Bone and Mineral Metabolism

VITAMIN D, DIABETES AND ENERGY METABOLISM

Hemoglobin A1c of 7% is the Threshold For Bone Impairment in Men With Type 2 Diabetes Mellitus.

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Background: Emerging data suggest that type 2 diabetes mellitus (T2DM) is associated with increased risk for fractures despite relatively normal or increased bone mineral density (BMD). Furthermore, it is now known that decreased bone turnover mainly due to reduced bone formation is the hallmark for bone disease in T2DM. Whether glucose control is important in generating this impairment in bone metabolism remains unknown and to what extent it would reflect this abnormality is undetermined. The purpose of our study is to identify Hemoglobin A1c (A1c) level threshold by which reduction in bone turnover begins. **Method:** Baseline data from 217 men between age of 35–65 who were participants in 2 clinical trials conducted at the Michael DeBakey VA Medical Center and the New Mexico VA Health Care System were analyzed. A1c was measured by high performance liquid chromatography, testosterone and estradiol measured by liquid chromatography/mass spectrometry (LC/MS). Bone turnover markers (Osteocalcin [OC],C-telopeptide of type 1 Collagen [CTx]) and sclerostin were measured by enzyme-linked immunosorbent assay. Bone mineral density was assessed by dual energy X-ray absorptiometry. Patients were grouped into 4 categories based of A1c values (%) (group 1:<6, group 2:6.1–6.5, group 3: 6.6–7 and group 4: >7). Simple correlations were assessed by simple regression analysis and group comparisons among the different A1c categories were performed by analysis of variance (ANOVA). **Results:** The mean age of the participants was 55±9 years old with mean BMI of 36.15±6.44 kg/m^2. Participants mean A1c was 6.1±1.5%. Simple correlation analysis showed a significant negative correlation between A1C and OC (r=-0.32, p<0.001) and CTx (r=-0.32, p<0.001). Comparison of bone turn over markers among different A1c groups revealed significantly lower OC in group 4 (A1C>7%), compared to groups with A1Cs ≤7%, i.e. 1, 2 and 3 (4.04 ± 2.64 vs 6.53 ± 3.18, 5.99 ± 3.16 and 6.09 ± 3.16 ng/mL, respectively, p = 0.002). Similarly, CTx was lower in group 4 compared to groups 1, 2, and 3 (0.19 ± 0.12 ng/mL vs 0.34 ± 0.17, 0.32 ± 0.18 and 0.28 ± 0.14 ng/mL, respectively, p=0.0002). Sclerostin levels were comparable among all the A1c categories. Analysis of the subgroup of men with T2DM (n=71) again showed lower OC (3.95 ± 2.68 vs. 6.34 ± 2.77, p=0.007) and CTx (0.18 ± 0.13 vs. 0.31 ± 0.15, p<0.001) in those with A1c >7% compared to those ≤7%, respectively. The significance between the groups persisted even after adjusting for medications, p=0.003. Analysis adjusted for baseline age, weight and testosterone showed no significant difference in areal BMD at all sites in the general population and in the subset of men with T2DM according to A1C categories. **Conclusion:** Our data analysis showed breakpoint A1c level of 7% or greater is associated with lower bone turnover irrespective of medication use in patients with T2DM.

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In a Clinical Trial There Was No Effect of Vitamin D on Physical Performance in Either Black or White Women

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Introduction: The effect of vitamin D supplementation on physical performance is controversial. Longitudinal cohort studies show very low levels of serum 25OHD (< 15-20ng/ml) are associated with lower physical performance. There are few clinical trials of the effect of vitamin D on physical performance and results are mixed. **Design:** 163 white and 110 black independent living women entered a 12-month double blind randomized dose ranging study of daily vitamin D,400,800,1600,2400,3200,4,000,4800IU or placebo together with calcium supplement as needed for a total intake of 1200mg and mean diet vitamin D of 114 IU. Inclusion criteria: total serum 25OHD ≤ 20ng/ml (Diasorin RIA); no known disease or drugs affecting calcium or bone metabolism. Physical performance tests were performed at baseline and end as described in the Short physical performance battery (SPPB) that included Balance, Timed walk, Chair rising test. Additional tests included Timed up and Go, Grip strength and Balance (Biodex). Fall history was recorded at baseline and at 3-monthly visits. Serum 25OHD was measured by Diasorin RIA and LCMS, Free 25OHD was measured by Elisa (Future Diagnostics). Changes in physical performance and fallers were analyzed by dose groups and by quintiles of total and free serum 25OHD. This was a secondary analysis using Intent to treat strategy. Chi square and ANOVA determined association between dose, quintiles and tests. **Results:** Mean age 66.2 years (SD 7.3, range 57–87), mean BMI 30.3 kg/m2 (SD 5.9). Compliance, measured every 3 months, was 94% for vitamin D and 91% calcium. 147 White and 89 Black women completed study. There was significant better performance in physical performance in women < age 70 years compared to > age 70 years. Black women performed better with all tests except grip strength after adjustment for age and BMI. When the absolute change in test performance was examined according to serum total or free 25OHD quintiles there was no correlation between serum levels of 25OHD and change in any physical performance test except for an improvement in chair rising test in younger Black women. **Conclusions:** There is no significant effect of vitamin D on physical performance in either black or white women. In a previous analysis we found a significant U-shaped response in fall incidence in the serum 25OHD range 30-40ng/ml but in this analysis there is no correlation between physical performance of fallers versus non- fallers