OSTEONECROSIS OF THE JAW

Overview

Reports of bisphosphonate-associated osteonecrosis of the jaw (BON) associated with the use of Zometa (zolendronic acid) and Aredia (pamidronate) began to surface in 2003. The majority of reported cases have been associated with dental procedures such as tooth extraction; however, less commonly BON appears to occur spontaneously in patients taking these drugs[1]. Zolendronic acid and pamidronate are intravenous (i.v.) bisphosphonates used to reduce bone pain, hypercalcemia and skeletal complications in patients with multiple myeloma, breast, lung and other cancers and Paget's disease of bone.

Several cases of BON have also been associated with the use of the oral bisphosphonates, Fosamax (alendronate), Actonel (risedronate) and Boniva (ibandronate), for the treatment of osteoporosis; however, it is not clear if these patients had other conditions that would put them at risk for developing BON.[2]

The table below lists all oral and i.v. bisphosphonates currently on the market in the U.S.

Orally Administered Bisphosphonates

Brand Name	Manufacturer	Generic Name
Actonel	Procter & Gamble Pharmaceuticals	risedronate
Boniva	Roche Laboratories	ibandronate
Fosamax	Merck & Co.	alendronate
Fosamax Plus D	Merck & Co.	alendronate
Skelid	Sanofi Pharmaceuticals	tiludronate
Didronel	Procter & Gamble Pharmaceuticals	etidronate

Intravenously Administered Bisphosphonates

Brand Name	Manufacturer	Generic Name
Aredia	Novartis	pamidronate
Zometa	Novartis	zolendronic acid
Bonefos	Schering AG	clodronate

Clinical Presentation

The typical clinical presentation of BON includes pain, soft-tissue swelling and infection, loosening of teeth, drainage, and exposed bone[3]. These symptoms may occur spontaneously, or more commonly, at the site of previous tooth extraction. Patients may also present with feelings of numbness, heaviness and dysesthesias of the jaw. However, BON may remain asymptomatic for weeks or months, and may only become evident after finding exposed bone in the jaw.

Dental Management

It is important to understand that, based on the information currently available, the risk for

developing BON is much higher for cancer patients on i.v. bisphosphonate therapy than the risk for patients on oral bisphosphonate therapy. Therefore, there are different recommendations for dental management of these patients.

For patients on oral bisphosphonate therapy
The risk of developing BON in patients on oral bisphosphonate therapy appears to be very low;[4] however, though the risk is small, currently millions of patients take these drugs. Therefore, recommendations for dental management of patients on oral bisphosphonate therapy | PDF file/125k were developed by an expert panel assembled by the ADA's Council on Scientific Affairs.[5] These panel recommendations focus on conservative surgical procedures, proper sterile technique, appropriate use of oral disinfectants and the principals of effective antibiotic therapy. There is currently no data from clinical trials evaluating dental management of patients on oral bisphosphonate therapy, and therefore, these recommendations are based on expert opinion only. A comprehensive oral evaluation is recommended for all patients about to begin therapy with oral bisphosphonates (or as soon as possible after beginning therapy).These recommendations do not address treatment of patients on i.v. bisphosphonate therapy or patients with BON. Refer to the information below regarding their treatment.

For patients on i.v. bisphosphonate therapy
It is important for dentists to be aware that while on treatment, invasive dental procedures should be avoided in patients receiving i.v. bisphosphonates, if possible. Dentists need to exercise their professional judgment, perhaps after consultation with the patient's physician, in deciding whether invasive treatment is needed under the particular clinical situations.

The prescribing information for these drugs recommends that cancer patients:

- Receive a dental examination prior to initiating therapy with intravenous bisphosphonates (Aredia and Zometa); and
- Avoid invasive dental procedures while receiving bisphosphonate treatment. For patients who develop osteonecrosis of the jaw while on bisphosphonate therapy, dental surgery may exacerbate the condition. Clinical judgment by the treating physician should guide the management plan of each patient based on an individual benefit/risk assessment.

Among tools useful to the dentist is a patient's medical history, including medications. Dentists should be aware that patients may not relay information about receiving i.v. bisphosphonates, because these drugs are administered in oncology wards. Therefore, patients with a history of multiple myeloma, metastatic cancer, Paget's disease and osteoporosis may need to be questioned about receiving i.v. bisphosphonates. In addition, it may be important to know of any history of i.v. bisphosphonate administration, because these drugs have a long half-life (years).[6]

An expert panel convened by Novartis Pharmaceuticals Corporation (the manufacturer of Zometa and Aredia) in 2004, made the following recommendations for prevention, diagnosis and treatment of osteonecrosis of the jaw in patients on i.v. bisphosphonate therapy:[3,7]

- Patients should be educated on maintaining excellent oral hygiene to reduce the risk of infection.
- Dentists should check and adjust removable dentures to avoid soft-tissue injury.
- Routine dental cleanings should be performed with care not to inflict any soft-tissue injury.
- Dental infections should be managed aggressively and nonsurgically (when possible).
- Endodontic therapy is preferable to extractions; and, when necessary, coronal amputation with root canal therapy on retained roots to avoid the need for extraction.

For patients with BON
Recommendations for the treatment of patients with BON have been published[7] and are posted on the Web site for the *Journal of Oncology Practice*.

Obtaining Informed Consent

- Obtaining Informed Consent Relating to Risks Associated with Oral Bisphosphonate Use | PDF file/27k

This document is designed to provide general information to patients and to guide dentists in fully and clearly explaining risks, benefits and treatment alternatives to patients. However, this document contains only a general discussion of issues surrounding treating patients taking oral bisphosphonates. It does not contain the specific information likely required to be in an informed consent form. The requirements for informed consent forms may vary from one jurisdiction to another. Dentists should consult with an attorney to develop a form which will be effective in a particular state.

Endnotes

1. Woo S-B, Hande K, Richardson PG. Osteonecrosis of the jaw and bisphosphonates. N Engl J Med 2005;353:100.
2. Ruggiero SL, Mehrotra B, Rosenberg TJ, Engroff SL. Osteonecrosis of the jaws associated with the use of bisphosphonates: A review of 63 cases. J Oral Maxillofac Surg 2004;62:527-34.
3. Expert Panel Recommendations for the Prevention, Diagnosis, and Treatment of Osteonecrosis of the Jaws: June 2004 | PDF file/56k.
4. Migliorati CA, Casiglia J, Epstein J, Jacobsen PL, Siegel MA, Woo S-B. Managing the care of patients with bisphosphonate-associated osteonecrosis: An American Academy of Oral Medicine position paper. JADA 2005;136:1658-68.
5. ADA Council on Scientific Affairs. Expert Panel Recommendations: Dental Management of Patients on Oral Bisphosphonate Therapy. June 2006 . | PDF file/125k
6. Ott SM. Long-term safety of bisphosphonates. J Clin Endocrinol Metab 2005;90:1897-9.
7. Ruggiero S, Gralow J, Marx RE, Hoff AO, Schubert MM, Huryn JM, Toth B, Damato K, Valero V. Practical Guidelines for the Prevention, Diagnosis, and Treatment of Osteonecrosis of the Jaw in Patients With Cancer. J Oncol Prac 2006;2:7-14.