Lower Doses of Vitamin D Can Prevent Bone Fractures in Older Women with Vitamin D Insufficiency

Written by Rita Buckley

The first dose response study on multiple doses of vitamin D shows that older Caucasian women need less vitamin D to prevent vitamin D insufficiency than previously thought. J. Christopher Gallagher, MD, Creighton University Medical Center, Omaha, Nebraska, USA, presented findings from the Vitamin D Response Study: Effect on Serum 25-Hydroxyvitamin D and Parathyroid Hormone trial, a randomized, double-blind, placebo-controlled trial that involved healthy Caucasian postmenopausal women.

Participants included 160 women aged 57 to 90 years who had been postmenopausal for at least 7 years and who had vitamin D insufficiency, defined by the World Health Organization (WHO) as serum 25OHD less than 20 ng/ml. Subjects were randomized in eight groups of 20 and to one of seven vitamin D doses—400, 800, 1600, 2400, 3200, 4000, and 4800 IU/day—or placebo. All were given calcium supplements to maintain a total intake of 1200–1400 mg/day, based on 7-day food diaries. Exclusion criteria included significant comorbidities or drugs that interfered with vitamin D metabolism. The primary outcomes of the study were serum 25OHD and parathyroid hormone (PTH) levels after 12 months.

The mean age of participants was 67 years, and mean dietary intake of vitamin D was 115 IU/day. Serum 25OHD and serum PTH were collected every 6 months—the former was measured by radioimmunoassay; the latter, by immunoradiometric assay. Analysis of the vitamin D dose response data showed that a quadratic model was the best fit to the change in serum 25OHD, and a linear model was the best fit for change in serum PTH.

Of the total participants, 89% completed the study, with 91% compliance for vitamin D. On 400 IU/day, all of the subjects exceeded a serum 25OHD greater than 20 ng/ml. On 1600 IU/day, 90% exceeded a serum 25OHD greater than 30 ng/ml. On higher doses of between 4000–8000 IU/day, mean serum 25OHD plateaued between 40–45 ng/ml. The absolute increase in mean serum 25OHD per 100 IU for participants on 400 IU/day was 5 times that for those on the 4800-IU/day dose. Hypercalcemia and hypercalciuria were the only adverse events: hypercalcemia >10.6 mg/dL occurred in 4 subjects, and hypercalciuria >400 mg/dL 24 hours occurred in 17 subjects. These events were unrelated to dose.

All women who received 400 IU/day of vitamin D had adequate mean serum levels of 25OHD; ie, in excess of 20 ng/ml. Most of the women in the group that received 1600 IU/day reached a mean serum level of 30 ng/ml.

Prior to this report, the recommended daily dose of vitamin D was based on clinical trials that were limited by the small number of doses that was studied. The outcomes from this dose response study in subjects with vitamin D insufficiency suggest that 400 IU/day of vitamin D corrects vitamin D insufficiency and can be used to supplement the normal intake of vitamin D as a Recommended Dietary Allowance for bone health in older women. This finding is consistent with the 2011 report from the Food Nutrition Board/Institute of Medicine, which defined 400 IU/day as adequate for bone health.

Laparoscopic Gastric Banding Can Lead to Significant Weight Loss in Morbidly Obese Adolescents

Written by Lori Alexander

Data from a study of morbidly obese adolescents show that significant weight loss is achievable in a large percentage of adolescents following laparoscopic gastric banding. In addition, significant metabolic improvement is likely when at least 20% of excess body weight is lost. Shulamit E. Lerner, MD, Columbia University Medical Center, New York, New York, USA, reported the results of the study.

The rate of severe childhood obesity has tripled in the past 25 years, which has profound implications for the early-adult onset of cardiovascular disease and diabetes. Dietary interventions have typically resulted in limited weight loss (up to 10% of total body weight), leaving surgical interventions as the best options for morbidly obese adolescents [Skelton JA et al. *Acad Pediatr* 2009]. With gastric bypass surgery the standard of care for this population, the frequency of laparoscopic gastric banding has increased since 2005 [Jen HC et al. *Pediatrics* 2010].

The aim of the study was to determine the preoperative anthropometric and metabolic parameters that predicted significant weight loss after banding and the metabolic outcomes that are associated with significant weight loss. The study involved 63 adolescents who were followed up for at least 1 year after surgery. Thirty-eight of the 63 (9 male and 29 female) subjects lost an average of 50.5% excess body weight (29.7 kg), and 25 (12 male and 13 female) subjects lost an average of 2.9% excess body weight (3.2 kg).

The investigators evaluated the findings by analyzing and comparing the data from two groups of patients according to weight loss: those who lost at least 20% of excess body weight with those who had lost less than 20% of excess body weight.

Dr. Lerner said that predictors of weight loss were drawn from data that were collected at the patients' initial visits. Several factors were significant predictors of weight loss of at least 20% of excess body weight, including older age, taller height, lower body mass index (BMI) and BMI z-score, waist circumference/height, 30-minute glucose and 120-minute insulin levels on an oral glucose tolerance test, 1,25 dihydroxy vitamin D level, and no history of polycystic ovary syndrome; these factors were predictive at a significance of $0.01<p< 0.05$.

Thus, the ideal adolescent patient for gastric banding is characterized by achievement of 95% of final height, based on bone age assessment; a BMI >30 to 40 kg/m^2 with significant obesity-related comorbidity or BMI >40 kg/m^2 in the presence of milder obesity-related comorbidity; demonstration of ability to adhere to a lifestyle modification program prior to surgery and to both comprehend and be able to cope with nutritional and behavioral ramifications of bariatric procedures; no presence of eating disorders or other psychiatric illnesses, such as depression or exposure to abuse; and a supportive family environment [Keidar A et al. *Curr Opin Clin Nutr Metab Care* 2011].

Among the adolescents who lost at least 20% of excess body weight, decreased glucose and insulin levels on oral glucose tolerance test, lower systolic and diastolic blood pressures, alkaline phosphatase, uric acid, and sex hormone-binding globulin, and higher levels of high-density lipoprotein ($p<0.05$) were observed. These data indicate the potential for improved metabolic parameters for morbidly obese adolescents who lose at least 20% of excess body weight.

GH Replacement Improves CV Risk Factors in Viscerally Obese Premenopausal Women

Written by Rita Buckely

Effects of Growth Hormone (GH) on Body Composition and Cardiovascular (CV) Risk Markers in Women with Visceral Adiposity was a 6-month randomized, double-blind, placebo-controlled trial to determine whether low-dose GH administration would reduce abdominal adiposity and CV risk markers in premenopausal women with reduced GH secretion due to abdominal obesity. Miriam Bredella, MD, Massachusetts General Hospital, Boston, Massachusetts, USA, presented findings from the study.

Abdominal adiposity confers a 3-fold increased risk for heart disease in women compared with accumulation of body fat in the gluteal femoral region [Rexrode KM et al. *JAMA* 1998]. Data also suggest that visceral adiposity may be associated with reduced endogenous growth hormone and that decreased growth hormone secretion may be associated with increased CV risk markers [Utz A et al. *J Clin Endocrinol Metab* 2008].

The study included 79 obese premenopausal women. The primary outcome measure was abdominal fat depots, including: visceral adipose tissue and the muscle area of the mid-thigh, as determined by computed tomography scan; fat and lean body mass, determined by dual-emission X-ray absorptiometry; intramyocellular (IMCL) and intrahepatic lipids (IHL), determined by proton magnetic resonance spectroscopy; high-sensitivity C-reactive protein (hs-CRP); total cholesterol, high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C); apolipoprotein B (apo B); fibrinogen; tissue plasminogen activator (tPA); carotid intima-media thickness (CIMT); and endothelial function.

At 6 months, the mean GH dose was 1.7±0.6 mg/day. This resulted in a mean increase in the IGF-1 standard deviation score (SDS*) from -1.7±0.5 to -0.1±1.4 in the GH group. Compared with placebo, administration of GH led to an increase in muscle area (2.0±5.4 vs -3.0±6.8 cm^2; p=0.03) and total lean mass (2.0±1.7 vs 0.1±2.1 kg; p=0.001), and a decrease in the trunk:extremity fat ratio (0.01±0.05 vs -0.03±0.06; p=0.006)

Change in IGF-1 level was associated with a 6-month decrease in visceral adipose tissue (VAT) (r=-0.56; p=0.002). This suggested that subjects with the greatest increases in IGF-1 levels had the greatest decreases in VAT. VAT decreased within the GH group, but the change was not significant when compared with placebo.

Compared with placebo, GH decreased hsCRP (-1.1±1.2 vs 0.07±1.2 mg/L; p=0.01), apo B (-9.1±17.9 vs 6.1± 17.5 mg/dL; p=0.005), apo B/LDL-C (a measure of LDL-C size and atherogenecity) (-0.009±0.1 vs 0.1±0.2; p=0.01), and tPA (-0.4±5.0 vs 4.5±10.3 ng/ml; p=0.03). Total cholesterol, LDL-C, HDL-C, fibrinogen, IMCL, and IHL did not change compared with placebo, but IMCL increased compared with baseline in the GH group. No effect on CIMT or endothelial function was observed.

GH increased fasting glucose (2.4±7.2 vs -0.9±3.6 mg/dL) and 2-hour glucose (18.6±32.8 vs -0.7±26.7 mg/dL)