Jaw Osteonecrosis Risk Increases With More Bisphosphonate Infusions

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CHICAGO — The risk of jaw osteonecrosis increases with the number of bisphosphonate infusions, according to studies presented at the annual meeting of the American Society of Clinical Oncology.

Osteonecrosis of the jaw (ONJ) is a rare, but serious side effect of bisphosphonates that has popped up in a number of case reports in the literature. Three groups of researchers conducted retrospective analyses to understand the natural history, incidence, and risk factors of this side effect.

In one study, Dr. Tracey L. O’Connor of Roswell Park Cancer Institute in Buffalo, N.Y., and colleagues identified 354 patients with metastatic cancer involving bones on intravenous bisphosphonates between 2002 and 2006 at the Institute. Using dental records, they identified 25 patients (7%) with ONJ. Most (80%) had breast cancer, and 27% had a medical comorbidity such as diabetes mellitus, hypertension, or chronic osteoporosis treatment for deep vein thrombosis or pulmonary embolism. In general, patients who developed osteonecrosis underwent a greater number of bisphosphonate infusions and greater total infusion hours, suggesting a positive correlation between osteonecrosis and drug dose, the authors wrote. Four women had full-blown ONJ. Patients with ONJ had a significantly greater number of infusions (21), versus controls (11) and a significantly greater mean number of hours of infusion time (43 vs. 18). All ONJ patients presented with exposed bone. In four, ONJ occurred after dental treatment. The mandible was affected in five patients; the maxilla in one. Bisphosphonates were discontinued in five patients after ONJ diagnosis. The patient who did not stop had a small area of exposed bone covered surgically using viable mucosa. Another patient recovered from ONJ and resumed bisphosphonates.

Dr. Minni I. Hu of the department of endocrine neoplasia and hormonal disorders at the University of Texas M.D. Anderson Cancer Center in Houston, and colleagues performed a retrospective analysis of patients treated with intravenous bisphosphonates between 1996 and 2004. They identified 4,025 patients; 35 had ONJ. Fourteen were followed for over 6 months at a dental clinic. Patients were evenly split between having breast cancer or multiple myeloma. The average length of exposed bone at the initial evaluation was 11 mm. Most (10) were treated with pamidronate, followed by zoledronic acid. Four were treated with zoledronic acid alone. The median cumulative dose was 11 mm. Most (10) were treated with pamidronate, followed by zoledronic acid. Four were treated with zoledronic acid alone. The median cumulative dose was 11 mm. However, the fracture data were inconclusive. In the FLEX (Fracture Intervention Trial [FIT]; Long-Term Extension) study, published late last year, researchers assessed the effects of continuing or stopping alendronate after 5 years of treatment (JAMA 2006;296:2927-38).

For women on placebo for years 5-10, total hip BMD returned to baseline levels. Women on 5 mg/day of alendronate had slightly fewer vertebral and total hip fractures than those who stopped treatment after 5 years. There was no difference between the groups in terms of nonvertebral or morphometric vertebral fractures.

“Combination of alendronate for 10 years maintains bone mass and reduces bone remodeling, compared with discontinuation after 5 years,” said Dr. Khosla.

Discontinuation did not increase the risk of nonvertebral fractures or a ray–detected vertebral fractures, but the risk of clinically detected vertebral fractures was significantly increased in those who discontinued therapy after 5 years.

“For many women, stopping alendronate after 5 years for up to 5 years does not significantly increase fracture risk, but women at high risk of vertebral fractures—such as those who already have a vertebral fracture or those who might have very low bone density—may benefit by continuing beyond 5 years.”

—Kerr Wachter