Osteonecrosis in 1% of IV Bisphosphonate Users

BY SHARON WORCESTER
Southeast Bureau

ATLANTA — A retrospective analysis of data from nearly 4,000 patients treated with intravenous bisphosphonates suggests that osteonecrosis of the jaw in patients with metastatic cancer is an important but rare event in these patients, Dr. Ana O. Hoff reported in a poster at the annual meeting of the American Society of Clinical Oncology.

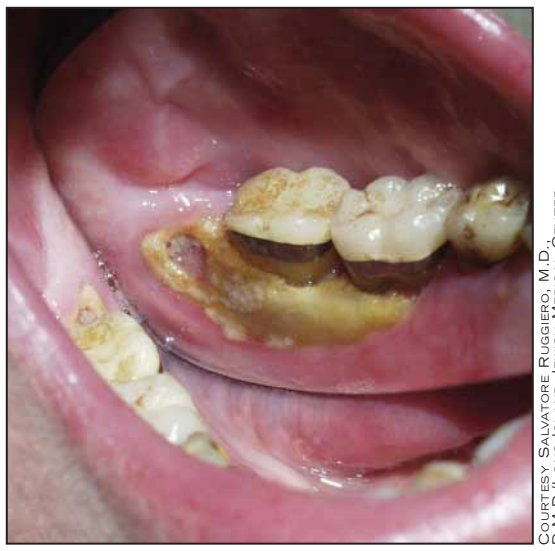
Reports of an association between bisphosphonate treatment and osteonecrosis of the jaw (ONJ) in patients with metastatic bone disease prompted this study examining the frequency of and risk factors for ONJ, explained Dr. Hoff of the University of Texas M.D. Anderson Cancer Center, Houston.

The cohort studied included patients treated from September 1996 to February 2004. The most common diagnoses were breast cancer (in more than 1,300 patients) and multiple myeloma (in 550 patients), and the indications for intravenous bisphosphonate treatment included metastatic bone disease, hypercalcemia, and osteoporosis.

ONJ, which developed in 29 patients (0.73% overall, including about 1% of breast cancer patients and 2% of multiple myeloma patients), was defined as exposed nonhealing bone of at least 3 months' duration.

Mean cumulative doses of the bisphosphonates used (pamidronate and zoledronate) were significantly higher, and duration of disease and follow-up were significantly longer, in ONJ patients than in those who didn't develop ONJ.

Dental extractions, estrogen-receptor–positive tumors, and treatment with pamidronate and zoledronate were shown to be significant risk factors for ONJ in breast cancer patients. In multiple myeloma patients, significant risk factors were dental extractions, periodontal disease, and osteoporosis.



COURTESY SALVATORE RUGGIERO, M.D., D.M.D./LONG ISLAND JEWISH MEDICAL CENTER

Spontaneous osteonecrosis of the jaw in a patient after long-term bisphosphonate therapy.

About 70% of ONJ patients reported no pain with bone exposure, Dr. Hoff noted.

Management of patients with ONJ included aggressive oral hygiene, oral rinses, debridement of necrotic bone, and antibiotic therapy. Of 15 ONJ patients followed longer than 6 months, 1 healed, 1 improved, 1 remained stable, and 9 experienced disease progression.

The finding of 0.73% ONJ occurrence in this population suggests that this is a rare, albeit important, event. Good dental care and avoidance of dental interventions are important recommendations for all patients being treated with intravenous bisphosphonates, Dr. Hoff concluded. ■

Race, Number of Infusions Possible Risks for Osteonecrosis

White cancer patients on intravenous bisphosphonate therapy for bone metastases may be at higher risk for osteonecrosis of the jaw, Dr. Tamer Aiti reported in a poster at the meeting.

A retrospective study by Dr. Aiti and his colleagues at John H. Stroger Jr. Cook County Hospital, Chicago, found that 6 (3.7%) of 161 patients with metastatic breast cancer developed this rare complication in the mandible bone. Five of the six patients were white. Yet whites accounted for less than a third of the population reviewed. All but 29 patients were nonwhite.

The investigators calculated that white patients had significantly more bisphosphonate infusions, 21 on average, compared with a mean of 13.5 infusions in nonwhite patients. Logistic regression analysis established that significantly more whites developed osteonecrosis of the jaw even after the study investigators controlled for dose (odds ratio 45.7).

The patients were treated with zoledronic acid and/or pamidronate between January 1, 2001, and October 30, 2005. None had prior glucocorticosteroid therapy.

As of Dec. 30, 2005, only two patients had resolution of their osteonecrosis of the jaw. Three patients had exposed bone—two with intermittent pain, and one with chronic pain. The lone African American patient with the complication developed sepsis and died.

Dr. Aiti of the department of surgical oncology at the University of Illinois at Chicago called for larger studies to consider not only race, but also confounding variables such as type of bisphosphonate therapy and cumulative dose, as well as other possible risk factors. Dr. Aiti and his colleagues also urged prospective imaging of high-risk patients, doing oral surgery before bisphosphonate treatment, and surveillance for osteonecrosis of the jaw.

"The study is small. I would not say it is confirmatory. We need larger numbers to see if this is really the fact," he said in an interview.

—Jane Salodof MacNeil

Relative Risk Data Favor Acceptance of Bisphosphonate Tx

BY JANE NEFF ROLLINS
Contributing Writer

LOS ANGELES — Physicians and patients are less likely to favor bisphosphonate therapy for osteoporosis when efficacy is expressed in terms of absolute risk reduction, as health literacy experts recommend, rather than relative risk reduction, Dr. Christine A. Sinsky reported at the annual meeting of the Society of General Internal Medicine.

Despite the widespread use of relative risk reduction (RRR) values to describe the benefits of osteoporosis therapy, health literacy experts favor focusing on absolute risk reduction (ARR). That's because RRR tends to overstate risk reduction when there is a low baseline frequency of a condition, such as hip fracture in osteoporosis, said Dr. Sinsky, an internist in private practice in Dubuque, Iowa.

Data cited by the U.S. Preventive Services Task Force (USPSTF) suggest that after 5 years of treatment with bisphosphonates, the RRR for hip fracture is 35%, while the absolute risk of fracture in the at-risk population decreases from 3% to 2%, yielding a 1% ARR (Ann. Int. Med. 2002;137:526-8).

Investigators administered a 10-item questionnaire to 641 consecutive female patients (aged 50 years or older) and all general medicine physicians at a university-based practice and a community practice. The patients were asked: "You have a bone density test that indicates osteoporosis. You have full drug coverage. Are you interested in treatment?" The physicians were asked: "Your 65-year-old patient has a [dual-energy x-ray absorptiometry] scan that indicates osteoporosis. The patient has full drug coverage. Would you recommend treatment?" Other scenarios presented out-of-pocket costs to the patient ranging from 0% to 90%. Subsequent questions presented similar scenarios but with efficacy of treatment presented as either RRR or ARR.

When treatment benefit was presented as RRR, 86% of patients expressed interest, which was significantly higher than the 57% rate when benefit was expressed as ARR. Similarly, physicians were significantly more likely to recommend osteoporosis treatment for their patients when treatment benefits were presented as RRR (97%) as opposed to ARR (53%). One limitation of the study is that patients may not have understood the clinical consequences of hip fractures, Dr. Sinsky noted. ■

TSH Stimulation Before Radioiodine Enhances Goiter Shrinkage

BY JOHN R. BELL
Associate Editor

Recombinant human thyrotropin before radioiodine therapy was associated with a 35% greater reduction in volume of nontoxic nodular goiters than that achieved with radioiodine alone, but with a fivefold increase in the rate of hypothyroidism, Danish researchers reported in the first large, double-blind, randomized, controlled trial of this therapy for nontoxic nodular goiter.

Dr. Viveque E. Nielsen of Odense (Denmark) University Hospital and colleagues assessed the effect of recombinant human thyrotropin (rhTSH) administered prior to treatment with radioiodine (iodine-131) in patients with nontoxic nodular goiter who were seen at the investigators' outpatient clinic (Arch. Intern. Med. 2006;166:1476-82).

Patients received 0.3 mg of either rhTSH or a placebo saline injection 24 hours before treatment with radioiodine doses customized to each patient, based in part on radioiodine uptake measured at baseline and 12 months. End points of thyroid size and function were assessed at 3, 6, 9, and 12 months, as were patient satisfaction before therapy and at 3 months and 1 year post treatment, via a visual analog scale.

In all, 57 patients were included in the final study results. In the placebo group, the median goiter volume had dropped from the baseline measure of 51 mL to 27 mL. The rhTSH group saw a decline from a median of 59 mL at baseline to a median of 20 mL at 12 months. Moreover, mean reduction at 12 months was 46% for the group receiving radioiodine alone and 62% for the group treated first with rhTSH—a difference of 16 percentage points, which constitutes a 35% advantage over the reduction achieved solely with radioiodine.

However, in terms of thyroid function, hypothyroidism developed in 62% of the rhTSH group versus 11% of the placebo group. And adverse events were more common in the rhTSH group—namely, hypothyroid symptoms, nausea, and headache. ■