

Bisphosphonates, Oral Health, and Osteonecrosis of the Jaw



Bisphosphonates are a type of drug that limits bone-mass loss. They have proven successful in treating patients with osteoporosis, and studies have shown them to help prevent osteoporotic fractures in patients who have previously suffered fractures.¹ In recent years, though, dental researchers have noticed a correlation between the incidence of osteonecrosis of the jaw and the use of bisphosphonates. Osteonecrosis is characterized by the breaking down of bone in the body's joints as the result of reduced blood flow to those bones. For patients taking bisphosphonates, this condition often affects the jaw even though these drugs limit bone loss in other parts of the body. Osteonecrosis of the jaw usually occurs as the result of dental surgery. Although rare,² bisphosphonate-related osteonecrosis of the jaw, or BONJ, is a serious condition. Dentists should therefore understand the risks of BONJ developing in their patients who take bisphosphonates and what they can do to prevent this condition. Bisphosphonate therapy has become more popular in recent years, so dentists are more likely to treat patients at risk of developing BONJ.

How Bisphosphonates Can Lead to Osteonecrosis

Although researchers have established a correlation between bisphosphonates and the development of BONJ, the reasons why bisphosphonates lead to BONJ are not yet fully understood. Hypotheses propose a few possible links. The body directs bisphosphonates to bones with high turnover rates, such as the maxilla and mandible. They might therefore inhibit osteoclasts in these bones to the point that trauma resulting from dental surgery does not properly heal, leading to the development of osteonecrosis.³ The occurrence of osteonecrosis in patients taking bisphosphonates remains low enough that some researchers have proposed genetic causes linked to patients' skeletal homeostasis and the rate at which they metabolize bisphosphonates.⁴

Although the links between the use of bisphosphonates and the development of osteonecrosis of the jaw remain to be proven, it is known that an open bony wound with limited ability to heal is more susceptible to infection by microflora. Osteomyelitis can develop as a result, which might then become osteonecrosis. Bones that remain unexposed are not at risk of osteonecrosis developing as the result of a surgical procedure.⁵

¹ Wells GA, Cranney A, Peterson J, Boucher M, Shea B, Welch V, Coyle D, Tugwell P. Risedronate for the primary and secondary prevention of osteoporotic fractures in postmenopausal women. Cochrane Database of Systematic Reviews 2008, Issue 1. Art. No.: CD004523. DOI: 10.1002/14651858.CD004523.pub3.

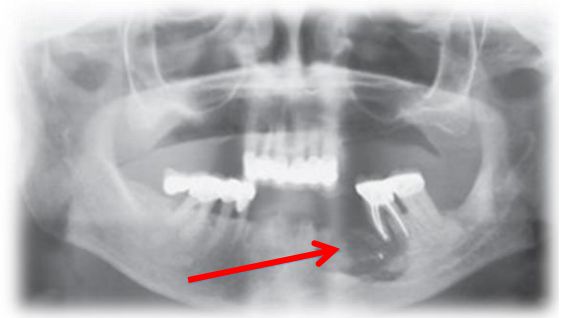
² <http://www.sdcep.org.uk/index.aspx?o=3120>

³ <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2781180/>

⁴ Ibid

⁵ <http://onlinelibrary.wiley.com/doi/10.1111/j.1834-7819.2005.tb00384.x/pdf>

Preventing Osteonecrosis of the Jaw in Patients Who Take Bisphosphonates



As researchers learn more about why bisphosphonates lead to osteonecrosis in the jaw, dentists should take steps to ensure that their patients do not develop BONJ. By assessing risk and making the right decisions regarding how to manage oral health issues, dentists can help prevent BONJ.

Risk Assessment

The risk of developing BONJ has been estimated at about 0.7 per 100,000 person-years for patients taking alendronate-based bisphosphonates. The risk is thought to be similar for patients taking other nitrogen-based oral bisphosphonates.⁶ Dose, however, affects risk. A 2007 found that 95 percent of BONJ occurred in cancer patients receiving high-dose intravenous bisphosphonates, with osteoporosis patients receiving low-dose bisphosphonate therapy comprising the remaining 5 percent of instances.⁷ The following conditions also put patients at greater risk of developing BONJ:

- Age older than 65 years
- Other conditions that affect bone
- Coagulopathy, chemotherapy, or radiotherapy
- Periodontitis
- Taking antiresorptive agents for more than two years
- Concurrent use of systemic corticosteroids or other immunosuppressants
- Smoking
- Wearing dentures
- Diabetes⁸



Dentists should develop a risk profile for patients who take bisphosphonates. Those who take them to treat osteoporosis remain at low risk. Patients at higher risk include those with the habits and conditions described above. Risk profiles help dentists determine how to treat oral health issues in ways that minimize the chance for BONJ to develop.

⁶ <http://www.jada.info/content/137/8/1144.full>

⁷ <http://press.endocrine.org/doi/full/10.1210/jc.2007-0098>

⁸ <http://www.ada.org/2594.aspx>

⁸ <http://www.sdcep.org.uk/index.aspx?o=3120>

Managing Oral Health Issues for Patients Who Take Bisphosphonates

Any procedure that impacts the maxilla or mandible bones could lead to osteonecrosis of the jaw if the patient is taking bisphosphonates. Dentists should therefore conduct a preliminary evaluation to determine the patient's level of risk for developing BONJ and then determine whether or not to perform the prescribed procedure.

Preliminary Evaluation

Many patients who take bisphosphonates are not aware that they are prescribed this specific class of medication. Dentists should therefore understand which malignant and nonmalignant conditions might be treated with bisphosphonates.⁹

| Malignant | Nonmalignant |
|-----------------------------|-----------------------------|
| Multiple myeloma | Osteoporosis |
| Breast cancer | Paget's disease |
| Prostate cancer | Osteogenesis imperfecta |
| Bony metastatic lesions | Fibrous dysplasia |
| Hypercalcemia of malignancy | Primary hyperparathyroidism |
| | Cystic Fibrosis |

Patients with these conditions should be encouraged to consult their primary-care physician to confirm whether or not their medication includes bisphosphonates.

After confirming that a patient is indeed taking bisphosphonates, dentists should assess the risk of BONJ developing using the factors listed in the previous section.

Implants

At the time of this writing, limited research has been undertaken studying the influence placing of dental implants has on the risk of developing BONJ. A couple of studies using small sample sizes have indicated that a link might exist, but the methodology could not conclusively determine the strength of this link.¹⁰

The extent to which the osteotomy site must be prepared, the extent to which implants are called for, and the amount of bone regeneration necessary could influence the likelihood of BONJ developing after placing implants. Dentists should therefore discuss these risks with their patients, review alternative treatments, and obtain written consent from patients who decide to proceed with the implant procedure.¹¹

⁹ <http://www.sdcep.org.uk/index.aspx?o=3120>

¹⁰ <http://www.ncbi.nlm.nih.gov/pubmed/23278625>

¹⁰ <http://www.ncbi.nlm.nih.gov/pubmed/23866309>

¹¹ <http://www.jada.info/content/137/8/1144.full>

Oral Surgery

Dentists should be able to proceed with oral surgery on low-risk patients, though these patients should also be aware that a risk does exist and sign an informed consent if they choose to proceed with the surgery. Low-risk patients who require invasive surgery should be dentally fit for the procedure. Dentists should address any periodontal or dental diseases and adjust or replace poorly fitting dentures. Patients should practice good oral hygiene, cease smoking, limit alcohol intake, and reduce the amount of sugar in their diet. Dentists should follow up four weeks after the procedure. If bone remains exposed, the patient should be referred to a specialist in oral or maxillofacial surgery.

Dentists should avoid performing oral surgery on patients at a high risk for developing BONJ. These patients should instead consult with a specialist in oral or maxillofacial surgery. Temporarily reducing or suspending a bisphosphonates regimen does not reduce the risk of the patient developing BONJ because bisphosphonates remain in the skeletal tissue for years.¹²

Restorative Procedures, Prosthodontics, and Endodontics

No evidence exists linking restorative procedures and prosthodontics with the development of BONJ, so dentists can undertake these treatments without concern. An endodontic procedure to restore the tooth should also be fine so long as it does not require manipulation beyond the apex. Paraendodontic surgery should follow the same guidelines as oral surgery.¹³

Diagnosing and Treating BONJ

Diagnosing BONJ relies mainly on observation. MRI can show the extent of the necrosis, but there are presently no tools that can identify the condition before it sets in. Once dentists have diagnosed BONJ, treatment focuses on healing or stabilizing the lesions and preventing further infection.

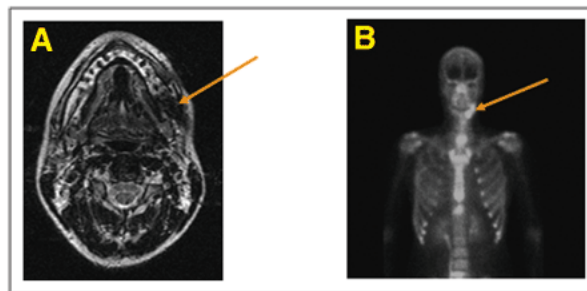


Figure 3: Advanced Osteonecrosis of the Jaw—This often shows lytic changes or "mottled bone" on MRI scans (A). Bone scan may reveal increased uptake in the area of osteonecrosis of the jaw (B).

Symptoms

Exposed, necrotic bone in the maxillofacial region that has remained for more than eight weeks is the primary symptom of BONJ. The patient must also have or be currently undergoing treatment with a bisphosphonate with no history of radiation therapy to the jaws. Exposed maxillofacial bone for less than

¹² <http://www.sdcep.org.uk/index.aspx?o=3120>

¹³ <http://www.jada.info/content/137/8/1144.full>

eight weeks constitutes a suspected case of BONJ with these two caveats also in place.¹⁴

BONJ might be present for months or years before patients begin to experience symptoms related to it. Examination of the area should reveal inflammation of the tissues surrounding the bone. Pain, a loose tooth, mucosal swelling, erythema, and ulceration might also indicate the onset of BONJ before it becomes visually discernible. Patients with BONJ in the maxillary bone might develop chronic maxillary sinusitis. BONJ lesions tend to occur more often in the mandible than the maxilla at a ratio of 2:1. Pus discharge at the site of BONJ lesions indicates a secondary infection.¹⁵



Stages

American Association of Oral and Maxillofacial Surgeons describes the following symptoms associated with the three stages of osteonecrosis of the jaw:

| Stage | Symptoms |
|-------|--|
| 1 | Exposed bone, but no pain or infection |
| 2 | Suppuration or infection and formation of intraoral sinus tract; possibly painful |
| 3 | Exposed necrotic bone beyond the alveolar bone, extraoral fistula, osteolysis extending to the inferior border or oroantral communication, pathological fracture |

AAOMS has also proposed a Stage 0 in which exposed bone is absent, but pain and loose teeth not associated with periodontal disease and intra-oral fistula not resulting from pulp necrosis are present.¹⁶

Treatment

Pain reduction and limiting secondary infection remain the primary goals of treatment for osteonecrosis of the jaw. Dentists can also remove necrotic debris if the patient's BONJ reaches Stage 3. Patients should

¹⁴ <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2781180/>

¹⁵ Ibid

¹⁶ <http://www.jada.info/content/140/7/864.full>

still ensure they intake adequate nutrients even if pain makes chewing difficult.¹⁷ Antimicrobial rinses and antibiotic therapy have been shown to resolve or stabilize lesions in up to 90 percent of Stage 3 BONJ cases.¹⁸



Conclusion

BONJ remains a low-risk condition, but bisphosphonate therapy continues to become more prevalent among osteoporosis and cancer patients. Dentists should know whether or not their patients take or have taken bisphosphonates and how much risk of developing BONJ exists for these patients if they require an oral health procedure. Having patients who take or have taken bisphosphonates sign an informed consent before agreeing to the procedure remains an important part of the protocol, and dentists should follow important steps to minimize the risk of the patient developing BONJ as the result of an oral health procedure. As research reveals more about the connection between bisphosphonates and osteonecrosis of the jaw, perhaps the dental community will further understand how to prevent and treat BONJ.

¹⁷ <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2464788/>

¹⁸ <http://www.jada.info/content/140/7/864.full>