Does vitamin D influence energy metabolism in children and adolescents?

Anna Wędrychowicz, Jerzy B. Starzyk
Department of Pediatric and Adolescent Endocrinology, Pediatric Institute, Medical College, Jagiellonian University in Cracow, Poland

Abstract

Background: Recent years bring a lot of data of the important role of vitamin D in different physiological processes, including a prevention from pathological states.

Objective and hypotheses: The aim of the study was to analyze associations between serum level of vitamin D and some markers of glucose and lipid metabolism but also as well bone-related molecules as adiponectin in children and adolescents.

Method: Fifty-seven patients, 40 with type 1 diabetes mellitus (T1DM), 17 with obesity, and 11 controls, healthy age, and BMI-matched children were included in the study. Fasting blood samples for measurement of vitamin D, lipid profile, glucose, HbA1c concentrations, but also as well bone-derived molecule: osteocalcin (OC), sclerostin and Receptor Activator of Nuclear Factor-KB ligand (RANKL), as fat tissue-derived leptin and adiponectin were taken at 0:00 AM. Vitamin D was measured by HPLC, hormones by immunochrometry, and other parameters by routine chemistry methods. Statistical analysis was performed in all groups using ANOVA with post-hoc Turkey test and multiple regression analysis.

Results: Vitamin D levels did not differ among these three groups: patients with T1DM, obese patients, and healthy ones. There were significant differences regarding C-peptide, HbA1c, fasting glucose, leptin, LDL-cholesterol, HDL-cholesterol, HOMA-IR, and HOMA-B levels among groups p<0.001. In multiple regression analysis vitamin D was negatively correlated with HOMA-IR, adiponectin, and HOMA-B in children (p<0.01). The partial regression coefficient of vitamin D for HOMA-IR was strong (β= -0.64). The group of patients with T1DM vitamin D correlated negatively with HbA1c (r=-0.3, p<0.03). In the control group vitamin D was positively related to OC (p=0.029).

Conclusion: The results of our study suggest that vitamin D could influence energy metabolism in children and adolescents. Its action seems to be associated with well insulin action as with bone-derived osteocalcin.

The authors have NOTHING TO DISCLOSE.

Background

Recent decades bring some studies confirmed that vitamin D plays an important role not only in skeletal health but also vitamin D might provide additional major health problems such as autoimmune disease, cardiometabolic disease, and cancer.

Receptor for vitamin D (VDR) is present in most cells and tissues in the body. 1,25(OH)2D3 is one of the most potent regulators of cellular growth in both normal and cancer cells. It has been suggested that increased vitamin D intake or increased exposure to sunlight, raising blood concentrations of 25(OH)D above 78 nmol/L (30 ng/mL), is necessary for maximal extramural production of 1,25(OH)2D3 in a wide variety of tissues and cells in the body, including colon, breast, prostate, lung, activated macrophages, and parathyroid cells.

The local production of 1,25(OH)2D3 is thought to be important for keeping cell growth in check and possibly preventing the cell from becoming autonomous and developing into a recurrent cancer cell. Activin A and B and 8-hydroxyproline VDRs, 1,25(OH)2D3 is a very effective modulator of the immune system. In a variety of animal models, it has been demonstrated that pretreatment with 1,25(OH)2D3 in vivo is effective in mitigating or preventing the onset of type 1 diabetes mellitus, multiple sclerosis, rheumatoid arthritis, and Crohn’s disease. In addition, in a mouse model, 1,25(OH)2D3 was an effective inhibitor of the blood pressure hormone renin. Deficiency of vitamin D was presented to have significant associations with diabetes mellitus and metabolic syndrome. In obese children vitamin D is related to hyperinsulinemia. It was reported that hypovitaminosis D is a risk factor for developing insulin resistance independent of adiposity.

The question is how vitamin D could influence metabolism? The possible explanation is that vitamin D action significantly acts on insulin action via osteocalcin. Osteocalcin, the most abundant noncollagenous protein in bone, is a marker of bone turnover in normal and disease states. Its synthetic production is controlled by parathyroid hormone, the active hormonal form of vitamin D, through the vitamin D receptor and a specific vitamin D-responsive element in the osteocalcin gene promoter. On the other hand vitamin D depletion induces RANKL-mediated osteoclastogenesis and bone loss.

Bone-derived osteocalcin is a hormone pharmacologically active on glucose and fat metabolism. There was shown that osteocalcin stimulates insulin secretion and β-cell proliferation. Insulin signaling in osteoblasts integrates bone remodeling and energy metabolism.

The hypotheses of our study built on the base of above-mentioned information granted that the influence of vitamin D on metabolism is visible via its antidiabetic, antiinflammatory, and bone-related role and since it is related with bone-derived osteocalcin, RANKL, adiponectin leptin and adiponectin and insulin action. Therefore we decided to test these hypotheses in two groups: the patients with type 1 diabetes mellitus – an autoimmune disease and in the obese patients with probable insulin resistance.

Table 1.

<table>
<thead>
<tr>
<th>Group</th>
<th>OC [mg/L]</th>
<th>RANKL [ng/mL]</th>
<th>Leptin [ng/mL]</th>
<th>Adiponectin [µg/mL]</th>
<th>HbA1c [%]</th>
<th>FG [mmol/L]</th>
<th>BMI [kg/m²]</th>
<th>Insulin [mU/L]</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1DM</td>
<td>26.3±5.0</td>
<td>143.6±13.3</td>
<td>6.13±0.9</td>
<td>6.25±0.63</td>
<td>7.7±0.3</td>
<td>0.9±0.2</td>
<td>20.9±4.8</td>
<td>0.9±0.1</td>
</tr>
<tr>
<td>obese</td>
<td>30.6±1.7</td>
<td>44.3±5.1</td>
<td>5.1±0.9</td>
<td>5.2±0.0</td>
<td>7.1±0.6</td>
<td>0.8±0.5</td>
<td>27.6±12.7</td>
<td>0.7±0.3</td>
</tr>
</tbody>
</table>

Results

The aim of the study was to analyze associations between serum level of vitamin D and some markers of glucose and lipid metabolism: fasting glucose level, HbA1c, lipid profile, as well as bone-related molecules: osteocalcin (OC), sclerostin and Receptor Activator of Nuclear Factor-KB ligand (RANKL), as adiponectin leptin and adiponectin in children and adolescents in different metabolic conditions: type 1 diabetes mellitus (T1DM) and obesity.

Methods

Patients

Forty children, 21 girls and 19 boys, mean age 12.2±4.6 yrs with T1DM and 17 obese children, 9 girls and 8 boys, mean age 11.3±3.8 yrs were included into the study. Control groups consist of 11 children, mean age 11.5±4.9 yrs (figure 1).

Figure 1. Characteristics of the groups included in the study.

Anthropometrical measurements

Height was measured to the nearest centimeter using a rigid stadiometer. Weight was measured unclocked to the nearest 0.1 kg using a calibrated balance scale. Reference data for Polish Children were used (Paczowska, 1999). Body mass index (BMI) will be calculated as weight in kilograms (kg) divided by the height in meters (m²). Homeostatic model assessment (HOMA) was used to quantify insulin resistance (IR).

Material

Blood samples were drawn once from the antecubital vein in the fasting state, at 08:00 hours. HbA1c level was measured at once. After clotting, blood samples were centrifuged. Serum was stored in −80°C until the time of measurement of required parameters.

Biochemical methods

25(OH)D3 was measured with HPLC. Serum levels of osteocalcin (Diasource), RANKL (Biomedica), leptin (Diasource), and adiponectin (Diasource) were measured by ELISA methods.

HbA1c was measured by standardized ICS chemistry method. Serum glucose level was measured by dry chemistry, and lipids with an enzymatic method (routine chemistry method).

Statistical analysis

Statistical analysis was performed using the Statistica software package. In statistical analysis ANOVA with post-hoc Turkey test, and multiple regression analysis were used.

Results

There were significant differences regarding C-peptide, Insulin, HbA1c, fasting glucose, insulin, C-peptide, LDL-cholesterol, HOMA-B, and moreover leptin levels among groups p<0.001 (Table 1 and Table 2).

Vitamin D levels did not differ among three groups: patients with T1DM, obese patients, and healthy ones (Table 2).

Table 2. Differences in lipid profile and vitamin D levels (mean±SD data are presented) among the group of patients with T1DM, obese patients and controls.

<table>
<thead>
<tr>
<th>Group</th>
<th>Chol [mmol/L]</th>
<th>Trig [mmol/L]</th>
<th>HOMA [mmol/L]</th>
<th>LDL [mg/dL]</th>
<th>HDL [mg/dL]</th>
<th>Insulin [mU/L]</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1DM</td>
<td>4.5±1.1</td>
<td>2.8±1.0</td>
<td>0.7±0.3</td>
<td>3.6±0.8</td>
<td>9.7±1.0</td>
<td>0.8±0.3</td>
</tr>
<tr>
<td>obese</td>
<td>5.0±1.2</td>
<td>3.1±1.2</td>
<td>1.2±0.3</td>
<td>3.8±0.9</td>
<td>7.8±1.0</td>
<td>0.9±0.4</td>
</tr>
</tbody>
</table>

Conclusion

The results of our study suggest that vitamin D could influence energy metabolism in children and adolescents. Its action seems to be associated with bone-derived osteocalcin and insulin action.

Acknowledgements

This study was supported by a grant of K2DS5/00113/12, from Medical College, Jagiellonian University in Cracow.