

Don't Stop Bisphosphonate Therapy After Early Bone Loss

BY SHERRY BOSCHERT
San Francisco Bureau

SAN FRANCISCO — If the first bone density reading after starting bisphosphonate therapy shows bone loss, don't stop or alter therapy, Steven R. Cummings, M.D., advised at a meeting on osteoporosis sponsored by the University of California, San Francisco.

In all likelihood, the therapy is working, but "noise" in the bone density test results in a lower density measurement. The next time the patient's bone density is taken, it probably will be higher, said Dr. Cummings, professor emeritus of epidemiology and biostatistics at the university and director of clinical research at the California Pacific Medical Center Research Institute.

He and his associates analyzed data from the 6,459-patient Fracture Intervention Trial and found that among women who lost at least 4% of hip bone density in the first year of treatment with alendronate, 92% gained an average of 5% of hip bone density in the second year of therapy.

The study involved postmenopausal women, aged 55 to 80 years, who were randomized

to receive alendronate at 5 mg/day for 2 years and 10 mg/day thereafter, or placebo for up to 4.5 years.

"If you were to change treatment or add another drug" after that first follow-up, "they would gain bone and you would look like a hero, but in fact they would have improved even without" any changes, Dr. Cummings said.

Among women who partici-



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DR. CUMMINGS

pated in the study and who gained up to 4% of hip bone density in the first year on alendronate, 67% continued to gain an average of 1% bone density in the second year on therapy.

Of the women who gained a lot of hip bone—8% or more—the first year, 64% lost an average of 1% of hip bone the second year. So patients with the largest gains in bone density during the first year ought to be told: "Watch out—the next year you're likely to lose bone," he said.

Continuing therapy also is important for reducing the risk of fracture. A comparison of the 18% of women who lost bone after a year of alendronate with the 18% of women who lost the most bone while on placebo indicated a 50% reduction in fracture risk among patients who gained bone density on treatment.

A slightly greater reduction in fracture risk was seen in those women who lost as much as 4% of bone if they were taking alendronate, compared with placebo.

The greatest overall benefits of the therapy occurred in women who lost more than 4% of bone density during the first year. In members of this subgroup, taking alendronate reduced the risk of fracture by about 80%-90%, compared with placebo.

"Stopping treatment in those patients who lose bone is exactly the wrong thing to do," said Dr. Cummings, who also works as a consultant and speaker for two companies that manufacture bisphosphonate medications.

If a patient consistently loses bone density over multiple follow-up measurements in a period of years, then it would be reasonable to reassess treatment options, Dr. Cummings advised. ■

Strategies to Reduce Steroid-Induced Fractures

BY ROBERT FINN
San Francisco Bureau

SANTA BARBARA, CALIF. — About half of patients using glucocorticoids for long periods will suffer compression fractures of the vertebrae if nothing is done to intervene, Barbara P. Lukert, M.D., said at a symposium sponsored by the American College of Rheumatology.

Bisphosphonate therapy is clearly effective in reducing fractures, whether started when initiating glucocorticoids or after a patient has been on them for a while.

But bisphosphonates aren't enough, and other steps should be taken to manage these patients, said Dr. Lukert of the University of Kansas Medical Center in Kansas City.

Other opportunities to intervene are listed below:

► **Diet is critical.** Since glucocorticoids are catabolic, patients need adequate protein intake, not just calcium and phosphorus.

► **Heavily encourage patients to exercise,** not only because of its benefits on bone. Glucocorticoids often cause myopathy, ranging from mild to severe, and exercise can help to offset this. Strengthening the quadriceps and related muscle groups also has been shown to help prevent falls. ■

► **Control urinary calcium.** A very large percentage of patients who use glucocorticoids will develop hypercalciuria, and restricting sodium in the diet will go a long way toward resolving this.

► **Replace hormones as appropriate.** Women taking steroids often have low estrogen levels. If premenopausal women become amenorrheic on glucocorticoids, consider prescribing estrogen or progesterone. Dr. Lukert noted that estrogen replacement in postmenopausal women remains controversial.

Patients who have a bone mineral density (BMD) T score of less than -1.5 or are taking more than 10 mg/day of prednisone or the equivalent should receive bisphosphonates as soon as corticosteroids are started.

Patients with a higher BMD taking lower doses of prednisone may hold off on starting bisphosphonates at first and retest BMD after 6 months.

Another reasonable strategy is simply to give a bisphosphonate to all patients who anticipate taking steroids for several weeks or longer.

This strategy is certain to prevent fractures, but at the cost of treating 40%-50% of patients who probably would not have suffered a fracture, even without the bisphosphonate prescription. ■

Decision to Measure Bone Mineral Density Can Be Complex

BY ROBERT FINN
San Francisco Bureau

SANTA BARBARA, CALIF. — While it's well known that bone mineral density testing should be routine for women over the age of 65, it can be difficult to decide whether to test other patients and difficult to know what to do with the results, Barbara P. Lukert, M.D., said at a symposium sponsored by the American College of Rheumatology.

The International Society for Clinical Densitometry and the National Osteoporosis Foundation list similar indications for testing bone mineral density (BMD), said Dr. Lukert of the University of Kansas Medical Center, Kansas City. While these guidelines appear straightforward, there are complexities.

The guidelines say that in addition to all women over 65, postmenopausal women under 65 should be tested if they have any risk factors. But studies have not succeeded in identifying all of those risk factors, so in Dr. Lukert's view it's probably prudent to measure BMD in all postmenopausal women.

Premenopausal women, on the other

hand, should not have their BMD measured routinely.

Similarly, the guidelines call for BMD testing in any adult who has had a fragility fracture, but in practice this is done only about 15% of the time, an oversight that Dr. Lukert described as "appalling."

BMD testing should also be done in adults with any disease or condition associated with bone loss or low bone mass. The conditions include Cushing's disease, hyperthyroidism, hyperparathyroidism, and rheumatoid arthritis.

Some medications are associated with bone loss, most notably the glucocorticoids, and the guidelines say any adult taking one of these medications should have BMD testing.

Any adult who is being considered for pharmacologic therapy for bone loss should have his or her BMD assessed, and anyone receiving that therapy should have BMD testing to monitor the treatment effect.

"If we follow these indications, we would greatly increase the number of patients who are having their bone density measured," Dr. Lukert said.

One complexity comes in interpreting the BMD results in some of these groups. For postmenopausal women one typically uses the T score, which compares the individual's BMD to that of a healthy young adult.

The T score is expressed in terms of the number of standard deviations the individual's BMD falls above or below this norm. The World Health Orga-

nization defines osteoporosis as a T score of -2.5 or below, and osteopenia as a T score between -1 and -2.5.

But in premenopausal women, the use of T scores can be misleading. Instead, one should use the z score, which compares an individual's BMD with that of an age-matched sample.

The use of T scores would imply a relationship with fracture risk that may not

exist or may differ from group to group.

A postmenopausal woman with a certain BMD would have many times the fracture risk of a premenopausal woman with the same BMD.

Once one has a T score or z score, the question becomes whether to treat the patient's osteoporosis or osteopenia. The National Osteoporosis Foundation recommends treating all women with a T score of -2 or below, and women with at least one additional risk factor and a T score of -1.5 or below.

On the other hand, a recent study determined that it was not cost effective to treat osteopenic women because treatment does not significantly reduce their fracture risk over a 5-year period (Ann. Intern. Med. 2005;142:734-41).

But Dr. Lukert pointed out that it's unknown whether pharmacotherapy would improve fracture risk more than 5 years down the road.

"If we start treating the patient with a T score of -2 when she is 50 years old, maybe we won't change her fracture rate in the next 5 years, but at 65 will she have a reduced risk for fracture? That is a big unknown." ■

Postmenopausal women under 65 should be tested if they have any risk factors, but studies have not identified all of those risk factors.