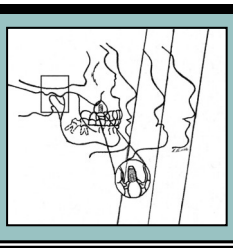

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Bisphosphonate-Related Osteonecrosis of the Jaw (BRONJ)

excerpts from a Position Paper from AAOMS

Intravenous bisphosphonates are primarily used and effective in the treatment and management of cancer-related conditions. These include hypercalcemia of malignancy, skeletal- related events associated with bone metastases in the context of solid tumors such as breast cancer, prostate cancer and lung cancer, and in the management of lytic lesions in the setting of multiple myeloma. The IV bisphosphonates are effective in preventing and reducing hypercalcemia, stabilizing bony pathology and preventing fractures in the context of skeletal involvement. While they have not been shown to improve cancer-specific survival, they have had a significant impact on the quality of life for patients with advanced cancer that involves the skeletal system. Before 2001, pamidronate (Aredia) was the only drug approved in the United States for treatment of metastatic bone disease. In 2002, zoledronic acid (Zometa) was approved for this indication by the US FDA.

Oral bisphosphonates are approved to treat osteoporosis and are frequently used to treat osteopenia as well. They are used for a variety of less common conditions such as Paget's disease of the bone, and osteogenesis imperfecta of childhood. By far the most prevalent and common indication, however, is osteoporosis. Osteoporosis may arise in the context of other diseases such as inflammatory bowel disease or primary biliary cirrhosis, as the result of medications, most commonly steroids, or as a consequence of postmenopausal aging. Whatever the underlying etiology of the osteoporosis, bisphosphonates may play a role, perhaps in conjunction with calcium and vitamin D, in its management.

In 2003-04, oral and maxillofacial surgeons were the first clinicians to recognize and report cases of non-healing exposed, necrotic bone in the maxillofacial region in patients treated with IV bisphosphonates. Since these initial reports, several case series and reviews have been published. In September 2004, Novartis, the manufacturer of the IV bisphosphonate pamidronate (Aredia) and zoledronic acid (Zometa), notified healthcare professionals of additions to the labeling of these products, which provided cautionary language related to the development of osteonecrosis of the jaws. This was followed in 2005 by a broader drug class warning of this complication for all bisphosphonates including oral preparations.

BRONJ Case Definition

To distinguish BRONJ from other delayed healing conditions, the following working definition of BRONJ has been adopted by the AAOMS:

Patients may be considered to have BRONJ if all of the following three characteristics are present:

1. *Current or previous treatment with a bisphosphonate;*
2. *Exposed, necrotic bone in the maxillofacial region that has persisted for more than eight weeks; and*
3. *No history of radiation therapy to the jaws.*

continued on reverse

Dental Fun Fact

DID YOU KNOW THAT...

IN THE EARLY MIDDLE AGES IN EUROPE, MONKS PRACTICED MEDICINE, SURGERY, AND DENTISTRY. IN THE 12TH CENTURY, A SERIES OF PAPAL EDICTS PROHIBITED MONKS FROM PERFORMING ANY TYPE OF SURGERY, BLOODLETTING, OR TOOTH EXTRACTION. BARBERS, WHO HAD OFTEN ASSISTED MONKS, ASSUMED THE MONKS' SURGICAL DUTIES.

- ADA

News You Can Use

Cannabis smoking may be a risk factor for periodontal disease, according to a prospective cohort study in *JAMA*.

The study, conducted in New Zealand, followed about 900 adults from age 18 to 32. After controlling for tobacco use and other risk factors, the researchers found that by age 32, heavy cannabis users (41 or more times in the previous year) were three times more likely to have periodontal disease (at least one site with 5 mm or greater combined attachment loss) than those who'd never used cannabis.

The authors say caregivers "should take steps to raise awareness of the strong probability that regular cannabis users may be doing damage to the tissues that support their teeth." An editorialist notes that the study adds to evidence that destructive periodontal disease occurs at earlier ages than previously thought.

Bisphosphonate-Related Osteonecrosis of the Jaw

It is important to understand that patients at risk for BRONJ or with established BRONJ can also present with other common clinical conditions not to be confused with BRONJ. Commonly misdiagnosed conditions include, but are not limited to, alveolar osteitis, sinusitis, gingivitis/periodontitis, caries, periapical pathology and TMJ disorders.

Estimated Incidence and Factors Associated with Development of BRONJ

IV bisphosphonates and incidence of BRONJ

The clinical efficacy of IV bisphosphonates for the treatment of hypercalcemia and bone metastases is well established. Based on these studies, estimates of the cumulative incidence of BRONJ range from 0.8%-12%.

Oral Bisphosphonates and incidence of BRONJ

The clinical efficacy of oral bisphosphonates for the treatment of osteopenia/osteoporosis is well established and is reflected in the fact that over 190 million oral bisphosphonates prescriptions have been dispensed worldwide. Based on data from the manufacturer of alendronate (Merck), the incidence of BRONJ was calculated to be 0.7/100,000 persons/years of exposure. While this is the best available data to date, there may be serious underreporting and, as noted above, none confirmed.

Based on the above cited data, the risk of BRONJ for patients receiving IV bisphosphonates appears to be significantly greater than the risk for patients receiving oral bisphosphonates.

Risk Factors

Risk factors for the development of BRONJ can be grouped as drug-related, local risk factors and demographic/systemic factors.

I. Drug - related risk factors include:

A. Potency of the particular bisphosphonate: zoledronate (Zometa) is more potent than pamidronate (Aredia) and pamidronate (Aredia) is more potent than the oral bisphosphonates; the IV route of administration results in a greater drug exposure than the oral route.

B. Duration of therapy: longer duration appears to be associated with increased risk.

II. Local risk factors include:

A. Dentoalveolar surgery, including, but not limited to
1. Extractions
2. Dental implant placement
3. Periapical surgery
4. Periodontal surgery involving osseous injury

Patients receiving IV bisphosphonates and undergoing dentoalveolar surgery are at least seven times more likely to develop BRONJ than patients who are not having dentoalveolar surgery.

B. Local anatomy
1. Mandible
   a. Lingual tori
   b. Mylohyoid ridge
2. Maxilla
   a. Palatal tori

It has been observed that lesions are found more commonly in the mandible than the maxilla (2:1 ratio) and more commonly in areas with thin mucosa overlying bony prominences such as tori, bony exostoses and the mylohyoid ridge.

C. Concomitant oral disease

Patients with a history of inflammatory dental disease, e.g., periodontal and dental abscesses, are at a seven-fold increased risk for developing BRONJ.

III. Demographic and systemic factors

A. Age: With each passing decade, there is a 9% in creased risk for BRONJ in multiple myeloma patients treated with IV bisphosphonates.

B. Race: Caucasian

C. Cancer diagnosis: Risk is greater for patients with multiple myeloma than for patients with breast cancer; and those with breast cancer have a greater risk than those with other cancers.

D. Osteopenia/osteoporosis diagnosis concurrent with cancer diagnosis.

The following factors are thought to be risk factors for BRONJ:

1. Corticosteroid therapy
2. Diabetes
3. Smoking
4. Alcohol use
5. Poor oral hygiene
6. Chemotherapeutic drugs

For more information, please visit www.aaoms.org.

BRONJ Staging	Treatment Strategies
Stage 1 Exposed/necrotic bone in patients who are asymptomatic 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/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 broad-spectrum oral antibiotics, e.g. penicillin, cephalexin, clindamycin, or 1st generation fluoroquinolone - Oral antibacterial mouth rinse - Pain control - Only superficial debridements to relieve soft tissue irritation
Stage 3 Exposed/necrotic bone in patients with pain, infection, and one or more of the following: pathologic fracture, extra-oral fistula, or osteolysis extending to the inferior border	- Antibacterial mouth rinse - Antibiotic therapy and pain control - Surgical debridement/resection for longer term palliation of infection and pain

"We must remember that one determined person can make a significant difference, and that a small group of determined people can change the course of history." Sonia Johnson