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International Journal of Medicine and Medical Research
2016, Volume 2, Issue 2, p. 10-13
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DOI 10.11603/IJMMR.2413-6077.2016.2.7021

VITAMIN D AND DIABETES MELLITUS TYPE 2

N. V. Pasyechko, V. M. Kulchinska, L. V. Radetska, L. V. Naumova, I. V. Smachylo, A. O. Bob, I. P. Savchenko, M. Ye. Havryliuk,N. I. Yarema, A. I. Balaban, O. O. Bob, M. A. Dzhula, T. I. Krytskyi
I. HORBACHEVSKY TERNOPIL STATE MEDICAL UNIVERSITY, TERNOPIL, UKRAINE

Background. *As it is established that diabetes mellitus causes metabolic disturbances of all types (first of all because of carbohydrate metabolism), affection of blood vessels, nerves, different organs and tissues. However, the influence of DM on the level of microelements is still not investigated enough. Despite the sufficient variety of medicaments, compensation of diabetes mellitus is achieved in less than 30% of patients. For this reason, the search of new ways of treatment which are aimed at the improvement of carbohydrate metabolism is an urgent issue.*

Objective. *The research was aimed to reveal the* deficiency of 25-hydroxyvitamin D3 [25(OH)D3] and its *correlation with carbohydrate metabolism.*

Methods. Thirty five patients with diabetes mellitus Type 2 aged 55–74 with illness duration *2–4 years* were examined. *The control group included 35 healthy people of the same age and sex. Levels of 25-hydroxyvitamin D3 [25(OH)D3] were tested by means of radioimmunoassay. The level of glycated haemoglobin was tested by means of liquid chromatography.*

Results. *Correlation of the level of vitamin D with the degree of diabetes mellitus Type 2 compensation has been detected.*

Conclusions. *A clear tendency to the improvement of diabetes mellitus Type 2 compensation after medication correction with vitamin D was evidenced.*

KEY WORDS: **diabetes mellitus, vitamin D, glycated haemoglobin, glycemic control.**

INTERNAL MEDICINE

Introduction

Diabetes mellitus (DM) — is a non-infectious epidemic of XXI century. According to World statistics data, the amount of people with DM doubles every 13-15 years. Today there are 415 million patients with DM in the world, and their amount will increase to 642 million in 2040. New drugs do not contribute to the disease suppression, and the intensification of diagnostic criteria causes rapid increase in the number of patients. Mainly the increase of patients mainly with DM type 2.

Today, in Ukraine the DM compensation is unsatisfactory because the average rate of glycated haemoglobin (HbA1c) within DM type 1 is about 9.0%, and within DM type 2 – about 8.5% [2]. In our day, it is ultimately important to search for pathogenetic links for efficiency of patients' with DM treatment improvement.

Corresponding author: Veronika Kulchinska, Department of Internal Medicine № 1, I. Horbachevsky Ternopil State Medical University, 1 Klinichna, Ternopil, Ukraine, 46000
Phone number: +380978484206
E-mail: v.m.kulchinska@gmail.com

So, much attention is paid to the study of vitamin D influence on different organs and systems in case of different diseases, DM as well. Recently scientists began to study the influence of vitamin D on the course of DM type 2 [4,5,6,7]. Some authors suggest, that vitamin D insufficiency is a risk factor of DM type 2 [6], other — that vitamin D supports glucose homeostasis and is inversely proportional to the level of glycated haemoglobin in DM type 2 [8]. Also there is a suggestion, that an adequate vitamin D intake may be connected with lower risk of a gestational diabetes mellitus development [9].

Physiological effects of vitamin D is polyhedral, it is difficult to select some less significant factors. Vitamin D influences the phosphorus-calcium exchange: calcium and other microelements cannot be absorbed in its deficiency. Activity of vitamin D is directly connected with many physiological processes in organism, in particular with vitamin E admission, liver function and function of intestine, lipid metabolism. Vitamin D is necessary for providing

normal functioning of immune system, reproductive and sexual health, and hematopoietic system. That is why, cholecalciferol and its active metabolites is applied for treatment of immunodeficiency, anaemia, various pathological conditions of liver, gastrointestinal tract, diabetes, cardiovascular system, tuberculosis, cancers of breast and bowel, prostate, locally for the treatment of psoriasis.

According to statistical data [3], among all residents of Ukraine, only 4.6% of the examined people had normal level of vitamin D, 13.6% of the population was diagnosed with its failure, and in 81.8% of residents the deficit was pronounced.

However, how the level of vitamin D can change, and whether its change can influence on indicators of compensation for diabetes remains poorly examined.

According to the literature [10], objective criterion of vitamin D security, is the determination of 25-hydroxy vitamin D3 [25 (OH) D3] contents.

The study is **aimed** to reveal the deficiency of 25-hydroxy vitamin D3 and its cross-correlation with glycated haemoglobin of patients with diabetes type 2.

Material and Methods

35 patients with diabetes mellitus type 2 were examined, the individuals were aged from 55 to 74, illness duration was 2–4 years. The control group included 35 healthy people of the same age and sex. The patients, who suffered from DM type 2, took oral hypoglycaemic drugs of biguanides in therapeutic doses (1000-2500 mg daily). Additionally patients of both group received the drug Alpha D3 Teva, dose 1 mkg daily during 3 month. Levels of 25-hydroxyvitamin D3 [25(OH)D3] were tested by means of radioimmunoassay. The level of glycated haemoglobin (HbA1c) was tested by means of liquid chromatography.

The results of 25(OH)D3 and HbA1c were determined before the start of Vitamin D taking and after 3 months of treatment with it.

Statistical evaluation of results was realized by methods of variation statistics with calculation of frequency performance indicators (P) and averages (the arithmetic mean X). Statistical significance of the result if compared the patient groups with the control one was evaluated using Student t-test. Regression analysis was used to determine the relationship between HbA1c levels and 25(OH)D3.

Results

After examination of patients with DM type 2, all of them were identified either with the deficiency or insufficiency of vitamin D.

In accordance to classification (Holick MF et al) at the level of 25(OH)D3 50 nmol/L (20 ng/ml) to 75 nmol/L (30 ng/ml) D-vitamin failure is diagnosed, and decreased level of 25(OH)D3 below 50 nmol/L (20 ng/ml) — vitamin D3 deficiency.

We have found out that among 35 patients with DM type 2 nobody has normal level of vitamin D. 62.9% of patients were diagnosed with the deficiency of vitamin D ($p<0.01$), moreover in 22.7% of them good compensation was observed ($p<0.01$), in 31.8 % of the patients compensation was satisfactory ($p<0.01$), and in 45.5% of the patients — unsatisfactory ($p<0.01$). Inverse correlation connection between the decrease level of vitamin D and increase level of glycated haemoglobin was detected ($r=-0.40$, $p<0.05$). We considered that compensation of DM was good when the level of glycated haemoglobin was <7.5%, satisfactory — at the level of glycated haemoglobin 7.5-8.5%, unsatisfactory — when the level of glycated haemoglobin was >8.5%. We justified the increased rate of glycated haemoglobin compensation because we examined patients of older age who were recommended to maintain higher indicators of $HbA1_c$ to avoid hypoglycaemia and brain hypoxia.

37,1% of the patients with DM type 2 ($p<0,01$) suffered from vitamin D failure, moreover 61.5% of them had satisfactory compensation of diabetes (the level of glycated hemoglobin was 7.5-8.5%) ($p<0,01$), and 38.5% – unsatisfactory (the level of glycated haemoglobin > 8.5%) ($p<0,01$). Inverse correlation between the decrease of vitamin D and increase of glycated haemoglobin was detected ($r=-0.39$, $p<0.05$).

In the control group (without diabetes mellitus) there were only 25.7% of patients with a good level of vitamin D ($p<0.01$), 54.2% of people in the same group suffered from vitamin D insufficiency ($p<0.01$), and 20.1% of people were diagnosed with vitamin D deficiency ($p<0.01$).

The low implementation of vitamin D for the older patients without diabetes may be associated with alimentary factor and age features of the body.

In the control groups the level of glycated haemoglobin was 5.1±0.05% ($p<0.01$).

The patients of both groups (except those with no deficiency) were provided with a drug Alpha D3 Teva – 1 mkg daily for three month to correct vitamin deficiency. After that, the levels of 25(OH)D3 and HbA1c were tested again.

The improvement of diabetes mellitus compensation is clearly stated for patients: decrease the number of patients with unsatisfactory compensation and increase of number of patients with good and satisfactory compensation. 51.4% ($p<0.01$) of the patients were diagnosed with optimal levels of vitamin D and 11.5% ($p<0.01$) had its failure. Inverse correlation connection between the increased level of vitamin D and decrease level of glycated haemoglobin was detected ($r=-0.38$, $p<0.05$).

We have established that a number of the patients with unsatisfactory compensation decreased, a number of the patients with satisfactory compensation increased, and

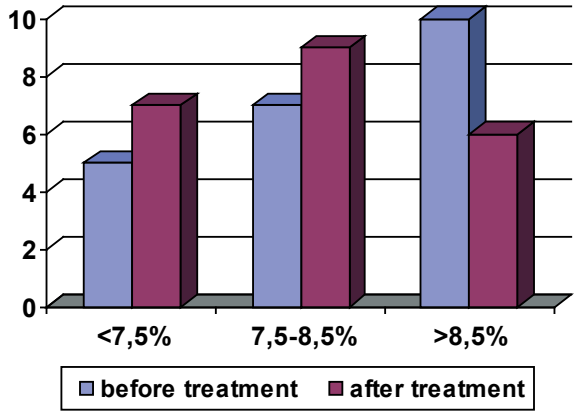

Figure 1. The levels of glycated haemoglobin of the patients with diabetes mellitus type 2, who were diagnosed with Vitamin D deficiency (before and after treatment with Alpha D3 Teva).

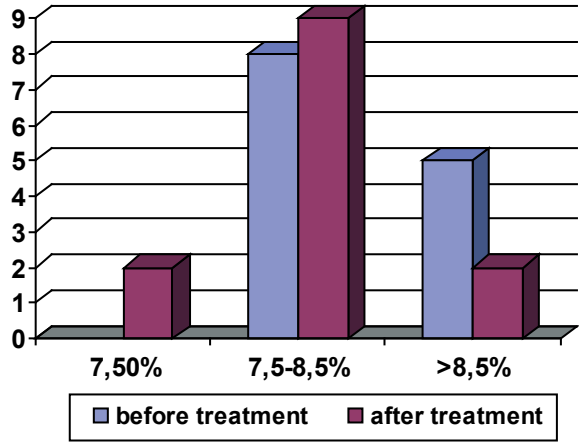

Figure 2. The levels of glycated haemoglobin of the patients with diabetes mellitus type 2, who were diagnosed with vitamin D failure (before and after treatment with Alpha D3 Teva).

patients with high compensation of diabetes was in evidence. After treatment with Alpha D3 Teva, 34.2% out of 37.1% of the patients with vitamin D failure had normal vitamin D level ($p<0.01$), and 2.9% still had its insufficiency ($p<0.01$). Inverse correlation between the increased level of vitamin D and decreased level of glycated haemoglobin has been detected ($r=-0.39$, $p<0.05$).

In the control group, after three months of treatment with Alpha D3 Teva, 74.2% of the patients had normal vitamin D level ($p<0.01$), 20% had its failure ($p<0.01$), 5.8% were diagnosed with the of vitamin D deficiency ($p<0.01$).

Discussion

Many authors consider the matter of vitamin D deficiency, which is a predictor of various diseases and also promotes decompensation of chronic diseases [11]. It is a topical issue in whole world and in Ukraine as well [12]. So, its deficiency correction should not seem less important. The drugs of cholecalciferoli are applied the most for its treatment [13], which, according to research literature, are first-line drugs that include ergocalciferol and structural analogue of vitamin D3-dyhidrotahisterol. The second-line drugs are calcitriol and alfacalcidol. As first-line drugs are exposed to 25-hydroxylation in liver, afterwards are converted into active metabolites in kidneys, therefore, the metabolism of these drugs is decreased in elderly patients with different types of primary and secondary osteoporosis and then don't have positive effect on bone system.

These defects are absent in the second-line drugs [14]. We suggest the drug alphacalcidol for vitamin D deficiency correction, because in our research we examined elderly patients.

Also, many patients suffer from osteoporosis; in such case this drug is more efficient.

The efficiency of alphacalcidol (1 mkg per day) compared to the combination of vitamin D (880 MO per day) and calcium carbonate (1000 mg per day) for patients with postmenopausal osteoporosis and absence of vitamin D deficiency in blood plasma is presented in research literature.

In 12 months in the females, who took alfacalcidol, mineral density of lumbar bone was increased by 2.33% (from base level) and in 18 months by 2.87% ($p<0.001$), and in the group of patients, who received vitamin D and Ca — only by 0.7% [15].

There are various conclusions on calcitriol efficacy. Some researches proved significant

effect of vitamin D on mineral density of bone for patients with postmenopausal osteoporosis [16, 17], others stated that such outcome was not obtained that may be associated with low doses [18].

Thus, we can argue that the drug alphacalcidol can be recommended for patients with vitamin D deficiency, diabetes type 2 and age-related osteoporosis.

Conclusions

A clear tendency to the improvement of diabetes mellitus type 2 compensation after medication correction with vitamin D was evidenced.

So, by correcting vitamin D deficiency the compensation of diabetes is improved.

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Received: 2016-12-05