25-Hydroxyvitamin D Concentration Correlates With Insulin-Sensitivity and BMI in Obesity

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The prevalence of hypovitaminosis D is high among obese subjects. Further, low 25-hydroxyvitamin D (25(OH)D) concentration has been postulated to be a risk factor for type 2 diabetes, although its relation with insulin-sensitivity is not well investigated. Thus, we aimed to investigate the relationship between 25(OH)D concentration and insulin-sensitivity, using the glucose clamp technique. In total, 39 subjects with no known history of diabetes mellitus were recruited. The association of 25(OH)D concentration with insulin-sensitivity was evaluated by hyperinsulinemic euglycemic clamp. Subjects with low 25(OH)D (<50 nmol/l) had higher BMI ($P = 0.048$), parathyroid hormone (PTH) ($P = 0.040$), total cholesterol ($P = 0.012$), low-density lipoprotein (LDL) cholesterol ($P = 0.044$), triglycerides ($P = 0.048$), and lower insulin-sensitivity as evaluated by clamp study ($P = 0.047$). There was significant correlation between 25(OH)D and BMI ($r = -0.58$; $P = 0.01$), PTH ($r = -0.44$; $P < 0.01$), insulin-sensitivity ($r = 0.43$; $P < 0.01$), total ($r = -0.34$; $P = 0.030$) and LDL ($r = -0.40$; $P = 0.023$) (but not high-density lipoprotein (HDL)) cholesterol, and triglycerides ($r = 0.45$; $P = 0.01$). Multivariate analysis using 25(OH)D concentration, BMI, insulin-sensitivity, HDL cholesterol, LDL cholesterol, total cholesterol, and triglycerides, as the cofactors was performed. BMI was found to be the most powerful predictor of 25(OH)D concentration ($r = -0.52$; $P < 0.01$), whereas insulin-sensitivity was not significant. Our study suggested that there is no cause–effect relationship between vitamin D and insulin-sensitivity. In obesity, both low 25(OH)D concentration and insulin-resistance appear to be dependent on the increased body size.

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INTRODUCTION

25-Hydroxyvitamin D (25(OH)D) is well known for its role in regulating calcium absorption and bone metabolism. There are accumulating data suggesting its pleiotropic effects and possible involvement in the pathogenesis of cardiovascular diseases (1) and metabolic syndrome (2). Metabolic syndrome with low 25(OH)D concentration has been reported to be highly prevalent among severely obese patients (3–5). Obesity is therefore considered to be a risk factor for hypovitaminosis D. The cause of low 25(OH)D concentration in obese individuals is still under debate, where enhanced uptake by adipose tissue (4), sunlight underexposure (6), or low dairy consumption of calcium and vitamin D (7) are the most plausible explanations. Interestingly, although high parathyroid hormone (PTH) is usually viewed as a compensatory mechanism for low 25(OH) vitamin D, PTH has also been reported as an independent risk factor for diabetes (8,9). On the contrary, there is evidence to suggest that the association between 25(OH)D and impairments in glucose metabolism may be independent of PTH concentration, supporting a direct role for 25(OH)D in pancreatic β-cell function and insulin-sensitivity (10). Further, low 25(OH)D concentration has been found to be associated with reduced glucose tolerance (11,12), dyslipidemia (13,14), hypertension (15,16), and obesity (3–5), strengthening the hypothesis that vitamin D may play a role in the etiology of "metabolic syndrome" either via an association with individual components of metabolic syndrome or via insulin-resistance. Several studies examined the vitamin D status and insulin-resistance, with conflicting results (17–19). Such controversy is most probably due to variability of the method used. It is recognized that indirect indexes of insulin-resistance derived from fasting values of insulin and glucose mostly reflect hepatic insulin-sensitivity, whereas post-oral glucose tolerance test indexes do not take into account all variables influencing the results, including insulin secretion. Thus, the present study was designed to examine the relationship of 25(OH)D with insulin-sensitivity, as evaluated by hyperinsulinemic euglycemic clamp, the gold-standard method for measuring insulin-sensitivity independently from insulin secretion and obesity.

METHODS AND PROCEDURES

Thirty-nine subjects who attended our division were considered for inclusion (18 males and 21 females, aged 41.4 ± 12.4 years, BMI 30.1 ± 5.4 kg/m^2) after approved consent. None of the study participants had relevant endocrine or nonendocrine diseases, including diabetes mellitus.

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