Bisphosphonate Medications and Oral Surgery

As more is learned about the ramifications of long-term use of oral and intravenous bisphosphonate medications, an association between bisphosphonate medications, oral surgery and development of osteonecrosis of the jaw (ONJ) is also becoming more apparent. This condition is usually referred to as bisphosphonate-related osteonecrosis of the jaw (BRONJ).

Bisphosphonate Medications

Bisphosphonates are a classification of medications typically used to treat osteoporosis, Paget’s Disease, bone metastasis and some cancer-related conditions. They can be taken orally or administered intravenously (depending on the indication for treatment). The oral bisphosphonate medications most commonly seen in dentistry and oral and maxillofacial surgery are Fosamax (Alendronate), Actonel (Risedronate) and Boniva (Ibandronate). Reclast (Zolendronic Acid) is a bisphosphonate infusion that has also become more common.

Characteristics of Bisphosphonate Related Osteonecrosis of the Jaw (BRONJ)

Bisphosphonate-related osteonecrosis of the jaw (BRONJ) is characterized by delayed healing or non-healing of the bone and soft tissue following an oral surgery procedure such as tooth extraction, dental implant placement, periapical surgery and some periodontal surgeries. It may also occur spontaneously without having had any recent surgery in the area. The delayed healing or non-healing condition is typically considered to be BRONJ when the following three conditions exist:

- Current or previous history of treatment with a bisphosphonate medication;
- Exposed bone in the maxillofacial region that has persisted for more than eight weeks;
- No history of radiation therapy to the jaws.

BRONJ lesions are more commonly found in the mandible, but also occur in the maxilla. Studies have indicated that patients with a current or previous history of treatment with intravenous bisphosphonates may be at a greater risk of developing BRONJ than those that have used or are using oral bisphosphonates. That is most likely due to the fact that intravenous bisphosphonate dosages are more potent. Additionally, there seems to be a correlation between the duration of a patient’s exposure to bisphosphonates and development of BRONJ.

Management Strategies for Bisphosphonate Patients
It is recommended that before beginning treatment with IV bisphosphonates, patients undergo a thorough oral examination, have all unsalvageable teeth removed, all necessary invasive dental procedures performed and achieve optimal periodontal health. Findings suggest that, while the risk of BRONJ is not eliminated, it is greatly reduced in patients that have all necessary dental work done prior to initiating IV bisphosphonate treatment. The risk of development of BRONJ associated with oral bisphosphonates, though small, appears to increase when the duration of treatment exceeds three years. This time frame may be shortened in the presence of other factors, such as chronic corticosteroid use. If systemic conditions permit, a patient taking oral bisphosphonates for a period of three years or greater should discontinue the medication for a period of three months prior to and three months following oral surgery or invasive dental procedures, in order to lower the risk of BRONJ. No alteration of bisphosphonate treatment is necessary for patients taking oral bisphosphonate medications for fewer than three years, unless there has also been concomitant corticosteroid use. Oral surgery and dental treatment for patients currently receiving IV bisphosphonates or with a recent history of IV bisphosphonate therapy should be carefully prioritized with the input of the physician administering the IV bisphosphonate care. Elective oral surgery and invasive dental procedures in asymptomatic patients currently receiving IV bisphosphonate therapy should be avoided.

### BRONJ Staging and Treatment Strategies

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<th>BRONJ† Staging</th>
<th>Treatment Strategies‡</th>
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| **At risk category** No apparent necrotic bone in patients who have been treated with either oral or IV bisphosphonates | - No treatment indicated  
- Patient education |
| **Stage 0** No clinical evidence of necrotic bone, but non-specific clinical findings and symptoms | - Systemic management, including the use of pain medication and antibiotics |
| **Stage 1** Exposed and necrotic bone in patients who are asymptomatic and have no evidence of infection | - Antibacterial mouth rinse  
- Clinical follow-up on a quarterly basis  
- Patient education and review of indications for continued bisphosphonate therapy |
| **Stage 2** Exposed and necrotic bone associated with infection as evidenced by pain and erythema in the region of the exposed bone with or without purulent drainage | - Symptomatic treatment with oral antibiotics  
- Oral antibacterial mouth rinse  
- Pain control  
- Superficial debridement to relieve soft tissue irritation |
**Stage 3** Exposed and necrotic bone in patients with pain, infection, and one or more of the following: exposed and necrotic bone extending beyond the region of alveolar bone, (i.e., inferior border and ramus in the mandible, maxillary sinus and zygoma in the maxilla) resulting in pathologic fracture, extra-oral fistula, oral antral/oral nasal communication, or osteolysis extending to the inferior border of the mandible or sinus floor

- Antibacterial mouth rinse
- Antibiotic therapy and pain control
- Surgical debridement/resection for longer term palliation of infection and pain

† Exposed bone in the maxillofacial region without resolution in 8-12 weeks in persons treated with a bisphosphonate who have not received radiation therapy to the jaws.
‡ Regardless of the disease stage, mobile segments of bony sequestrum should be removed without exposing uninvolved bone. The extraction of symptomatic teeth within exposed, necrotic bone should be considered since it is unlikely that the extraction will exacerbate the established necrotic process.
‡ Discontinuation of the IV bisphosphonates shows no short-term benefit. However, *if systemic conditions permit*, long-term discontinuation may be beneficial in stabilizing established sites of BRONJ, reducing the risk of new site development, and reducing clinical symptoms. The risks and benefits of continuing bisphosphonate therapy should be made only by the treating oncologist in consultation with the OMS and the patient.
‡ Discontinuation of oral bisphosphonate therapy in patients with BRONJ has been associated with gradual improvement in clinical disease. Discontinuation of oral bisphosphonates for 6-12 months may result in either spontaneous sequestration or resolution following debridement surgery. *If systemic conditions permit*, modification or cessation of oral bisphosphonate therapy should be done in consultation with the treating physician and the patient.

**Future Research**

The National Institute of Health has provided funding for research into many aspects of BRONJ. At this time, research remains ongoing and future research is planned. Our office will continue to stay abreast of the most current BRONJ information in order to continually serve our patients in the safest manner possible.

**References:**