Watch for Osteonecrosis With Long-Term Bisphosphonates

BY KATE JOHNSON
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Long-term bisphosphonate therapy can lead to osteonecrosis of the jaw—a previously unrecognized and potentially serious complication that can often be avoided, according to Salvatore Ruggiero, M.D., D.M.D.

Patients on intravenous therapy, whether for cancer or osteoporosis, face the highest risk regardless of whether they are taking the medication for cancer or for osteoporosis, but the risk is lower, although not absent in those taking oral bisphosphonates, said Dr. Ruggiero, who is chief of oral and maxillofacial surgery at Long Island Jewish Medical Center in New Hyde Park, NY.

"The push is to alert physicians that this is a potential problem, so that before they start a patient on bisphosphonates, they send them to a dentist to extract any teeth that are nonrestorable," he told this newspaper. "Prevention and early detection are important for preserving the jawbone in these individuals."

In his experience, the majority of cases have been associated with infections following dental surgeries such as tooth extractions. However, necrosis has also occurred spontaneously in a significant number of patients, he said.

For this reason Dr. Ruggiero recommends that all patients on long-term bisphosphonates have two or three preventive dental visits per year, and that physicians be alert for any early signs of necrosis. Patients should be alert to "things like tooth pain, swelling, numbness of the lip and chin, or pain within the jaw. This is not a very difficult diagnosis to make. You basically have to look in the mouth and if you see exposed bone it is very clear," he said.

Dr. Ruggiero’s research, published in the Journal of Oral and Maxillofacial Surgery (J. Oral Maxillofac. Surg. 62;2004:527-34), has prompted warnings from the Food and Drug Administration (FDA), as well as from Novartis, which manufactures the intravenous bisphosphonates pamidronate disodium (Aredia) and zoledronic acid (Zometa).

Novartis has also changed its package inserts to reflect this information. However, labeling for oral bisphosphonates has not changed.

His study identified 63 patients with osteonecrosis of the jaw (ONJ), all of whom were on long-term bisphosphonate therapy for a period ranging from 6 to 48 months. Fifty-six of the patients had used intravenous bisphosphonates for cancer chemotherapy, while the remaining 7 had used oral bisphosphonates for treatment of osteoporosis.

Until these cases were identified, ONJ had been a rare clinical scenario, Dr. Rug- giiero noted.

The typical presenting symptoms were pain and nonhealing exposed bone at the site of a previous tooth extraction. However, 9 patients (14%) had no history of a recent dentoalveolar procedure and presented with spontaneous exposure and necrosis of the alveolar bone. Biopsies of the lesions showed no evidence of metastatic disease, Dr. Ruggiero said.

Spontaneous jaw osteonecrosis can occur in patients treated with long-term bisphosphonates; however, the majority of cases occur after tooth extraction or other dental surgeries.

Dr. Ruggiero speculated that the impaired bone wound healing may result from a compromised vascular supply caused by the antiangiogenic effects of bisphosphonates. He suggests that the absence of bone problems elsewhere in the body may be due to the unique environment created by oral microflora.

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With modern biotechnology, it is now possible to develop drugs that target specific pathways and molecules responsible for the development of osteoporosis. This approach has the potential to improve the efficacy and safety of osteoporosis treatments while reducing the risk of adverse events. Novel therapies, such as selective estrogen receptor modulators (SERMs) and selective androgen receptor modulators (SARMs), are currently under investigation and may offer promising new options for the treatment of osteoporosis.

In addition to pharmacological interventions, nonpharmacological approaches, such as lifestyle modifications and physical activity, play a crucial role in the management of osteoporosis. Regular exercise, particularly weight-bearing activities, can help to preserve bone density and reduce the risk of fractures. Dietary modifications, including the consumption of foods rich in calcium and vitamin D, are also important for maintaining bone health.

The future of osteoporosis treatment is promising, with ongoing research aiming to identify new targets, develop more effective agents, and improve the accessibility and affordability of current treatments. Collaboration between researchers, healthcare providers, and patients is essential to achieve these goals and to ensure that all individuals with osteoporosis have access to the care they need to maintain their quality of life and independence.