EFFECT OF VITAMIN D STATUS ON LIPID METABOLISM OF CHILDREN

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Abstract: It has been proven that the functions of vitamin D are not limited to the control of calcium-phosphorus metabolism, but its other pleiotropic effects are being studied.
The aim of our study was to study vitamin D status and its effect on the lipid profile in children of risk group for the development of dyslipoproteinemia.
Materials and methods. 30 children aged 6–7 years (mean age 6.4±0.6 years) who were born to women with diabetes were examined. The control group – 30 children 6–7 years old (6.5±0.5 years) from healthy mothers.
An assessment of physical development was carried out with the calculation of body mass index.
We studied lipid metabolism indicators - total cholesterol, triglycerides, high density lipoprotein cholesterol, low density lipoprotein cholesterol (mmol/l) in blood, atherogenic index. All children were determined with the content of 25-OH-D in the serum, the level of glucose.
Results. 10 (33.3 %) children from mothers with diabetes are overweight, 5 (16.7 %) – obesity, which is 2 times higher than in the control group.
The fasting glucose level in all the examined children from mothers with diabetes was within physiological fluctuations.
The level of 25-OH-D in children from mothers with diabetes mellitus, compared with the control group, was significantly reduced.
Dyslipoproteinemia was found in children from diabetic mothers: a significant increase in serum triglyceride and cholesterol levels, higher levels of low-density lipoprotein cholesterol and lower levels of high-density lipoprotein cholesterol than in the control group ($p < 0.05$), atherogenic index was significantly higher.
Prospects for further research are to explore the possibility of using vitamin D for the primary prevention and treatment of metabolic syndrome, diabetes in children.
Conclusions. Vitamin D deficiency in the body of the surveyed can be one of the causes of their dyslipidemia, in addition, overweight and obesity are also risk factors for the development of atherosclerosis, metabolic syndrome. Children at risk need dynamic monitoring of anthropometric indicators, control of body mass index, lipid and carbohydrate blood profile, level 25-OH-D.
Keywords: children, diabetes, dyslipoproteinemia, obesity, cholesterol, vitamin D, lipoproteins, atherogenic index.

1. Introduction

Currently, there have been many studies on the supply of the human body with vitamin D (VD) and its biological role in the body.

It has been proven that VD functions are not limited to the control of calcium-phosphorus metabolism, but its other pleiotropic effects are being studied [1].

The active form of VD takes part in the regulation of cell differentiation, proliferation, apoptosis, thereby inhibiting tumor growth; stimulates insulin synthesis by β-cells of the pancreas and increases the sensitivity of human cells to insulin, regulates the function of T and B lymphocytes, macrophages, pro-inflammatory cytokines. The results of large-scale scientific studies of recent years indicate its important role in the development of the metabolic syndrome, endocrine disorders, including type 1 and type 2 diabetes, allergic, autoimmune, cardiovascular diseases in children.

Worldwide population studies have established that the prevalence of VD deficiency and hypovitaminosis reaches an epidemic level. Thus, when examining the adult population of Ukraine, it was noted that only 4.6 % of residents have a VD level within the normal range, 13.6 % have a deficiency, and 81.1 % have a VD hypovitaminosis. Population studies of the prevalence of VD hypovitaminosis in children in Ukraine have not been conducted, but according to some authors, its frequency is 88.5 % in children of school age [2].

Taking into account the above data, further study of the VD status in children of different ages and its pleiotropic effects is promising.

The aim of the research was to study the VD status and its possible effect on the lipid profile in children at risk for the development of dyslipoproteinemia.

2. Methods

The study was conducted on the basis of the Centre of primary health care No. 4 of the city of Kiev during 2016–2017 years.

A total of 30 children aged 6–7 years old (mean age 6.4± ±0.6 years) who were born to women with diabetes mellitus (DM) were examined comprehensively. As a control group, 30 children aged 6–7 years old (mean age 6.5±0.5 years) were examined, who were born to healthy mothers.

Children's anthropometric indicators (height, weight) were measured, the calculation of body mass index was done by the formula:

BMI=body weight,
kg/square of height, m^2.

Anthropometry was performed by the standard method with an accuracy of 0.1 cm for growth and 0.1 kg for body weight. BMI (kg/m^2) was estimated using percentile curves taking into account standard deviations (SD) for a certain age and sex [3]. Obesity in children was diagnosed with IMT>95 percentile (from +2 to +3 SD), overweight – with a BMI of 85–95 percentile (from + 1 to + 3 SD).

Children also were studied with lipid metabolism indicators – total cholesterol (CS), triglycerides (TG), high density lipoprotein (HDL), low density lipoprotein (LDL), mmol/l in the blood by the enzymatic-colorimetric method using RocheDiagnostics kits (Switzerland) on the analyzer Cobas 6000.

The atherogenic index (AI) was determined by an indirect calculation method according to the formula of A. N. Klimov:

IA=(CS–HDL)/HDL.

A qualitative assessment of the lipid profile was carried out according to the adapted NCEP/ATPIII and ADF criteria.

In addition, the state of carbohydrate metabolism was assessed by the level of glucose in the blood by the enzyme hexokinase method.

The content of 25-OH-D in serum was determined by the ELISA kit 25-OH-VitaminD-ELISA (BioVendor, Germany) according to the instructions of the manufacturer.

The obtained data were processed on a personal computer using the statistical package Statistica 7 StatSoftInc. with the use of parametric and non-parametric estimation methods.

3. Results

In assessing the health status of children who were under observation, they took into account the family history data, information about the state of health, the severity of diabetes

in the mother and the degree of compensation of carbohydrate metabolism, as well as the features of the course of pregnancy and childbirth.

It is known that 16 (53.3 %) women suffered from type 1 diabetes, 12 (40 %) – type 2, 2 (6.6 %) had gestational diabetes. Severe obstetric and gynecological anamnesis was detected in 24 (80 %) women (spontaneous abortion, premature birth, infertility, abortion for medical reasons, antenatal fetal death). All mothers of the examined children had diabetes combined with other chronic diseases — hypertension, chronic pancreatitis, cholecystitis, peptic ulcer. An analysis of the children's developmental histories showed that 20 (66.6 %) children were born by caesarean section, 23 (76.6 %) - in mild asphyxia, 5 (16.7 %) – moderate one; 4 (13.3 %) had respiratory distress syndrome on the background of lung atelectasis, 7 (23.3 %) children were born prematurely, all children showed signs of diabetic fetopathy, which is corresponds to the literature data on this issue [4, 5].

It should be noted that 80 % of the children we observed often had respiratory viral infections – 10 or more times throughout the year, had complications in the form of sinusitis, pneumonia, otitis. Most of the observed children were contingent with nidus of chronic infection – chronic tonsillitis was diagnosed in 10 (33.3 %) children, adenoid vegetations of II-III degree – in 10 (33.3 %) children.

As shown by the results of clinical studies, among all diseases in children who were born from mothers with diabetes, the pathology of the digestive system has a high proportion – so 80 % of the observed children had dysfunction of the biliary system, 23.3 % had functional dyspepsia.

An assessment of the physical development of the observed children showed that 10 (33.3 %) children from mothers with diabetes are overweight, 5 (16.7 %) are obese. Moreover, 23.3 % of the mothers of the children surveyed were also obese, and in many children the immediate maternal relatives also had an overweight. It should be noted that in the control group the number of children with excess body weight was significantly less than in the group of children from mothers with diabetes (a total of 5 children – 16.7 %), obesity was diagnosed in 2 children (6.6 %).

The state of carbohydrate metabolism in children from mothers with diabetes and in children of the control group was studied. The fasting glucose level in all the examined children from mothers with diabetes was within the range of physiological fluctuations and did not differ from that in children of healthy mothers.

The study of the provision of VD showed that the level of its transport form 25-OH-D in children from mothers with diabetes, compared with the control group, was significantly reduced and amounted to 19.63 ng/ml (in children of healthy women – 32.3 ng/ml). This indicates a marked deficiency of this active metabolite of VD, its transport form in the body in children from mothers with diabetes.

It is possible that VD deficiency may be the result of nutritional deficiency, which does not meet the increased needs of a growing organism, a decrease in its synthesis in the skin, metabolic disorders as a result of functional changes in target organs, connection disruptions of VD-receptor protein and the number of receptors to it [6].

In the study of lipid metabolism, there were significant impairments in the group of children from mothers with diabetes (**Table 1**). Thus, according to our data, dyslipoproteinemia was detected in the observed children: a significant increase in serum TG and cholesterol levels compared with the control group.

The analysis of the serum lipid spectrum showed that children from mothers with diabetes have higher LDL levels and lower HDL levels than in children from the control group ($p<0.05$). IA was significantly higher in the group of children from mothers with diabetes.

Table 1

Indicators of lipid metabolism in children 6–7 years old, who were born to mothers with diabetes (M±m)

Indicators	Children of mothers with diabetes, n=30	Control group, n=30
Triglycerides, mmol/l	3.20±0.15*	1.90±0.12
Cholesterol, mmol/l	8.70±0.90*	5.10±0.80
HDL, mmol/l	1.48±0.11*	2.07±0.16
LDL, mmol/l	2.44±0.19*	1.46±0.13
IA,c.u.	4.8*	1.46

Note: the difference is significant ($p<0.05$)

4. Discussion

Thus, a study of the content of 25-OH-D in children of mothers with diabetes revealed its deficiency in blood serum compared with the control group.

The study of lipid metabolism showed an increase in the level of TG, cholesterol, LDL cholesterol, as well as a decrease in HDL cholesterol.

At present, the regulatory effect of VD on all metabolic processes in the body, including the synthesis of proteins, lipids, and cellular hormones, including insulin, is known. In addition, VD has a positive effect on the functional activity of a number of tissue enzymes and hormones by modifying the lipid composition of cellular and subcellular membranes [6].

In this regard, we believe that the revealed VD deficiency in the body of the examined children can be one of the causes of the dyslipidemia identified in them. According to the results of the research, children from mothers with diabetes were diagnosed with excess body weight 2 times more often than in the control, and obesity is 2.5 times more often - and this can also be a factor in the development of lipid metabolism disorders. According to the literature, obesity and overweight significantly increase the risk of dyslipidemia [7], more often in the form of a decrease in HDL cholesterol levels, which is the case in our patients.

It is known that dyslipidemia is accompanied by the deposition of cholesterol, triglycerides in the vascular intima, as a result of which atheromatous plaques are formed. Atherogenic properties of LDL and apolipoprotein B. In contrast, HDL are involved in the so-called reverse cholesterol transport, taking it from the plasma membranes of the cells and transporting it to the liver. The final effect will depend on the ratio of these classes of lipoproteins, more precisely, on the ratio of cholesterol that is part of HDL and LDL ± the so-called IA. A high content of LDL cholesterol in serum with a low content of HDL cholesterol is an important factor in the development of atherosclerosis.

In our study, IA was significantly higher in the group of children from mothers with diabetes, which allows them to be included in the risk group.

A number of studies conducted in recent years demonstrate the association of VD levels with adverse changes in the lipid profile. A direct correlation was established between 25-OH-D values and HDL values, as well as a negative correlation with LDL and triglyceride levels [8]. Recent studies indicate that high levels of 25-OH-D are significant ($p<0.05$) lowering triglyceride levels and IA.

Pharmacotherapy of dyslipidemia is quite complicated. There are many drugs that reduce the level of cholesterol due

to the effect on different parts of its exchange. However, most of these drugs are not used in childhood due to numerous side effects. Given all the above, we believe that the use of VD for the correction of dyslipidemia in children is promising.

Currently, there are numerous researches in the world on the possibility of using VD as an adjuvant therapy for patients with hypercholesterolemia. In addition, it has been proven that VD regulates the immune inflammatory response in the vascular intima, which also allows its use for the prevention of atherosclerosis in risk groups.

It is well known that the presence of obesity, hyperlipidemia, arterial hypertension and disorders of carbohydrate metabolism are components of the metabolic syndrome in children, especially against the background of burdened heredity in type 2 diabetes. However, in the early stages of development, metabolic syndrome is asymptomatic, metabolic and functional changes are detected only during laboratory and instrumental examinations [9]. Therefore, an important task of family medicine is the early diagnosis of the preclinical stages of the metabolic syndrome by simple and accessible methods, especially among risk groups [10].

All things consider, research results indicate that:

1. Children who were born from mothers with diabetes may be considered at risk for the development of metabolic syndrome, atherosclerosis, diabetes.

2. One of the causes of the found violations may be a VD deficiency.

3. Children at risk need dynamic observation of anthropometric indicators, control of body mass index, lipid and carbohydrate blood profile, level 25-OH-D.

Prospects for further research are to explore the possibility of using VD for the primary prevention and treatment of metabolic syndrome, diabetes in children.

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