

THEMATIC ABSTRACT REVIEW

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Editors' note: Dr Clark Stanford, who was appointed the editor of this section earlier this year, has designed a new format for the presentation of abstracts of important studies from the literature. Beginning with this issue, abstracts of the latest research on a particular topic will be presented by Dr Stanford and associates along with a brief summary of the current state of that field. We hope you enjoy this new format.

Bisphosphonates, Osteonecrosis, and Implant Outcomes

The use of intravenous bisphosphonates has been a great asset in the management of bone loss associated with bone-related tumors, such as multiple myeloma and hypercalcemia related to breast and prostate tumors. The less potent oral forms have been used to manage osteopenia and osteoporosis. Given the number of case reports presented recently in the literature regarding the formation of necrotic lesions in the jaws (bisphosphonate-related osteonecrosis [BON]) in patients on intravenous bisphosphonates and the recent anecdotal reports of BON in patients after long-term use of the oral forms, this critically important topic was selected as the theme for this inaugural edition of "Thematic Abstract Review," JOMI's newly revamped literature review section. The studies cited below were identified by a Medline search using the terms *disphosphonates* and *osteonecrosis* and by a hand search of the literature for the period of 2005–2006 using inclusion/exclusion criteria. The NLM/MESH heading was used to find systematic reviews, consensus statements, or high-level evidence based randomized controlled trials or cohort studies. Individual case reports were excluded. Hand searching was used to find systematic consensus panel discussions and consensus statements derived from dis-

closed panels of experts on the topic. Significant clinical issues to consider when evaluating the relative risks for implant therapy include past history of potency of drug, dose and duration of exposure, confounding medications (eg, corticosteroids) and the presence of systemic conditions that could compromise wound healing (eg, diabetes mellitus). The most controversial questions appear to concern use of implant therapy in patients on the oral forms of bisphosphonate (eg, alendronate, ibandronate, risedronate). Each of these has different potencies and potentially may have a different clinical impact based on the medical history, current medications, and related confounding variables affecting the patient. Long-term monitoring of current restored implant patients and caution in proceeding with implant therapy appears to be the current consensus. Large flap procedures and grafts associated with implant procedures may increase the potential for complications. Proceeding in a quadrant-by-quadrant manner may minimize the risk for and degree of complications and multifocal diseases. If implant procedures are elected, chlorhexidine rinses may be both preventative and therapeutic in either short- or long-term application.

Dental management of patients receiving oral bisphosphonate therapy: Expert panel recommendations. *J Am Dent Assoc* 2006;137:1144–1150.

In light of the uncertainty surrounding the incidence of bisphosphonate-associated osteonecrosis of the jaw (BON) and concomitant risk factors, dentists have questioned how to manage the care of patients receiving oral bisphosphonate therapy. Expert panelists were selected by the American Dental Association Council on Scientific Affairs on the basis of their expertise in the relevant subject matter and on their respective dental or medical specialties, and the panel was tasked with developing guidance for dentists treating these patients. No data are available from clinical trials evaluating dental management of the care of patients receiving oral bisphosphonate therapy; therefore, these recommendations are based on a thorough review of the available literature relating to bisphosphonate use and osteonecrosis of the jaw. After reviewing the literature, the panel developed these recommendations based on their expert opinion. These panel recommendations focus on conservative surgical procedures, proper sterile technique, appropriate use of oral disinfectants, and the principles of effective antibiotic therapy. The recommendations are a resource for dentists to use in their practice, in addition to the dentist's own professional judgment, the information available in the dental and medical literature, and information from the patient's treating physician. The recommendations must be balanced with the practitioner's professional judgment and the individual patient's preferences and needs.

Reprints available from: http://www.ada.org/prof/resources/topics/topics_osteonecrosis_recommendations.pdf

JEFFCOAT M. Safety of oral bisphosphonates: Controlled studies on alveolar bone. *Int J Oral Maxillofac Implants* 2006;21:349–353.

Osteoporosis and osteopenia are characterized by reductions in bone mass and may lead to skeletal fragility and fracture. The latest generation of oral bisphosphonate drugs, including alendronate and risendronate, has been approved for the prevention and treatment of osteoporosis. These medications are chemically absorbed into bone, decreasing osteoclast number and activity and thereby decreasing bone resorption. The purpose of this report is to present safety data from 2 controlled studies in patients receiving oral bisphosphonates. Study 1 tested the effect of alendronate, an inhibitor of bone resorption, on alveolar bone. A total of 335 patients (162 men and 173 women, aged 30 to 79 years) with moderate or severe periodontal disease were randomized to either placebo or 70 mg alendronate once weekly. Alveolar bone height and safety were assessed over a 2-year period. Study 2 was a longitudinal single-blind controlled design comparing implant success in 50 consecutive patients (210 implants), 25 patients who received bisphosphonate therapy and 25 age-matched control subjects. Implant

success and safety, including incidence of osteonecrosis of the jaws (ONJ), was blindly assessed for at least 3 years. In study 1, no cases of ONJ were observed in either treatment group. Furthermore, a trend toward lower incidences of infection and tooth loss was observed in the alendronate group. In study 2, no cases of ONJ were observed in either group, and implant success was greater than 99% in both groups. On the basis of 2 controlled clinical studies, oral bisphosphonate usage was not associated with occurrence of ONJ.

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Woo SB, HELLSTEIN JW, KALMAR JR. Systematic review: Bisphosphonates and osteonecrosis of the jaws. *Ann Intern Med* 2006;144:753–761 [erratum 2006; 145:235].

Osteonecrosis of the jaws is a recently described adverse side effect of bisphosphonate therapy. Patients with multiple myeloma and metastatic carcinoma to the skeleton who are receiving intravenous, nitrogen-containing bisphosphonates are at greatest risk for osteonecrosis of the jaws; these patients represent 94% of published cases. The mandible is more commonly affected than the maxilla (2:1 ratio), and 60% of cases are preceded by a dental surgical procedure. Oversuppression of bone turnover is probably the primary mechanism for the development of this condition, although there may be contributing comorbid factors. All sites of potential jaw infection should be eliminated before bisphosphonate therapy is initiated in these patients to reduce the necessity of subsequent den-toalveolar surgery. Conservative debridement of necrotic bone, pain control, infection management, use of antimicrobial oral rinses, and withdrawal of bisphosphonates are preferable to aggressive surgical measures for treating this condition. The degree of risk for osteonecrosis in patients taking oral bisphosphonates, such as alendronate, for osteoporosis is uncertain and warrants careful monitoring.

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HELLSTEIN JW, MAREK CL. Bisphosphonate-induced osteochemonecrosis of the jaws: An ounce of prevention may be worth a pound of cure. *Spec Care Dentist* 2006;26:8–12.

Patient exposure to bisphosphonate drugs for the management of hypercalcemia of malignancy, osteolytic lesions of metastatic cancer and osteoporosis has led to increasing reports of osteochemonecrosis of the jaws (bis-phossy jaw). This serious and debilitating condition requires dental practitioners to be alert for signs and symptoms of this syndrome. Thus far, nitrogen-containing bisphosphonates have been implicated as a causative agent. While only a small fraction of patients who have

taken these agents will develop osteochemonecrosis, it seems that patients who have received intravenous bisphosphonates are at greater risk than those who have taken oral agents. Tooth extractions are the most frequently reported predisposing dental procedure. While appropriate management strategies for patients with osteochemonecrosis of the jaws are evolving, the authors suggest rational preventive protocols and therapies based upon current experience and knowledge. These recommendations may change over time as the profession gains more experience in managing these patients.

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RUGGIER S, GRALOW J, MARX RE, ET AL. Practical guidelines for the prevention, diagnosis, and treatment of osteonecrosis of the jaw in patients with cancer. *J Oncol Pract* 2006;2(1):7-14.

This article discusses osteonecrosis of the jaw (ONJ) and offers health-care professionals practical guidelines and recommendations for the prevention, diagnosis, and management of ONJ in cancer patients receiving bisphosphonate treatment. A panel of experts representing oral and maxillofacial surgery, oral medicine, endocrinology, and medical oncology was convened to review the literature and clinical evidence, identify risk factors for ONJ, and develop clinical guidelines for the prevention, early diagnosis, and multidisciplinary treatment of ONJ in patients

with cancer. The guidelines are based on experience and have not been evaluated within the context of controlled clinical trials. ONJ is a clinical entity with many possible etiologies; historically identified risk factors include corticosteroids, chemotherapy, radiotherapy, trauma, infection, and cancer. With emerging concern for potential development of ONJ in patients receiving bisphosphonates, the panel recommends a dental examination before patients begin therapy with intravenous bisphosphonates. Dental treatments and procedures that require bone healing should be completed before initiating intravenous bisphosphonate therapy. Patients should be instructed on the importance of maintaining good oral hygiene and having regular dental assessments. For patients currently receiving bisphosphonates who require dental procedures, there is no evidence to suggest that interrupting bisphosphonate therapy will prevent or lower the risk of ONJ. Frequent clinical assessments and conservative dental management are suggested for these patients. For treatment of patients who develop ONJ, a conservative, nonsurgical approach is strongly recommended. An increased awareness of the potential risk of ONJ in patients receiving bisphosphonate therapy is needed. Close coordination between the treating physician and oral surgeon and/or a dental specialist is strongly recommended in making treatment decisions.

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Erratum

In the Academy Abstracts section of the July/August 2006 issue of the *International Journal of Oral and Maxillofacial Implants*, the authors for the abstract of "The Relationship of Drill Diameter to Heat Generation During Implant Osteotomy Preparation" were incorrectly listed. Dr Ivan Roman, DDS, MS, should have been listed as the first author. Dr Roman was the primary investigator for this study.