Teriparatide Boosts Periodontal Surgery Recovery

Pilot study shows agent improves bone gain, probing depth, clinical attachment.

BY MITCHEL L. ZOLER

FROM THE NEW ENGLAND JOURNAL OF MEDICINE

Treatment for 6 weeks with teriparatide, a U.S.-approved drug that stimulates bone remodeling, led to significant, 1-year improvements in alveolar bone formation and clinical outcomes in a controlled pilot study of 40 patients undergoing periodontal surgery.

Bone gain in the osseous defects of the 20 patients who were randomized to receive daily teriparatide injections became detectable early after treatment began and continued to improve during 12 months of follow-up, leading to a highly significant improvement in overall alveolar bone gain, compared with the 20 patients on placebo, Jill D. Bashutski, D.D.S., and her associates reported online (N. Engl. J. Med. 2010 Oct. 16 [doi:10.1056/NEJMoa1005361]).

The patients who were treated with teriparatide also demonstrated significantly better 1-year improvements in periodontal probing depth and clinical attachment, reported Dr. Bashutski, a periodontist at the University of Michigan in Ann Arbor.

The article's online publication was timed to coincide with Dr. Bashutski's presentation of the study findings at the annual meeting of the American Society for Bone and Mineral Research in Toronto.

She and her coinvestigators used teriparatide, a recombinant agent that contains the first 34 amino acids of parathyroid hormone, because of its activity as an anabolic agent and evidence from prior studies that it enhances bone remodeling and wound healing in areas of high bone turnover, such as fractures and surgical sites.

"We know that parathyroid hormone stimulates formation of preosteoblast cells, and these cells go on to eventually form bone," said Dr. Bashutski.

The 6-week regimen consists of daily teriparatide injections, which produce "an initial incentive for bone formation to occur" during subsequent months, said Dr. Laurie K. McCauley, the principal investigator of the study and professor and chair of periodontics and oral medicine at the University of Michigan, in an interview.

The positive effects that teriparatide treatment had on the study outcomes of bone gain, probing depth, and clinical attachment were also all clinically significant, according to Dr. McCauley. Teriparatide increased 1-year bone gain at a rate that was 10-fold higher than placebo.

Parathyroid hormone stimulates formation of preosteoblast cells and bone.

DR. BASHUTSKI

"That's huge," she said.

The long-term sequence of events that teriparatide triggers likely explains how a 6-week course produced significant differences after 1 year, she said.

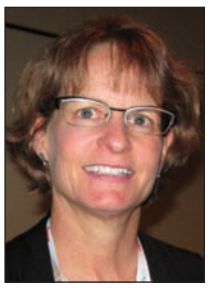
"We know that most connective tissue healing goes on during the first 6 weeks," according to Dr. McCauley. "The thought was to augment that healing with this agent."

The outcome from "this small trial provides preliminary evidence that an agent that stimulates bone formation might confer additional benefit over that achieved with standard care in patients with periodontitis," commented Dr. Andrew Grey in an editorial that accompanied the article (N. Engl. J. Med. 2010 Oct. 16 [doi:10.1056/NEJMe1010459]).

But many questions about this treatment remain, he said. "How durable is the effect of teriparatide? What is the optimal dosing regimen? Does teriparatide alter important end points such as tooth loss or the need for further operative intervention? Do antiresorptive agents, which cost considerably less than teriparatide, confer similar benefits?" asked Dr. Grey, an endocrinologist at the University of Auckland (New Zealand).

The study enrolled patients (aged 30-65 years) with severe periodontal disease at the University of Michigan from January 2005 to June 2009. All patients in the study had normal levels of calcium and parathyroid hormone, a minimum vitamin D level of 16 ng/mL, and no osteoporosis.

All patients underwent conventional surgery on an osseous defect. Starting 3 days before surgery, patients began daily treatment with either 20 mcg of teriparatide or placebo, administered daily by subcutaneous injection, for 6 weeks. All patients also received a daily supplement of calcium and vitamin D.



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DR. McCAULEY

Patients who were treated with teriparatide had significantly better resolution of their periodontal bone defects at 6, 9, and 12 months following baseline, compared with the placebo patients.

At 12 months, the teriparatide-treated patients averaged a bone gain of 1.86 mm (29%), compared with baseline, whereas the placebo patients averaged a 0.16-mm (3%) gain from baseline.

Teriparatide treatment was also associated with a 2.42-mm (33%) average reduction in probing depth at the surgical site after a period of 12 months, compared with baseline. The placebo group averaged a 1.32-mm (20%) reduction in probing depth from baseline, a statistically significant difference.

Clinical attachment improved by an average of 1.58 mm (22%) at 1-year follow-up, compared with baseline, in the teriparatide patients, significantly better than the average value of 0.42 mm (7%) for attachment improvement in the placebo group.

No improvements in probing depth occurred in the teriparatide and placebo patients in areas of severe, chronic periodontitis that did not undergo surgery.

At entry to the study, five patients in the teriparatide arm and nine in the placebo group had osteopenia on dual x-ray absorptiometry examinations. At the 12-month follow-up, patients in both of the study arms showed no significant changes in bone density scores or in quality of life scores.

Teriparatide treatment was not associated with any pattern of adverse events that differed from the placebo group.

Although teriparatide is available in the United States for treating osteoporosis, its widespread use in patients who are undergoing periodontal surgery should await results from studies involving larger numbers of patients, Dr. McCauley said. She also cautioned against extrapolating the results to other types of bone surgery.

Dr. McCauley said she would like to run studies on a delayed-release, topical formulation of teriparatide that would be implanted during surgery and would then release over the subsequent 6 weeks. Such a mode of delivery would preclude the necessity of administering daily injections. Teriparatide formulations of this type now exist, but they have not reached the clinical-testing stage. ■

VITALS

Major Finding: In patients undergoing periodontal surgery, daily 20-mcg injections of teriparatide for 6 weeks led to an average 29% bone gain at the surgery site after 1 year, compared with an average 3% gain in the placebo group.

Data Source: A randomized, single-center pilot study of 40 patients with severe periodontal disease.

Disclosures: The investigator-initiated study received partial funding from Eli Lilly & Co., the company that markets teriparatide (Forteo). Dr. McCauley has received research grants and transportation support from Lilly. She has also received research grants and has been a consultant to Amgen, but has not received any honoraria or consulting fees. Dr. Bashutski said she has received travel expenses from the Colgate-Palmolive Co. Dr. Grey said that he has received travel expenses from Merck Sharp & Dohme (NZ) Ltd.

Ten Years Between Osteoporosis Screenings Okay for Some

BY MITCHEL L. ZOLER

FROM THE ANNUAL MEETING OF THE AMERICAN SOCIETY FOR BONE AND MINERAL RESEARCH

TORONTO – Women aged 67 years or older with a bone mineral density T score higher than –1.50 on dual-energy x-ray absorptiometry can have their next DXA examination deferred for at least 10 years with a low risk that they'll progress to osteoporosis in the interim, according to an analysis of data from more than 5,000 U.S. women.

"Fewer than 10% of women with a BMD [bone mineral density] T score of more than –1.50 were estimated to transition to osteoporosis if followed for 15 years," Dr. Margaret L. Gourlay said.

For these women, "repeat testing before 10 years is unlikely to show osteoporosis," she said, and for women with a T score of –1.50 to –1.99, "a 5-year interval could be considered."

The results provide the first evidence-based guidance available on the appropriate interval for osteoporosis screening in elderly women.

"The value of these results is that we can be less concerned about women with good BMD," Dr. Gourlay said in an interview. "We don't need to go on autopilot and screen [all women] every 2 years."

Medicare reimburses for screening women aged 65 years or older with dual-energy x-ray absorptiometry (DXA) every 2 years, she noted, and hence U.S. physicians often recommend this screening interval.

Earlier this year, however, an updated review of osteoporosis screening by the U.S. Preventive Services

Continued on following page