

Decision to Measure Bone 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 with risk factors should be tested. 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.

The guidelines also call for BMD testing in men over 70. "We know very little about the development of osteoporosis in men, except that we do know that it's much more common than we had previously thought," Dr. Lukert said. "We aren't measuring bone density in men frequently enough."

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 that any adult taking one of these medications should have BMD testing.

Any adult who's 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.

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 a healthy young adult's. 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 Organization 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, men aged 50-64 with no risk factors, and in men aged 20-50 with risk factors, 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," she said. ■

Don't Halt Bisphosphonates Because of 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 55-80 years, 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, he said.

Among women in the study who gained

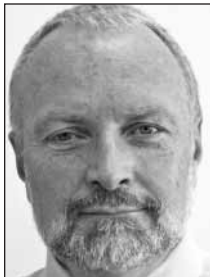
up to 4% of hip bone density in the first year on alendronate, 67% continued to gain an average of 1% bone density in the second year on therapy.

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 women who lost up to 4% of bone if they were taking alendronate, compared with placebo.

The greatest overall benefits occurred in women who lost more than 4% of bone density in the first year. In this subgroup, taking alendronate reduced the risk of fracture by 80%-90%, compared with placebo. "Stopping treatment in those patients who lose bone is exactly the wrong thing to do," said Dr. Cummings, who is a consultant and speaker for two companies that make 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, he said. ■



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DR. CUMMINGS

DHEA Demonstrates Mild Effect On BMD, But No Other Benefits

BY BETSY BATES
Los Angeles Bureau

SAN DIEGO — A long-term study of dehydroepiandrosterone supplementation in elderly men and women found no effect on body composition, muscle strength or performance, glucose metabolism, or quality of life.

There was a "trend... of borderline significance" for the effect of the popular supplement on bone mineral density, which was the only positive finding that approached statistical significance in the 2-year study, said K. Sreekumaran Nair, M.D., professor of endocrinology at the Mayo Medical School in Rochester, Minn.

Dr. Nair presented results of one of the few well-designed, long-term studies of dehydroepiandrosterone (DHEA) supplementation at the annual meeting of the Endocrine Society.

To provide an objective, long-term perspective, Dr. Nair and associates recruited 120 men and women (mean age, 69 and 70 years, respectively) with low dehydroepiandrosterone sulfate (DHEAS) levels, defined as concentrations below the 15th percentile for normal young adults. In men, bioavailable testosterone was also low, falling more than 1.5 standard deviations below the mean.

Eligible participants were randomized to receive supplemental DHEA (50 mg/day for women and 75 mg/day for men) or placebo for 20-24 months.

As expected, individuals taking DHEA had significant increases in DHEAS levels. Estradiol levels also rose significantly in both women and men taking DHEA. In women only,

testosterone levels increased significantly, from a mean 30 ng/dL to a mean 45 ng/dL.

At enrollment and upon completion of the study, researchers conducted a wide variety of tests to identify any potential changes in muscle function, fat distribution, and carbohydrate metabolism. These tests included maximum oxygen consumption, chest press, isometric and double-knee extension, thigh muscle mass by single-slice CT, and fat-free mass by DXA to evaluate muscle function, ratio of visceral to total fat to characterize fat distribution, and fasting glucose and insulin for carbohydrate metabolism. Also measured was bone mineral density at the L2-L4 spine, femur neck, total hip, distal radius, and ultradistal radius.

Quality of life was assessed by using both physical and mental competency scores. Dr. Nair ticked through the results methodically, demonstrating "no difference at all" in subjects taking DHEA vs. placebo on myriad measures. "Body fat-free mass? The same story," he said at one point.

Bone mineral density did improve slightly in subjects who were taking DHEA, compared with those taking placebo, mainly due to a 5.7% relative increase in ultradistal forearm BMD in women and a 2.6% relative increase in femur neck BMD in men. But Dr. Nair characterized the overall trend in BMD as "weak" evidence of DHEA's effectiveness.

On a more positive note, no adverse effects were associated with taking DHEA long term, Dr. Nair said during a symposium at the meeting. ■