Does vitamin D influence energy metabolism in children and adolescents?

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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 adipokines in children and adolescents.

Method: Fifty-seven patients, 40 with type 1 diabetes mellitus (T1DM), 17 with obesity, and 11 control, 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 sclerostin, osteocalcin (OC) and Receptor Activator of Nuclear Factor NF-κB ligand (RANKL), as fat tissue-derived leptin and adiponectin were taken at 8.00 AM. Vitamin D was measured by HPLC, hormones by immunochemistry, 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 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, HDL-cholesterol/Total Cholesterol levels among groups p<0.001. In multiple regression analysis vitamin D was negatively related to HOMA index in obese children (p=0.01). The partial regression coefficient of vitamin D for HOMA-IR was strong (r= -0.64). In 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=0.028).

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 as 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 protection against major health problems such as autoimmune disease, cardiometabolic disease, and cancer. I

Receptor for vitamin D (VDR) is present in most cells and tissues in the body. 1,25(OH)2D 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 extrarenal production of 1,25(OH)2D 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)2D is thought to be important for keeping cell growth in check and possible preventing the cell from becoming autonomous and developing into a unregulated cancer cell. Activated T and B lymphocytes have VDRs. 1,25(OH)2D 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)2D 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)2D 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 synthesis is induced by calcitriol, the active hormonal form of vitamin D, through the vitamin D receptor and a specific vitamin D-responsive element in the osteocalcin gene promotor. 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 association with some glucose and lipids paramethers and moreover it is related with bone-derived osteocalcin, RANKL, adipokines: 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.

Objective

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, lipids profile,
- as well bone-related molecules: osteocalcin (OC), sclerostin and Receptor Activator of Nuclear Factor NF-κB ligand (RANKL),
- as adipokines: leptin and adiponectin,

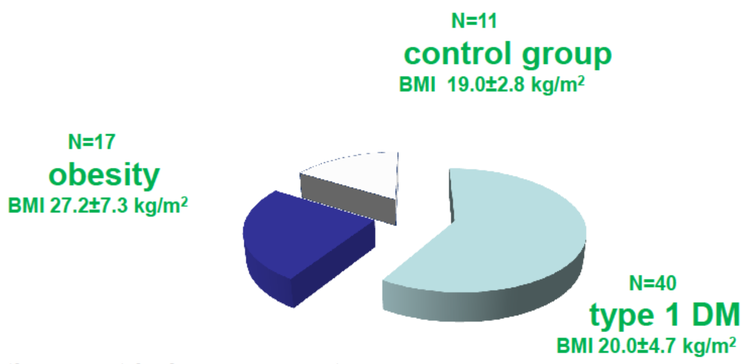
in children and adolescents in different metabolic conditions: type 1 diabetes mellitus (T1DM) and obesity.

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±5.0 yrs [Figure 1].

Figure 1. Characteristic of the groups included into the study.



Anthropometrical measurements

Height was measured to the nearest centimeter using a rigid stadiometer. Weight was measured unclothed to the nearest 0.1 kg using a calibrated balance scale. Reference data for Polish Children were used [Palczewska, 1999]. Body mass index (BMI) will be calculated as weight in kilograms (kg) divided by the square of height in meters (m^2). 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 ISCC 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, HDL-cholesterol/Total Cholesterol , 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 1.
Mean±SD data of OC, RANKL, leptin, adiponectin, HbA1c, fasting serum glucose (FG), Insulin and C-peptide in patietns with T1 DM, obese patients and in controls.

Group	OC [ng/ml]	RANKL [pmol/l]	Leptin [ng/ml]	Adipo-nectin [ug/ml]	HbA1c [%]	FG [mmol/l]	Insulin [ulU/ml]	C-peptide [ng/ml]
T1 DM	26.3±16.6	24.9±43.8	2.2±3.3	11.6±4.4	7.7±1.6	7.9±2.9	-	0.54±0.2
obese	28.9±17.4	44.3±51.6	8.1±5.9	6.2±5.3	5.2±0.2	4.4±0.5	15.6±4.5	1.52±0.6
control	21.7±15.9	28.2±40.7	2.4±0.9	7.7±3.3	5.4±0.1	4.4±0.6	11±5.8	0.96±0.3
p	NS	NS	<0.001	NS	<0.001	<0.001	NS	<0.0001

Results

Table 2.
Differences in lipid profile and Vitamin D levels (mean±SD data are presented) among the groups of patients with T1 DM, obese patients and controls.

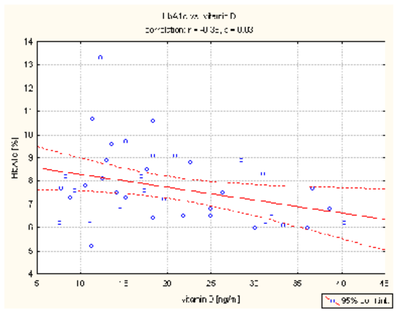
Group	Chol [mmol/l]	TGL [mmol/l]	HDL [mmol/l]	LDL [mmol/l]	HDL/TC [%]	25(OH)D_3 [ng/ml]
T1 DM	4.43±0.7	1.01±0.7	1.57±0.3	2.36±0.7	35.97±7.8	20.4±9.4
obese	4.67±1.1	1.5±1.0	1.18±0.3	3.04±0.8	26.0±7.2	17.2±9.2
control	3.94±0.8	1.02±0.5	1.42±0.3	2.04±0.6	37.3±10.1	19.2±9
p	0.07	0.07	<0.0001	<0.001	<0.001	NS

HOMA-IR in the group of obese patients was not significantly higher 2.89±1.14 uIU/ml x mmol/l than in healthy ones – 1.93±1.08 uIU/ml x mmol/l (p = 0.069).

Type 1 DM patients

Multiple regression analysis adjusted for age and BMI showed that serum level of vitamin D was negatively related to HbA1c level (p=0.03) [Figure 2]. Moreover HbA1c was negatively related to OC (p=0.004).

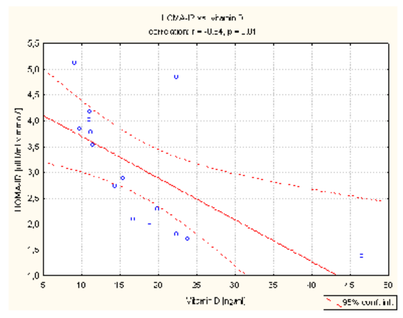
Figure 2
The linear association between vitamin D and HbA1c (r = -0.3, p=0.03) in children with type 1 DM



Obese patients

In multiple regression analysis vitamin D was negatively related to HOMA index in obese children (p=0.01). The partial regression coefficient of vitamin D for HOMA-IR was strong (r= -0.64) [Figure 3].

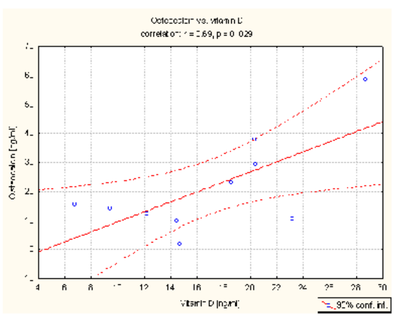
Figure 3
The linear association between vitamin D and HOMA index (r = -0.64, p=0.01) in obese patients.



Control group

In control group vitamin D was positively related to OC level (p=0.03) [Figure 4].

Figure 4
The linear association between vitamin D and OC level (r=0.7, p=0.028) in healthy children.



In multiple regression analysis vitamin D did not correlate with sclerostin. RANKL, adipokines: leptin and adiponectin, lipids parameters in any of examined groups.

Conclusions

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.

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