

Bisphosphonate-Induced Osteonecrosis: Dental Considerations

Howard B. Gross, DDS, MSD*

Bisphosphonates are drugs used for the clinical treatment of osteoporosis, multiple myeloma, Paget's disease, and metastatic breast, lung, and other cancers. Bisphosphonates inhibit bone resorption by decreasing the activity of the cells that remove old, injured, and dying bone (osteoclasts).¹ Bisphosphonates are dispensed two ways: orally, for the prevention of osteoporosis and osteopenia; and intravenously, to prevent skeletal fractures in cancer patients.

Recently, bisphosphonates have been linked to osteonecrosis of the jaws, also called bisphosphonate-related osteonecrosis of the jaws (BRONJ)^{1,2} and avascular necrosis of the jaws. Patients being treated with intravenous (IV) bisphosphonates are most at risk for BRONJ. According to Marx, < 1% of oral bisphosphonates are absorbed in the gastrointestinal tract while > 50% of the IV form reaches the patient's bone.² More than 90% of the reported cases of BRONJ are related to IV bisphosphonates, while < 10% are related to the oral forms. Predisposing factors for BRONJ include periodontal diseases, dental trauma, dental surgery, and poor oral hygiene.

The clinical features of BRONJ are a significant delay in wound healing, increased tooth mobility, exposure of the alveolar bone, suppuration, and bony sequestrations. The osteonecrosis lesions are more common on the mandible in areas where the mucosa is thin and a bony prominence, such as a mandibular torus or mylohyoid ridge, exists.

Radiographs are used to make the diagnosis of BRONJ and also may be used to rule out metastatic lesions. Bone turnover, the continuous action of bone resorption and replacement, can be evaluated using a newly developed test that measures carboxy-terminal collagen crosslinks (CTx) in

serum.² With this test, clinicians can assess their patients' risk for developing BRONJ:

- CTx < 100 pg/mL is associated with a high risk for developing BRONJ;
- CTx = 100 pg/mL to 150 pg/mL indicates a moderate risk; and
- CTx > 150 pg/mL indicates minimal to no risk.

In 2005, Marx first recognized and reported nonhealing bone in the mouths of patients taking IV bisphosphonates.² Since then, several reports have been published and guidelines established to treat IV and oral bisphosphonate users. All patients should get a comprehensive dental examination, and all treatment—restorative, periodontal, and especially extractive—should be performed before the start of oral or IV bisphosphonate therapy.²

TREATMENT STRATEGIES

Wade and Suzuki³ established a modification of the staging system proposed by the American Association of Oral and Maxillofacial Surgeons (AAOMS) to include treatment strategies using the CTx serum test measurements.

Stage 0

At this stage, patients typically are asymptomatic and have been receiving bisphosphonates, either orally or intravenously, for more than 3 years.

Treating IV Bisphosphonate Patients

- Educate patients about the need to maintain excellent oral hygiene.
- Treat nonrestorable teeth without the use of dentoalveolar surgery.

Treating Oral Bisphosphonate Patients

- In addition to the above recommendations, treatment should be deferred until a CTx serum measurement is obtained.

*Diplomate of the American Board of Periodontology;
Clinical Assistant Professor, Department of Periodontology,
School of Dental Medicine, University of Pennsylvania;
Private Practice, Philadelphia, Pennsylvania

- If CTx > 150 pg/mL, dentoalveolar surgery is relatively safe.
- If CTx < 150 pg/mL, a physician should be consulted, and the patient should stop bisphosphonate therapy, typically for 3 months or until CTx > 150 pg/mL, before dentoalveolar surgery is performed.
- If emergency dental treatment is performed, take a CTx serum measurement immediately after the procedure and contact the patient's physician. It would be appropriate to have an informed consent form signed by the patient before the procedure.

Bone turnover, the continuous action of bone resorption and replacement, can be evaluated using a newly developed test that measures carboxy-terminal collagen crosslinks (CTx) in serum.

Stage 1

In this stage, patients present with asymptomatic, exposed bone and have no evidence of infection.

Treating IV Bisphosphonate Patients

- Educate the patient about the exposed bone and proper hygiene procedures.
- Chlorhexidine oral rinses and frequent follow up visits are indicated.

Treating Oral Bisphosphonate Patients

- In addition to the above recommendations, a baseline CTx serum measurement is recommended.
- Further discussion with the prescribing physician is advisable to stop the patient's use of bisphosphonates until CTx > 150 pg/mL.

Stage 2

In this stage, patients present with exposed bone, pain, infection, and erythema.

Treating IV Bisphosphonate Patients

- Antibiotic therapy consisting of penicillin, 500 mg every 6 hours, is standard.
- Prescribe chlorhexidine 12% for use twice a day.

- In refractory cases, add to the regimen metronidazole, 500 mg every 6 hours, for 7 to 10 days.

Treating Oral Bisphosphonate Patients

- The treatment is the same as above with the addition of taking a CTx serum measurement.
- Consult the patient's physician, and take the patient off bisphosphonates until CTx > 150 pg/mL.

Stage 3

At this stage, patients present with exposed necrotic bone, pain, infection, and one or more of the following: fracture, extraoral fistula, or osteolysis extending to the inferior border. In these cases, conservative methods of therapy often fail.

- Antibiotic therapy is recommended along with chlorhexidine rinses.
- Pain control is important for patient's comfort.
- Surgically debride the area. Large areas of bone may need to be resected.⁴

CONCLUSION

To prevent and treat BRONJ, practitioners need to get an accurate and up-to-date medical history on all patients, especially those on bisphosphonate therapy. The CTx serum test is a significant addition to the staging system treatment strategies already proposed by the AAOMS. Although more research and testing are needed, the CTx serum test gives dentists a biochemical marker of bone resorption, allowing an estimation of the patient's response to therapy. BRONJ is a complex issue; therefore, medical and dental professionals need to communicate with each other and stay up to date on current literature.

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