Testosterone Tx Fortifies Bone in Hypogonadal Men

BY JEFF EVANS

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 (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 bone modification to those expected to decrease (the topologic erosion index).

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. 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.

Solvy 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

BETHESDA, MD. — Calcitonin nasal spray appears to preserve trabecular bone microarchitecture at the distal radius. The study associated temporally 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 include preservation of bone volume, number, spacing, and thickness of trabecular bone, Dr. Chestnut wrote in a poster presentation at the meeting, which was 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 losses in bone mineral density (BMD) at the distal radius or lumbar spine during the same period. In placebo patients, the number of trabecular declined significantly 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, he said. Dr. Chestnut noted that trabecular architecture is associated with bone mineral density.

The improvement in trabecular architecture could not be attributed to BMI or calcium intake during treatment since neither factor changed substantially. The improvement in trabecular architecture was significantly preserved—if not reinforced—in calcitonin patients compared with placebo patients, despite losses in bone mineral density at the distal radius or lumbar spine during the same period. In placebo patients, the number of trabecular declined significantly at those sites even if the women had gained BMD.

Search for Genes Controlling Bone Quality Narrows With New Findings

BY JEFF EVANS

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 comprised 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 16, 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

DEDHAM, MASS. — All calcium supplements are not created equal. The stomach absorptions vary and are often dependent on the fat content of a meal. Once in the small intestine, calcium absorptions are less influenced by the type of supplement.

Some experts recommend substituting 30 mg of calcium per day, but others say it’s better to take smaller amounts, two or three times a day. Caution is advised with high dosages of calcium, which can result in the blocking of other nutrients as well as produce high blood pressure.

In a new study, scientists found that calcium supplements may be better absorbed if taken with white vinegar. Vitamin C is known to increase bone mineral density and prevents bone loss. The study was designed to determine if vitamin C increased the absorption of calcium in the gut.

The researchers from the University of California, Davis, first measured baseline blood levels of calcium and vitamin C in their volunteers. Then, they gave each volunteer a supplement that contained 340 mg of calcium carbonate and 100 mg of vitamin C in a daily dose. The volunteers were given a glass of milk or water with one tablet of calcium carbonate, 15 minutes before breakfast and dinner.

After some investigating, Dr. Holick discovered that 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, because you find a good calcium supplement, “always take it with your meal,” he advised.

Teenagers need 1,300 mg; adults need 1,000 mg per day, and adults over age 50 require 1,200 mg per day, according to the Institute of Medicine.