recommendations for the care of these patients; however, denying oral comprehensive care to patients who are in pain and have an active area of infection and sending them home with a prescription of analgesics and antibiotics is not the best management strategy. Patients in treatment with antiresorptives can receive dental care with a relatively good safety margin.

This clinical practice statement was developed as an educational tool based on expert consensus of the AAOM leadership. Readers are encouraged to consider the recommendations in the context of their specific clinical situation, and consult, when appropriate, other sources of clinical, scientific, or regulatory information prior to making a treatment decision.

Originators: Juan M Bugueno, DDS, MS, ABOM; Cesar A Migliorati, DDS, MS, PhD
Review: AAOM Education Committee
Approval: AAOM Education Committee

PURPOSE

Routine dental care of patients treated with antiresorptive therapy has been a challenge since the first reported cases of medication-related osteonecrosis of the jaw (MRONJ) in 2003.[1,3,4,5] In spite of publications promulgating guidelines to care for these individuals, oral health care providers are still uncertain as to how or what type of dental care can be safely provided to patients because of the risk of this complication. The goals of this clinical practice statement are to:

1) Provide basic information to the clinician about the definition and diagnosis of MRONJ
2) Identify medical conditions in which antiresorptive drugs are being used
3) Describe epidemiology and risk assessment of MRONJ
4) Explain the pathogenesis and offer general guidance on best practices to follow when providing routine dental care to individuals who are taking antiresorptive drugs or who have had antiresorptive therapy in the past

It is important to keep in mind that the vast majority of patients taking antiresorptives will not develop MRONJ after receiving dental treatment. Therefore, having the knowledge about these drugs and their actions and assessing patients for risk factors can decrease the development of this complication even further.

METHODS

This statement is based on a review of the current dental literature related to dental care for the patient on antiresorptive drug therapy.[1,2,3,4,5,6] PubMed searches were conducted by using the terms “antiresorptive therapy,” “medication-related osteonecrosis of the jaw,” and “bisphosphonate.”

The identified case-based reviews, narrative reviews, and clinical recommendations provided the basis for this statement. Expert opinions and best current practices were relied upon when clinical evidence was not available.

BACKGROUND

Definition and drugs

MRONJ is defined as a condition of exposed bone or bone that can be probed through an intraoral or extraoral fistula in the maxillofacial region and that has

[a]Diagnostic Sciences and Oral Medicine, College of Dentistry, University of Tennessee Health Science Center, Memphis, TN, USA.
[b]Department of Oral and Maxillofacial Diagnostic Sciences, Associate Dean of Clinics and Quality Assurance, University of Florida College of Dentistry, Gainsville, FL, USA.
Received for publication Jun 6, 2017; returned for revision Jul 26, 2018; accepted for publication Aug 17, 2018.

2212-4403/$-see front matter
http://doi.org/10.1016/j.oooo.2018.08.021

persisted for more than 8 weeks in patients who are currently on, or have had previous exposure to, antiresorptive or antiangiogenic agents and have no history of radiation therapy of the jaws.[4,5]

Bisphosphonates (BPs; e.g., alendronate, risedronate, ibandronate, pamidronate, zoledronate) and other antiresorptive agents, such as denosumab are used in a large number of applications.[1,3,4,5] The oral formulation of BPs is used to treat patients with osteoporosis, osteopenia, or other less common conditions, such as Paget disease and osteogenesis imperfecta. The most common oral medication is alendronate (Fosamax), 70 mg once a week. BPs are also used to prevent bone loss in patients with breast cancer taking aromatase inhibitors and in patients with prostate cancer to prevent bone loss from androgen deprivation therapy. The subcutaneous injection of 60 mg of denosumab every 6 months is indicated in osteoporosis. Intravenous (4 mg zoledronic acid once a month) or subcutaneous (120 mg denosumab once a month) BPs are used in the management of cancer-related bone disease, including hypercalcemia of malignancy, skeletal-related events associated with bone metastases in the context of solid tumors, such as breast, prostate, and lung cancers, and for the management of lytic lesions found in multiple myeloma. More recently, patients with giant cell tumors of bone and those with Paget disease of bone have also been included in the populations at risk for MRONJ. Denosumab is approved to treat adults with giant cell tumors of bone. Zoledronic acid and risedronate are being used to treat patients with Paget disease of bone.[1,3,4,5]

Brief epidemiology and risk factors for MRONJ

The growing number of indications for antiresorptive agents has led to the increase in the number of patients worldwide using these medications. In general, the prevalence of MRONJ is higher in patients treated with BPs via the intravenous route of administration compared with the oral route.[6]

The prevalence of MRONJ in patients with osteoporosis treated with oral/intravenous BPs has been estimated to be very low (0.001%−0.01%). The prevalence of MRONJ in patients with breast or prostate cancer as well as multiple myeloma is 2% to 4%.[4,6]

The risk of developing MRONJ depends on several factors, including therapeutic indications, types of medication, and the duration of exposure to the drugs. Other risk factors to consider are current oral issues (i.e., ill-fitting dentures, extensive decay, periodontal disease), systemic diseases (i.e., cancer, diabetes, renal dialysis), lifestyle factors (i.e., smoking, drinking, obesity), and coadministered agents (i.e., anticancer agents, corticosteroids).[3,4,5]

Pathogenesis

The underlying mechanisms of pathogenesis of MRONJ are still unclear. It is not known whether necrosis precedes or follows infection. Infection and inflammation clearly play a significant role in the development of MRONJ. Numerous hypotheses attempting to explain the unique localization of this condition, exclusively to the jaws, have been considered. These include inhibition of bone remodeling and excessive suppression of osteoclast activity by antiresorptive drugs, pre-existing periodontal or periapical disease, altered production of proinflammatory cytokines and impairment of the immune response to infection by these medications, inhibition of angiogenesis, and soft tissue toxicity caused by the antiresorptive agents.[1,2,3,4,5,6] The current opinion is that MRONJ is a multifactorial complication that can develop as a result of various pathogenic mechanisms.

CLINICAL PRACTICE STATEMENT

Over the years, important information about BPs has emerged and can help providers make treatment decisions and minimize the risk for MRONJ. It is important to state that *there is limited clinical trial−related evidence to support* the recommendations for the care of these patients. Thus, in many instances, the best evidence available and expert opinion will be used. This clinical practice statement suggests the following recommendations for providing dental care to patients on antiresorptive therapy:

1. It is ideal to treat dental disease *before* the patient is exposed to antiresorptive drugs. With the better information about MRONJ, physicians who prescribe these drugs are sending their patients to have an oral evaluation prior to starting them on antiresorptive therapy. Thus, it is important for dental clinicians to have good communication with referring physicians in the management of the patient prior to initiation of antiresorptive therapy. Although there is no strong evidence, it appears that even if patients have already started therapy with a BP, dental care can be provided to prevent the development of adverse events.
2. A thorough dental evaluation prior to initiation of antiresorptive therapy must be performed. This evaluation should include systematic examination of the oral cavity as well as radiographic assessment. Such dental factors as tooth decay, periodontal disease with alveolar bone loss, bleeding on probing and mobility, existence of unsalvageable teeth and root fragments, caries, periapical

pathology, edentulism, and denture stability must be considered. *Radiographically, bone sclerosis and thickened lamina dura do not necessarily indicate the presence of MRONJ if the patient is asymptomatic.* There is also no evidence that these findings indicate risk of MRONJ, especially if the patient does not have symptoms.

3. Patients receiving antiresorptive therapy should undergo not only a complete dental evaluation but also review of the medical history prior to any dental treatment. It is essential to know the overall medical history, including medications, medical conditions, and concomitant medical therapies. It is important to know why the patient is taking the drug, how long the patient has been in treatment, if the patient has received dental care recently, the outcome of therapy, if any previous complication has occurred in the oral cavity, and whether or not discontinuation of therapy could be considered, if deemed necessary. Discontinuation of antiresorptive therapy should be a medical decision based primarily on the risk of skeletal-related events, secondary to low bone density or to skeletal complications resulting from cancer and not on the potential risk of MRONJ. Thus, being in contact with the patient's medical team is warranted. It is important to keep in mind that the risk for MRONJ is higher when injectable formulations of antiresorptives are being used.
4. After the patient's oral health and the risk factors have been assessed and a treatment plan is completed, patients must be informed about the risks and benefits of having any type of invasive dental care. Treatment options should be clearly presented to the patient, especially treatment that may place the patient at risk of MRONJ. Additionally, the patient must be informed about the risk incurred by not undergoing the recommended dental preventive measures before initiation of antiresorptive therapy.
5. In general, routine dental care can be provided to patients on antiresorptive therapy if the dental treatment does not involve major surgical procedures. Restorative procedures, scaling and root planning, and endodontic therapy can be performed by following standard treatment protocols. *Less invasive procedures (e.g., endodontic treatment) should be recommended over more invasive procedures (extractions), whenever possible.*
6. When invasive dental care is necessary and there is a risk of MRONJ, it is recommended that informed consent be obtained from the patient. Procedures that involve direct osseous injury, such as dental implants, should be avoided in the patient with cancer receiving intravenous antiresorptive therapy. Placement of implants is possible in patients taking oral formulations, such as those for the treatment of osteoporosis or osteopenia. However, the clinician must consider if placing dental implants is the best treatment option. Informed consent should be obtained because of the possibility of implant failure over the long term if the patient continues to take an antiresorptive agent.
7. If dental extractions are indicated, they should be done per quadrant and after observing healing before moving to the next areas of the oral cavity. If the area in question is painful, is swollen, and has an active infection or a fistula is present, with active pus drainage, oral surgical procedures should be done under cover of antibiotic therapy. Clinicians must keep in mind that these signs and symptoms may indicate that necrotic bone has been already established in the area. Penicillin remains the first choice; in case of penicillin allergy, a combination of quinolones−metronidazole or erythromycin−metronidazole is a valuable alternative. Antibiotics should be started 1 day before the procedure and maintained for at least 1 week until there is evidence of effective healing. It is also recommended that the patient be placed on twice-daily chlorhexidine rinses. Certain protocols recommend the use of antibiotics anytime an invasive dental procedure is needed in a patient on an antiresorptive. We recommend that the decision on using or not using antibiotics must be evaluated on a case-by-case basis. Dental providers should keep in mind that the healing process can be slower in patients on antiresorptive therapy. Thus, patients must be carefully followed up until healing is complete. An important aspect to remember is that the majority of patients using oral antiresorptives, fortunately, will not develop ONJ. Thus, it is unacceptable to deny dental care to a patient only because the patient is on an antiresorptive. In summary, denying comprehensive oral care to patients who are in pain and have an active area of infection and sending them home with a prescription of analgesics and antibiotics is not the best management strategy. Patients in treatment with antiresorptives can receive dental care with a relatively good safety margin.

REFERENCES

1. Hellstein JW, Adler RA, Edwards B, et al. American Dental Association Council on Scientific Affairs. 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;142:1243-1251.
2. Japanese Allied Committee on Osteonecrosis of the JawYoneda T, Hagino H, Sugimoto T, et al. Antiresorptive agent-related osteonecrosis of the jaw: position paper 2017 of the Japanese allied committee on osteonecrosis of the jaw. *J Bone Miner Metab*. 2017;35:6-19.
3. Khan AA, Morrison A, Kendler DL, et al. Case-based review of osteonecrosis of the jaw (ONJ) and application of the international recommendations for management from the international task force on ONJ. *J Clin Densitom*. 2017;20:8-24.
4. Migliorati CA, Saunders D, Conlon MS, et al. Assessing the association between bisphosphonate exposure and delayed mucosal healing after tooth extraction. *J Am Dent Assoc*. 2013;144:406-414.
5. Ruggiero SL, Dodson TB, Fantasia J, et al. American association of oral and maxillofacial surgeons position paper on medication-related osteonecrosis of the jaw—2014 update. *J Oral Maxillofac Surg*. 2014;72:1938-1956.
6. Rugani P, Walter C, Kirnbauer B, Acham S, Begus-Nahrman Y, Jakse N. Prevalence of medication-related osteonecrosis of the jaw in patients with breast cancer, prostate cancer, and multiple myeloma. *Dent J*. 2016;4:32.

Reprint requests:
Juan M. Bugueno, Assistant Professor,
Diagnostic Sciences and Oral Medicine,
College of Dentistry,
University of Tennessee Health Science Center,
875 Union Avenue, Memphis,
Tennessee, 38163,
USA.
ddsjb@hotmail.com