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FAST FACTS AND CONCEPTS #196

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Introduction Osteonecrosis of the jaw (ONJ) is a potentially devastating complication associated with bisphosphonate therapy. In cancer, bisphosphonates are indicated for the treatment of malignant hypercalcemia and to prevent skeletal complications including pain, need for radiation therapy, and fractures in those with bone metastases (see *Fast Fact* #113). Drugs approved for use in cancer in the US include pamidronate and zoledronic acid.

Epidemiology The reported incidence of ONJ in patients on bisphosphonates ranges from 1-11% in different studies, varying by type of bisphosphonate, patient population, and time-frame of surveillance. ONJ is mostly a disease of long-term intravenous bisphosphonate treatment; risk of developing ONJ depends on the duration and dose of therapy. There is a cumulative risk of ONJ of ~3% after 2 years and up to 11% after 4 years of exposure. Almost all (~94%) cases of ONJ occur in patients receiving intravenous bisphosphonate as compared to oral bisphosphonates. Other risk factors include:

- Prior radiation treatment to the head and neck.
- Periodontal disease or poorly fitting dentures.
- Dental procedures involving bone surgery.
- Caucasian race and age greater than 65 years.

Diagnosis Symptoms of ONJ are localized pain, swelling, loosening of teeth, exposed bone, non-healing oral ulcers, purulent gingival discharge, and numbness or heaviness of the jaw. Signs of ONJ include local swelling, exposed bone on examination, and a radio-dense bony appearance on imaging studies. Differentiating ONJ from other oral diseases (alveolar osteitis, periodontitis, dental caries, sinusitis, osteonecrosis from radiation therapy, and recurrent or metastatic cancer) can be difficult, and *early involvement of an oral surgeon is important*. If ONJ is suspected, imaging studies can help to rule out cysts, impacted teeth, or metastatic disease; however radiographic changes may be absent during early stages. A biopsy should be performed if metastatic cancer is suspected.

Prevention All patients should have a complete dental examination with removal of any unsalvageable teeth prior to initiating bisphosphonate therapy. Patients should be well informed of the importance of good oral hygiene, regular dental follow-ups, and the avoidance of invasive dental procedures while on bisphosphonates. *Instruct patients to let their dentists know they have received a bisphosphonate*. Although empiric, stopping bisphosphonates for ~3 months before and after invasive dental procedures such as extractions has been recommended.

Treatment Asymptomatic patients with exposed/necrotic bone can be managed with antibacterial mouth wash (e.g. chlorhexidine 0.12%) and followed up quarterly. Superficial debridement to relieve soft tissue irritation can also be performed. Oral antibiotics, in addition to antibacterial mouth washes, are indicated if there are signs of local infection. Severe ONJ manifested as a pathologic mandible fracture, extraoral fistulae, and/or osteolysis extending to the inferior border of the mandible necessitates surgical debridement. Pain management is often very challenging for these patients and best managed through an interdisciplinary approach including oral surgeons, pain management experts, psychologists, and others.

There is no consensus about when it is appropriate to stop bisphosphonates, particularly with early ONJ. Brief interruption of therapy offers no benefit. Clinicians need to evaluate the benefits of initiating and continuing the

use of bisphosphonates on an individual basis.

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