

Testosterone Tx Fortifies Bone in Hypogonadal Men

BY JEFF EVANS
Senior Writer

BETHESDA, MD. — Testosterone replacement therapy in hypogonadal men appears to significantly improve trabecular bone architecture, according to the results of a small study.

Findings from previous studies suggest that testosterone replacement therapy increases bone mineral density in hypogonadal men, but none of these investigations looked at the effect of the hormone on trabecular architecture.

Maria Benito, M.D., reported at a meeting on bone quality the improvements seen in trabecular architecture in 10 hypogonadal men (median age 51 years) after 2 years of testosterone gel (AndroGel) therapy.

Each patient applied 5 g of a transdermally absorbed gel once per day and then received doses titrated to keep their serum testosterone level within the normal range of 400-900 ng/dL. The men increased their serum testosterone level from a mean of 88 ng/dL at baseline to 468 ng/dL after 2 years, said Dr. Benito of the division of endocrinology, diabetes, and metabolism at the University of Pennsylvania, Philadelphia.

Using micro MRI scans of the distal tibia taken at baseline, 6, 12, and 24 months, Dr. Benito and her colleagues matched architectural parameters in the images from each subject at

each time point to ensure that the same volume was analyzed each time. They measured the ratio of surface voxels (representing trabecular plates) to curve voxels (representing trabecular rods) and the ratio of topologic parameters expected to increase during trabecular deterioration to those expected to decrease (the topologic erosion index).

The improvement in trabecular architecture could not be attributed to BMI or calcium intake during treatment since neither factor changed substantially.

After 24 months of treatment, the ratio of surface to curve voxels increased significantly by 11% while the topologic erosion index decreased significantly by 8%; both measures indicate that trabecular architecture improved. Bone mineral density also rose significantly in the L1-L4 vertebrae by 7%.

The improvement in trabecular architecture could not be attributed to body mass index or calcium intake during treatment since neither factor changed substantially. Testosterone's effect on trabecular architecture suggests that it may exert an anabolic effect on bone, she said.

Men with a calcium intake of less than 750 mg per day, a history of disease, or on medications that could affect bone, were excluded from the study, Dr. Benito said at the meeting, sponsored by the National Institute for Arthritis, Musculoskeletal, and Skin Diseases and the American Society for Bone and Mineral Research.

Solvay Pharmaceuticals provided the AndroGel used in the study. Dr. Benito had no financial conflicts of interest to report. ■

Calcitonin Nasal Spray May Preserve Bone Architecture

BY JEFF EVANS
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BETHESDA, MD. — Calcitonin nasal spray appears to preserve trabecular bone microarchitecture at the distal radius without substantially altering bone mineral density, Charles H. Chestnut III, M.D., said at a meeting on bone quality.

In a 2-year, randomized, double-blind trial involving 91 women with an average age of 67 years, high-resolution MRI analysis of the distal radius showed that calcitonin nasal spray preserved significantly more trabecular bone architecture than placebo.

Calcitonin's effects included preservation of the volume, number, spacing, and thickness of trabecular bone, Dr. Chestnut wrote in a poster presentation at the meeting, which as sponsored by the National Institute for Arthritis and Musculoskeletal and Skin Diseases and the American Society for Bone and Mineral Research.

Trabecular bone microarchitecture was significantly preserved—if not reinforced—in calcitonin patients, compared with placebo patients, despite loss in bone mineral density (BMD) at the distal radius or lumbar spine during the same period. In placebo patients, the number of trabeculae declined

slightly at those sites even if the women had gained BMD.

The results are consistent with earlier reports showing that calcitonin spray was associated with reductions in osteoporotic fractures in postmenopausal women with a history of vertebral fracture, despite producing minimal increases in BMD, said Dr. Chestnut, professor of medicine and radiology at the University of Washington, Seattle.

Almost none of the measurements of BMD in the lumbar spine or midradius were significantly correlated with measures of trabecular microarchitecture change as shown on high-resolution MRI, suggesting that "BMD is a poor marker for trabecular microarchitecture," Dr. Chestnut wrote.

In the calcitonin group, trabecular microarchitecture in the lower trochanter was preserved, according to T2-MRI findings, regardless of whether patients lost or gained total hip BMD. By comparison, trabecular microarchitecture deteriorated in the placebo group.

All women in the trial received calcium supplementation.

Dr. Chestnut reported that he has received research grants and consulting fees from Novartis Pharmaceuticals Corp., which funded the trial and manufactures calcitonin-salmon nasal spray (Miacalcin). ■

Search for Genes Controlling Bone Quality Narrows With New Findings

BY JEFF EVANS
Senior Writer

BETHESDA, MD. — New chromosomal regions that possibly contain genes controlling bone quality were recently identified in the first genome-wide linkage scan of cross-sectional bone geometry in humans.

The few reported genetic studies of cross-sectional geometry have shown that the heritability is greater than 50%, "which means that in the general population, more than 50% of the phenotypic variation can be attributable to genetic events," Hui Shen said at a meeting on bone quality.

In a prospective study of 79 white pedigrees composed of 1,816 individuals, Mr. Shen of Creighton University, Omaha, Neb., and his colleagues calculated logarithmic odds (LOD) scores for bone geometry parameters at the femoral neck, including cross-sectional area, cortical thickness, endocortical diameter, sectional modulus, and buckling ratio in relation to 451 microsatellite markers.

On chromosome 10q26, the researchers calculated an LOD score of 3.29, the highest recorded in the study, for the buckling ratio at the femoral

neck. This indicates that the odds are nearly 2,000 to 1 in favor of genetic linkage between the two loci.

Three bone geometry parameters (cross-sectional area, cortical thickness, and buckling ratio) were linked to a broad region on chromosome 20p12-q12 with LOD scores ranging from 1.95 to 2.29. A candidate gene called bone morphogenetic protein 2 (BMP2) is located in that region.

BMP2 is known to regulate bone growth and in a recent study was identified as a genetic determinant of risk for osteoporosis (PLoS Biol. 2003;1:E69).

The researchers also observed some difference in the linkages for buckling ratio and cortical thickness between males and females. "Taken together, this evidence suggests a gene or a group of genes appearing in this area may have significant effects on [bone mineral density], bone geometry, and probably other fracture-related factors," said Mr. Shen, a doctoral student at Creighton's Osteoporosis Research Center.

The meeting was sponsored by the National Institute of Arthritis and Musculoskeletal and Skin Diseases and the American Society for Bone and Mineral Research. ■

Simple White Vinegar Test Gauges Bioavailability of Calcium Supplements

BY COLIN NELSON
Contributing Writer

DEDHAM, MASS. — All calcium supplements are not created equal. The stomach absorbs some better than others, Michael F. Holick, M.D., told a gathering of clinicians at a symposium on bone health sponsored by Boston University School of Medicine.

Dr. Holick said patients can use a simple test to gauge the ability of the GI system to absorb these pills. Toss one in white vinegar and see if the pill dissolves, said the Boston University professor and director of the Bone Healthcare Clinic at Boston Medical Center.

Though there is some controversy about the need for calcium supplements in teenagers and many adults, most experts agree there is one group of individuals who are likely to benefit from them—and also likely to suffer from an indigestible concoction. They are the frail elderly—frequently women, often institutionalized, and occasionally malnourished. The scientific literature and clinical experience generally agree that these individuals are at particular risk for hip fracture.

Healthy people generally get their calcium from their diet, Dr. Holick said. "There's 300 mg in an 8-ounce glass of milk, guaranteed." Other good sources of calcium in-

clude sardines, Tums, and calcium-fortified orange juice, he said.

As with calcium supplements, all sources of dietary calcium are not equal, he noted. At 100 mg calcium per cup, for example, "you'd have to be a cow in order to get enough calcium from broccoli."

For those individuals who don't get enough calcium in their diet, there are supplements. A huge industry has grown up around them, producing variable results.

A recent ER visit by a 17-year-old woman prompted Dr. Holick to share his calcium pills acid test with his colleagues. The patient arrived with serious abdominal pain. After some investigating, Dr. Holick discovered her calcium supplements were leaving her body in the same state they entered. They were not "bioavailable," he said.

"Take white vinegar and mix in the calcium preparation," Dr. Holick said. "In 20 minutes, if it doesn't dissolve in white vinegar, guess what? It's not going to dissolve in your stomach." In addition, when you find a good calcium supplement, "always take it with your meal," he advised.

Teenagers need 1,300 mg calcium/day, young and middle-aged adults need 1,000 mg/day, and adults over age 50 require 1,200 mg/day, according to the Institute of Medicine. ■