PET Tracks Monostatic Forms of Paget's Disease

Scans taken during follow-up might be helpful in determining course of bisphosphonate therapy.

BY MIRIAM E. TUCKER
Senior Writer

FORT LAUDERDALE, FLA. — The use of ^{18}F-fluoride positron emission tomography may be useful in the follow-up of patients with monostotic forms of Paget's disease, Dr. Jean-Pierre Devogelaer said at a meeting sponsored by the Paget Foundation for Paget's Disease of Bone and Related Disorders.

In Paget's disease of bone, biochemical markers are used to monitor treatment response. However, in patients with limited bone involvement, these global indices often remain in the normal range, said Dr. Devogelaer, professor of rheumatology at Catholic University of Louvain and Saint-Luc University Hospital, Brussels.

Positron emission tomography (PET) using ^{18}F-fluoride as an imaging agent appears to be of value in measuring regional skeletal metabolism, and therefore may be helpful in determining whether bisphosphonate therapy should be stopped or prolonged depending on the local level of pagetic activity, he said.

Twelve patients with monostotic Paget's disease of bone underwent 1-hour dynamic ^{18}F-fluoride PET scans at baseline and at 1, 6, and 12 months after bisphosphonate treatment (intravenous pamidronate in nine, oral risedronate in two, and oral tiludronate in one). Biochemical markers were measured at the same time points. The affected areas were pelvis in three patients, tibia in three, femur in two, and humerus, vertebral body, skull, and scapula in one patient each.

Changes in bone metabolism as measured by the PET scans were assessed in two ways: via dynamic plasma clearance of ^{18}F-fluoride to bone mineral, which requires arterial blood sampling; and with a standardized uptake value, a semiquantitative index that averages the tracer uptake with respect to the injected dose and the body weight. Calculation of the standardized uptake value does not require arterial sampling and therefore is a far more convenient method for measuring pagetic activity in a clinical setting, Dr. Devogelaer added.

The two values correlated with each other at all time points. Both showed huge activity prior to treatment and significant drops thereafter, by about 30% at 1 month, 40% at 6 months, and nearly 50% at 1 year.

In contrast, the biochemical markers correlated with the PET scan results at baseline but not after treatment: Total alkaline phosphatase dropped by about 25% at 1 year, but remained within the normal range throughout the study. Fasting levels of urinary N-terminal cross-linking telopeptide of type I collagen (NTX) decreased significantly up to 6 months, but not thereafter. Bone-specific alkaline phosphatase dropped by about 30%-35% at 1 month, but remained significant only up to 6 months. Such changes in biochemical markers are not adequate for follow-up, he said.

An audience member noted that PET scans are expensive and not covered for Paget's disease in the United States. Dr. Devogelaer replied, "We hope that the cost will decrease. But we see that with the biological parameters, there is no correlation after treatment. To appreciate the activity of monostotic Paget's disease of bone, we need something else." ■

Level of Cathepsin K Predicts Response in Paget's Disease

BY MIRIAM E. TUCKER
Senior Writer

FORT LAUDERDALE, FLA. — Serum cathepsin K levels could serve as a useful measure in the management of patients with Paget's disease of bone, Dr. Daniela Merlotti said at a meeting sponsored by the Paget Foundation for Paget's Disease of Bone and Related Disorders.

ALP levels in the zoledronate group continued to drop after 6 months but increased with pamidronate.

DR. MERLOTTI

Cathepsin K, a cysteine protease enzyme, is the most abundantly synthesized protein of the resorbing osteoclast, and plays an important role in the degradation of the organic matrix of bone. Recent studies have suggested that the enzyme may serve as a marker for fracture prediction and bone mineral density (J. Lab. Clin. Med. 2005;146:13-7) and as a parameter for bone metabolism in patients with early rheumatoid arthritis (Arthritis Res. Ther. 2005;7:R65-70), noted Dr. Merlotti of the University of Siena, Italy.

Serum cathepsin K levels were assessed before and after bisphosphonate treatment in 60 patients with Paget's disease and in 50 age-matched controls without the disease. Serum total alkaline phosphatase (ALP), carboxyterminal cross-linked telopeptide of type I collagen (sCTX), and bone-specific ALP were also measured.

At baseline, serum cathepsin K levels were significantly higher in the Paget's disease patients, compared with the controls, and were higher in patients with polyostotic disease than in those with monostotic disease. Baseline cathepsin K correlated positively with sCTX and urinary calcium, but not with total or bone-specific ALP. Similar but weaker correlations were seen in the controls, Dr. Merlotti said.

Overall, intravenous bisphosphonate treatment reduced cathepsin K levels by 28% at 3 days, 34% at 30 days, 45% at 3 months, 29% at 6 months, and 32% at 1 year. At each time point, the reduction in cathepsin K was significantly greater among the 20 patients treated with zoledronate than in the 40 who received pamidronate. With pamidronate, serum cathepsin K levels increased between 3 and 6 months, while on zoledronate the levels decreased continuously.

For the group as a whole, serum ALP dropped by 33% at 30 days and 24% at 90 days, then increased slightly thereafter up to 1 year. However, when examined separately, ALP levels in the zoledronate group continued to drop, while they increased after 6 months with pamidronate. At 6 months, serum ALP had normalized in 88% of the zoledronate patients, compared with just 31% of the pamidronate group, Dr. Merlotti reported.

The evaluation of cathepsin K levels at 3 months predicted the response to bisphosphonate treatment: The Paget's disease patients in whom cathepsin K was decreasing at 3 months had an 18% reduction in total serum ALP levels at 6 months, while those in whom cathepsin K was rising at 3 months showed a 5% increase in total serum ALP at 6 months, she said. ■

PTH Appropriate for a Select Few Patients With Bone Loss

BY TIMOTHY F. KIRN
Sacramento Bureau

SNOWMASS, COLO. — The current evidence suggests it is a very small group of individuals with low bone density who should be treated with parathyroid hormone, Dr. Lenore Buckley said at a symposium sponsored by the American College of Rheumatology.

Probably the only patients who are proper candidates for parathyroid hormone (PTH) therapy, according to a recent cost-effectiveness analysis, are those patients who have an extremely low T score, below –3.5, and who are at least 70 years old or have had a vertebral fracture, said Dr. Buckley, a professor of internal medicine at Virginia Commonwealth University, Richmond.

Combining PTH with a bisphosphonate seems to dampen density gains seen with PTH alone—likely because bone resorption is inseparable from formation.

The cost-effectiveness analysis to which she referred considered the case of a postmenopausal woman with osteoporosis and compared four different treatment strategies: calcium and vitamin D supplementation, 5 years of treatment with alendronate, 2 years of PTH therapy, and 2 years of PTH followed by 5 years of alendronate.

The analysis said that vitamin D supplementation and the alendronate treatment fell within the cost range that is considered economical. The 5 years of alendronate treatment cost $15,800 per quality-adjusted life year gained. The 2 years of PTH therapy alone was not as effective as the alendronate alone regimen, and cost more. And the combined PTH followed by alendronate regimen cost $157,500 per quality-adjusted life year gained, which is considered well outside the range of cost effectiveness.

It was only when the risk of fracture became very high that the combined regimen began to become cost effective.

Those findings appear to be practical and to reflect what recent research indicates about PTH treatment, Dr. Buckley said.

PTH does seem to produce greater increases in bone density than bisphosphonates, and in patients who are at high risk of fracture, the hormone appears to reduce the rate of fracture by approximately 65% over 2 years, she said. But PTH also costs about $7,000 a year, and patients have a hard time with the required daily injections.

A number of recent studies have looked at combining PTH with bisphosphonates as a way to either improve on the density gains or make treatment easier.

Those studies have found that it is possible to get some additional benefit when PTH is used cyclically (3-month cycles) with continuous bisphosphonate treatment and that there may be some benefit in using PTH in patients who do not seem to be responding to bisphosphonate treatment.

But, in general, combining the two appears to dampen the gains in density that are achieved with PTH alone, probably because it is not possible to fully uncouple bone resorption, which is prevented with bisphosphonate treatment, from bone formation, which is stimulated by PTH, Dr. Buckley said.

She said that given the length of activity of bisphosphonates, it probably would take a patient about 1 year off bisphosphonate treatment to be ready to reap the full benefit of PTH.

However, the present evidence suggests it's possible to consolidate gains achieved with PTH treatment by following it with a bisphosphonate; a year of PTH followed by a year of alendronate can produce a 12% increase in bone mineral density in the lumbar spine. ■