Look Past First Cause of Secondary Osteoporosis

BY ROBERT FINN
San Francisco Bureau

SAN FRANCISCO — Finding one possible cause of secondary osteoporosis does not mean there aren't other causes as well, Dr. Diana Antoniucci reported at a meeting on osteoporosis sponsored by the University of California, San Francisco.

"Having one secondary cause of osteoporosis does not preclude you from having another, so even if one contributor is obvious from the history, you can still consider laboratory testing," said Dr. Antoniucci, of UCSF. (See sidebar for suggestions on which tests to order.) She listed four frequent causes of secondary osteoporosis for physicians to consider.

Glucocorticoid Use

This is the most common cause of drug-induced osteoporosis. In these patients, prevention is clearly the best strategy. All patients should be taking supplemental calcium and vitamin D, Dr. Antoniucci said, and if the patient has already been diagnosed with osteoporosis or is otherwise at high risk, the physician should measure bone mineral density (BMD) with dual-energy x-ray absorptiometry (DXA). Clinical trials have shown that bisphosphonates halt bone loss and reduce fractures in patients taking glucocorticoids, and alendronate and risedronate are both approved for this indication. They should be considered for any patient on glucocorticoids with low BMD.

Vitamin D Deficiency

This deficiency is very common in the general population. Depending on the study population, the prevalence appears to range between 9% and 50%.

When severe, vitamin D deficiency is associated with osteomalacia, which is indistinguishable from low bone density on DXA. Less-severe vitamin D deficiency is associated with secondary hyperparathyroidism.

One difficulty in the assessment and treatment of vitamin D deficiency is that there is no general agreement as to what constitutes a sufficient level of 25-hydroxyvitamin D, Dr. Antoniucci noted. A level of 20 ng/mL appears to be necessary for normal parathyroid dynamics, 32-36 ng/mL appears to be necessary for maximal intestinal calcium transport, and 30-40 ng/mL is the level that several randomized controlled trials have determined is necessary for fracture reduction.

"The good news is that vitamin D insufficiency is treatable," Dr. Antoniucci said. "Replacement reestablishes vitamin D stores, and it improves bone mineral density because it allows optimal calcification of preexisting osteoid."

Celiac Disease

Somewhere between 9% and 12% of patients with osteoporosis also have celiac disease. Conversely, about 50% of patients with celiac disease have a BMD that is two standard deviations or more under the mean. Among patients with celiac disease, those with a low BMD are more likely to have villous atrophy, an indication of more severe disease.The pathogenesis of bone disease in these patients is likely multifactorial, according to Dr. Antoniucci. They tend to have worse calcium absorption from the gut, especially before their disease is diagnosed, which can be many years in some patients. They also can have vitamin D deficiency from secondary hyperparathyroidism. Some women with celiac disease also have infertility and amenorrhea, both of which can lead to poor bone health.

At least one study has demonstrated that among patients with celiac disease, a strict gluten-free diet over the period of a year can improve bone mass in both men and women (Arch. Intern. Med. 2005;165:393-9). The authors of that study concluded that it's worth screening patients with unexplained osteoporosis for celiac disease. Dr. Antoniucci is not so sure that that's a good idea. "First of all, what exactly is 'unexplained osteoporosis'? And secondly, it might be a very expensive way to be treating the disease," she said.

Androgen Deprivation Therapy

The longer a man is on this common therapy forprostate cancer, the greater his BMD loss and the greater his chance of fracture. After 10 years on androgen deprivation therapy, about 20% of men will have experienced a fracture, a risk fivefold greater than in age-matched controls. Slender white men appear to be at greatest risk, she said, noting that both pamidronate and zoledronate have been shown to prevent bone loss caused by androgen deprivation therapy. ■

Labs to Detect Secondary Osteoporosis

There is no consensus on whom to evaluate for secondary osteoporosis, said Dr. Antoniucci. However, "most people would agree that we should evaluate virtually all men with low T-scores, premenopausal women with low Z-scores or fragility fractures, and postmenopausal women," she said.

Dr. Antoniucci said a standard laboratory work-up should include:

- Complete blood count.
- 24-hour urine calcium excretion (which can provide important information if the result is very high or very low).
- 25-hydroxyvitamin D levels.
- Testosterone levels.
- Thyroid-stimulating hormone levels (in patients on thyroid hormone replacement).
- Electrolyte levels.
- Renal and hepatic function.

Additional tests are dictated by the patient's history and physical exam and the physician's clinical judgment.

Denosumab at Least as Effective as Alendronate

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

BOSTON — The investigational antiresorptive denosumab is at least as effective as alendronate for increasing bone mineral density in postmenopausal women, Dr. Nelson Watts said at the annual meeting of the Endocrine Society.

The drug inhibits RANKL (receptor activator of nuclear factor kappa B ligand), which is a mediator of the resorptive phase of bone remodeling. Interfering with the binding of RANK to its ligand inhibits the differentiation and proliferation of osteoclasts, thus reducing bone turnover, said Dr. Watts, director of the bone health and osteoporosis center at the University of Cincinnati. He presented the 24-month bone mineral density (BMD) results of a phase II safety and efficacy trial of denosumab. The trial compared denosumab with open-label alendronate, 70 mg weekly, and placebo in 412 postmenopausal women with low bone mass. Three doses of denosumab were tested; Dr. Watts discussed the results for 60-mg doses given subcutaneously every 6 months. This dosage was selected for evaluation in phase III clinical testing.

At 24 months, denosumab was associated with a significantly higher mean increase in BMD than was alendronate at all skeletal sites measured, including lumbar spine (7% vs. 6%), total hip (5% vs. 3.5%), and distal radius (1.75% vs. 0.5%).

Adverse events occurred in about 93% of patients in both groups, and the types of events were not significantly different, with the exception of more dyspepsia among those taking alendronate, Dr. Watts said. There were no signs of increased immune problems, infections, or neoplasms in either group.

In a post hoc analysis, significantly more women in the denosumab group experienced a gain of more than 3% in BMD at each site measured, including lumbar spine (93% vs. 87%), total hip (80% vs. 56%), femoral neck (60% vs. 41%), and distal radius (25% vs. 11%).

The trial was sponsored by Amgen Inc., which manufactures denosumab. ■

IV Ibandronate Found to Boost Bone Density as Well as Daily Oral Dosing

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

BOSTON — Intermittent intravenous ibandronate is at least as effective as daily oral ibandronate for increasing bone mineral density and may be preferable to oral dosing in patients with esophageal disease or compliance problems.

There are no fracture data for the intravenous dosing schedule, but the risk reduction that has been shown with oral ibandronate can probably be extrapolated to the intravenous form of the drug, Dr. Mone Zaidi said at the annual meeting of the Endocrine Society.

Oral ibandronate has been shown to reduce the risk of new vertebral fractures by up to 60% (Curr. Med. Res. Opin. 2005;21:391-401; J. Bone Miner. Res. 2004;19:1241-9).

"If you can show equivalence or superiority in bone mineral density changes to [the form] with proven fracture data, which we have done, I think everyone would agree that you can extrapolate that data," said Dr. Zaidi, director of the Mount Sinai Bone Program, Mount Sinai School of Medicine, New York.

Dr. Zaidi presented 2-year bone mineral density (BMD) data from the ibandronate Dosing Intravenous Administration trial, a Roche-sponsored phase III study that compared two doses of intravenous ibandronate (2 mg every 2 months and 3 mg every 3 months) with the approved oral dosing schedule (2.5 mg daily). The study group included 1,400 postmenopausal women with low bone mass (T-scores of –3.3 for total spine and –2 for hip).

After 2 years, BMD at the lumbar spine increased significantly more in both intravenous groups than in the oral group (mean increase 6.4% for the 2 mg IV dose, 6.3% for the 3 mg IV dose, and 4.8% for the oral dose).

BMD increased similarly at all other sites measured, with consistently greater gains in both intravenous groups than in the oral group, Dr. Zaidi said.

At 2 years, the incidence of adverse events was similar across all groups. Flulike illnesses and gastrointestinal intolerance were seen primarily in the first year, with only slight increases in cumulative numbers during the second year.

There was no osteonecrosis of the jaw. Renal and urinary incidents were uncommon and similar across groups.

Fracture incident, which was reported as an adverse event, was low and similar in all groups, although Dr. Zaidi stressed that the study was not powered to prove fracture risk reduction.

The intermittent dosing would also be "a great way" to ensure compliance, according to Dr. Zaidi. ■

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