

Quantity vs. quality: Long-term use of bone-building osteoporosis drugs

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Bisphosphonate treatments, proven to enhance bone density and reduce fracture incidence in post-menopausal women, may adversely affect bone quality and increase risk of atypical fractures of the femur when used for four or more years, according to preliminary research presented today at the 2010 Annual Meeting of the American Academy of Orthopaedic Surgeons (AAOS).

Bisphosphonates are designed to slow or stop the bone loss that occurs during the body's bone remodeling cycle, or the natural process that involves removal and replacement of [bone tissue](#).

Two separate studies by researchers from Hospital for Special Surgery (HSS) and Columbia University Medical Center revealed data suggesting that long-term suppression of bone remodeling by bisphosphonate treatments may alter the material properties of bone, potentially affecting the bone's mechanical integrity and potentially contributing to the risk of atypical fractures.

"Although [bisphosphonates](#) have demonstrated an improvement in bone quantity, little if anything is known about the effects of these drugs on bone quality," said Brian Gladnick, BS, representing a team of investigators at HSS in New York.

Researchers at Columbia evaluated the bone structure of 111 [postmenopausal women](#) with primary osteoporosis, 61 of whom had been taking bisphosphonates for a minimum of four years and 50

controls taking calcium and vitamin D supplements.

This study found that bisphosphonate use improved structural integrity early in the course of treatment, but those gains were diminished with long-term treatment.

"In the early treatment period, patients using bisphosphonates experienced improvements in all parameters, including decreased buckling ratio and increased cross-sectional area," said Melvin Rosenwasser, MD, orthopaedic surgeon for Columbia University Medical Center. "However, after four years of use, these trends reversed, revealing an association between prolonged therapy and declining cortical bone structural integrity."

Scientists at both institutions noted that the culprit behind the diminishing results may be the fact that bisphosphonates suppress the body's natural process of remodeling bone. "Recent research suggests that suppressed bone remodeling from long-term bisphosphonate use might result in brittle bone that is prone to atypical fractures," said Gladnick.

The investigators added that more research is needed to determine the true efficacy of the long-term clinical use of bisphosphonates for the treatment of osteoporosis, and that the results of their studies will not likely affect clinical practice in the near future.

"Bisphosphonate use still is a very effective solution that prevents bone loss in most patients and no one is recommending that physicians avoid prescribing these," said Dr. Rosenwasser. "However, as baby boomers age and continue to remain active, it is important that we conduct more research and develop sustainable, safe and effective treatments for osteoporosis."

In a second unrelated prospective pilot study, conducted at HSS and funded in part by the NIH, researchers evaluated the bone composition of 21 post-menopausal women who were treated for femoral fractures. Of these, 12 patients had a history of bisphosphonate treatment for an average of 8.5 years, while nine had not had bisphosphonate treatment.

Samples of bone were removed from each patient's femur during surgical placement of a femoral nail. Both micro-architecture and material properties of the bone were analyzed.

The study found that, although there were no differences in bone micro-architecture between groups, the material properties of bone in bisphosphonate-treated patients displayed reduced bone tissue heterogeneity, which may be associated with reduced strength and potentially may contribute to the presentation of atypical fractures.

"Patients who had been treated with bisphosphonates showed a reduction in tissue heterogeneity, specifically with mineral content and crystal size compared with the control group," Gladnick said. "This tells us that there may be some measurable differences in bone quality parameters in patients on long-term bisphosphonate therapy, which might contribute to the development of atypical fractures."

Provided by American Academy of Orthopaedic Surgeons

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