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Effect of vitamin D on insulin resistance and anthropometric parameters in patients with type 2 diabetes mellitus

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INTRODUCTION

Prevalence of type 2 diabetes mellitus (DM) is increasing worldwide. Nowadays over 420 million people are suffering from DM and it is expected that its prevalence reach a staggering 552 million by 2030 [1]. Type 2 DM is defined by chronic hyperglycemia, altered insulin secretion, and complications that come from induction of oxidative stress [2]. One of novel strategy toward prevention and control of type 2 DM is vitamin D supplementation [3]. Besides the role of vitamin D in calcium homeostasis and bone metabolism, other effects also have been proposed. Vitamin D is essential for normal insulin secretion in response to glucose and also for maintenance of glucose tolerance [4]. In a study performed on 126 healthy adults with normal blood glucose, an association between vitamin D deficiency with beta cell dysfunction and insulin resistance was observed [5]. Such an association has also been established in type 1 DM [6].

Though little information is available regarding the association between vitamin D and type 2 DM. Human and animal studies have shown a negative correlation between serum levels of vitamin D with insulin levels and a positive correlation with insulin sensitivity [7, 8]. Several processes are responsible for effect of vitamin D on metabolism of glucose and insulin. Some animal studies have suggested that vitamin D may directly stimulate the insulin secretion from the pancreas. In non-diabetics and also subjects with high blood sugar, consumption of vitamin D supplement improved the insulin secretion [9]. However, interventional studies have shown conflicting results about the effect of vitamin D supplement on type 2 DM [8, 10]. These differences can be related to difference in race, dosage of vitamin D administration (oral or injection), or duration of usage. To best of our knowledge, no study has assessed the effect of injected mode of vitamin D supplement on DM in Ukrainian population.

The aim of this study is to evaluate the effect of vitamin D supplement on insulin resistance and anthropometric parameters.

MATERIALS AND METHODS

This randomized clinical investigation was performed with 55 diabetic patients. Inclusion criteria were type 2 DM subjects under treatment diet and oral hypoglycemic agents treatment with glycated hemoglobin (HbA1c) < 7.5 %. Exclusion criteria included: insulin therapy, current consumption of vitamin D. multivitamin or calcium, renal failure, nephrotic syndrome, liver failure, known cases of liver cirrhosis or liver dysfunction associated with ascites, coagulation disorders, and

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Table 1

Baseline anthropometric and biochemical characteristics of patients in both intervention and control groups

Variable	Intervention group (n = 26)	Control group (n = 26)	P value
Age (years)	58.2 ± 9.1	58.3 ± 9.7	0.942
Male/Female (%(n))	9 (17.3)/17 (32.7)	10 (19.2)/16 (30.8)	1.000
Duration of DM (years)	6.8 ± 4.2	7.4 ± 5.1	0.355
Systolic BP (mm Hg)	126.8 ± 9.2	128.1 ± 10.5	0.586
Diastolic BP (mm Hg)	84.6 ± 8.3	83.7 ± 8.1	0.371
WC (cm)	94.2 ± 6.9	93.3 ± 8.5	0.925
BMI (kg/m2)	29.6 ± 3.2	30.1 ± 3.7	0.464
FBG (mmol/l)	7.15 ± 1.02	7.31 ± 1.08	0.518
HbA1c (%)	6.9 ± 0.8	7.1 ± 0.9	0.602
Insulin (μIU/ml)*	9.2 ± 4.9	10.4 ± 4.7	0.354
HOMA*	3.4 ± 1.4	3.6 ± 1.5	0.245
25(OH)D (ng/ml)*	23.8 ± 4.6	24.3 ± 5.1	0.248

Legend. BP: Blood Pressure, WC: Waist Circumference, BMI: Body mass index, FBG: Fasting Blood Glucose, HbA1c: Glycated Hemoglobin, HOMA: Homeostasis Model Assessment Index, 25(OH)D: 25-Hydroxyvitamin D. The results are described as mean ± Standard Deviation (SD).
* The Wilcoxon and Mann–Whitney nonparametric test was used. Paired t-Test was used for other variables.
P ≤ 0.05 was considered as statistically significant.

uncontrolled high blood pressure. After obtaining the written consent, a baseline fasting blood samples was obtain from all the patients.

The patients were divided into two groups; intervention group who received 28,000 International Unit (IU) cholecalciferol per week, and control group. Each group included 26 subjects and examined in two time points: baseline and three months after vitamin D administration (mean of 94 days) for anthropometric characteristics (systolic and diastolic blood pressure, body mass index (BMI), waist circumference) and biochemical analysis including fasting blood glucose (FBG), 25-hydroxyvilanun D [25(OH)D], insulin, and HbAlc levels. Systolic and diastolic blood pressure was measured after 5—10 min rest, on the right arm in sitting position. For estimation of insulin resistance the Homeostasis Model Assessment Index (HOMA) based on the following equation was used. The HOMA index value <3 was considered as normal and > 3 as insulin resistant. 25(OH)D levels equal to: < 21, 21—29 and > 30 ng/ml were defined as deficient, inadequate, and adequate vitamin D [11], respectively. All of the laboratory tests were done in one hormone laboratory. The study was approved by local ethical committee.

The normal distribution of data was evaluated by Kolmogorov—Smirnov analytic test. All the statistical analysis was performed with SPSS software version 12. P < 0.05 was considered as statistically significant.

RESULTS AND DISCUSSION

Majority of the participants (63.5 %) were composed of female subjects. The age range of 52 patients was 36—78 years with a mean of 58.2 ± 9.4 years and DM duration of 7.2 ± 4.7 years (mean ± SD). All the patients were under oral hypoglycemic agents treatment. No significantly difference between two groups was present in regards to their antidiabetic treatment regimen (p > 0.36). Baseline characteristics of intervention and control groups are described in table 1.

All variables had normal distribution except 25(OH) D and insulin. Two groups showed no significant differences in anthropometric or clinical characteristics. Table 2 shows the mean differences in both anthropometric and clinical parameters, three months after vitamin D treatment between interventional and control groups.

In our study the effect of 28,000 IU vitamin D (cholecalciferol) in a short period (94 days) in patients with type 2 DM was evaluated. We found a significant increase in serum 25(OH)D levels in interventional group without any significant change in level of HbA1c, FBG and anthropometric factors. On the other word, administration of vitamin D in diabetic subjects produced positive effects on HOMA index and insulin resistance.

Detecting an increase in serum levels of 25(OH)D in patients with type 2 DM following vitamin D treatment

Table 2

Comparison anthropometric and biochemical characteristics before and three months after study according to mean differences

Variable	Intervention group	Control group	P value
Systolic BP (mm Hg)	+0.6±0.1	+1.1±0.3	0.783
Diastolic BP (mm Hg)	+0.4±0.1	+0.6±0.2	0.362
WC (cm)	-0.2±1.4	+0.3±1.8	0.625
BMI (kg/m^2)	0.06±0.4	-0.02±0.6	0.184
FBG (mmol/l)	-1.2±1.9	+0.7±1.3	0.263
HbA1c (%)	-0.02±0.8	-0.01±0.7	0.481
Insulin (μIU/ml)*	-2.6±3.4	-0.2±2.8	0.045**
HOMA*	-0.9±1.3	-0.2±1.4	0.029**
25(OH)D (ng/ml)*	+14.2±19.8	+0.3±11.2	0.007**

Legend. BP: Blood Pressure, WC: Waist Circumference, BMI: Body mass Index, FBS: Fasting Blood Glucose, HbA1c: Glycated Hemoglobin, HOMA: Homeostasis Model Assessment Index, 25(OH)D: 25-Hydroxyvitamin D. The results are described as mean ± Standard Deviation (SD). * Wilcoxon and Mann—Whitney analytic test was used. ** P ≤ 0.05 was considered statistically significant.

is in agreement to result of other investigations [12, 13]. In our study, the median level of serum 25(OH)D after 94 days was equal 37 ng/ml.

Series of studies have shown that a positive correlation between low levels of serum 25(OH)D and impaired insulin sensitivity, type 2 DM, arterial hypertension, hyperlipidemia and obesity is exist [14, 15]. An inverse relationship has been reported between serum 25(OH)D levels and HbA1c, particularly in obese patients [16]. Indeed a protective role for high levels of plasma vitamin D against type 2 DM progression has been reported [17]. However, in interventional studies, there are some conflicting results regarding the effect of vitamin D in prevention of type 2 DM.

Some studies performed that in population with concomitant vitamin D deficiency and impaired glucose tolerance or type 2 DM, vitamin D supplement was able to correct the insulin secretion and glucose tolerance, as well as HbA1c [18, 19]. In contrast, some studies failed to show an improvement in levels of blood sugar, glucose tolerance or insulin sensitivity following vitamin D supplement in both diabetic and non-diabetic subjects [20].

These controversy, or at least part of it, might be due to ethnicity difference in study's population. Other reasons for discrepancy seen in different studies might be related to duration of study, sample size, and lack of prospective studies or clinical trials specifically aimed to evaluate the effect of vitamin D deficiency on the incidence of type 2 DM.

In our study the baseline level of HOMA index in two groups were similar. Interestingly, remarkable changes in HOMA index following vitamin D supplementation in intervention group was found, while in control group a significant decrease at the end of study wasn't noticed.

It seems that the effect of vitamin D on glucose intolerance is more prominent in vitamin D deficient patients [21]. Due to our small sample size in each group, it is impossible to classify our patients according to their vitamin D status.

In our study such an association between vitamin D levels and BMI or WC was not found. In New Zealand study [22] also such a correlation was not observed.

One of limitation in our study was our small sample size.

Future studies to evaluate effects of concomitant consumption of vitamin D, effect of vitamin D in patients with vitamin D insufficiency, along with attention to larger sample sizes is suggested.

CONCLUSIONS

Based on previous results by this study we can be sure the effect of vitamin D on improvement of insulin resistance.

Three months after vitamin D treatment, HbA1c, anthropometric factors in intervention group stayed constant, however, serum 25(OH)D was significantly increased (p = 0.007). Administration of vitamin D in diabetic subjects produced positive effects on HOMA index and insulin resistance.

Association between vitamin D levels and BMI or WC was not found.

Taken our data together available information warrants exploring the possibility that vitamin D can be more efficient in reducing type 2 DM risk.

Moreover further studies are needed to show the definite effect of vitamin D on control of diabetes and its risk.

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SUMMARY

Effect of vitamin D on insulin resistance and anthropometric parameters in patients with type 2 diabetes mellitus

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Background. Prevalence of type 2 diabetes mellitus (DM) is increasing worldwide. To reduce its risk and progression, preventive programs are needed. Vitamin supplementation such as vitamin D is one of the strategies. Though little information is available regarding the association between vitamin D and type 2 DM. Human and animal studies have shown a negative correlation between serum levels of vitamin D with insulin levels and a positive correlation with insulin sensitivity.

The aim of the study. This study was designed to investigate the effect of vitamin D on insulin resistance and anthropometric parameters in type 2 DM.

Materials and methods. This randomized clinical investigation was conducted with 52 diabetic patients in two groups; intervention group with 28,000 International Unit (IU) of cholecalciferol and the control group. After recording demographic and anthropometric factors (waist circumference, blood pressure and body mass index), fasting blood samples was taken for measurement of blood glucose, 25-hydroxyvitamin D [25(OH)D], insulin, glycated hemoglobin (HbA1c) and estimation of Homeostasis Model Assessment Index (HOMA) in two times; before study and after three months.

Results and discussion. Two groups had similar baseline characteristics (each group = 26 subjects). Three months after vitamin D treatment, HbA1c, anthropometric factors in intervention group stayed constant, however, serum 25(OH)D was significantly increased (p = 0.007). We found a significant increase in serum 25(OH)D levels in interventional group without any significant change in level of HbA1c and anthropometric factors. Administration of vitamin D in diabetic subjects produced positive effects on HOMA index and insulin resistance. Association between vitamin D levels and BMI or WC was not found.

Conclusion. Taken our data together available information warrants exploring the possibility that vitamin D can be more efficient in reducing type 2 DM risk. Further studies with large sample sizes are needed to show the definite effect of vitamin D on control of diabetes and its risk.

Key words: type 2 diabetes mellitus, cholecalciferol, insulin resistance

РЕЗЮМЕ

Ефективність вітаміну D на інсулінорезистентність та антропометричні параметри у хворих на цукровий діабет типу 2

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Вступ. Захворюваність на цукровий діабет (ЦД) типу 2 зростає у всьому світі. На сьогодні необхідні ефективні програми профілактики для зменшення ризику виникнення ЦД та його прогресування. До однієї із стратегій належить застосування вітамінів, зокрема вітаміну D.

Мета роботи — вивчити ефективність додаткового призначення вітаміну D на інсулінорезистентність і антропометричні параметри у хворих на ЦД типу 2.

Матеріали та методи. У рандомізоване клінічне дослідження було включено 52 пацієнти з ЦД типу 2, розподілених на дві групи — контрольну та інтервенційну. Хворі інтервенційної групи додатково отримували 28000 міжнародних одиниць (МО) холекальциферолу. Після встановлення демографічних і антропометричних чинників (об'єм талії, артеріальний тиск і індекс маси тіла) двічі проводився забір крові для визначення глікемії натще, 25-гідроксивітаміну D [25(OH)D], інсуліну, глікованого гемоглобіну (HbA1c) і індексу інсулінорезистентності (HOMA): на початку дослідження і через три місяці.

Результати та обговорення. Хворі двох груп (по 26 осіб) не відрізнялися за основними показниками на початку дослідження. Через три місяці після

лікування холекальциферолом показник HbA1c, антропометричні дані в інтервенційній групі не змінювалися, однак встановлено достовірне збільшення вмісту 25(OH)D у сироватці крові (p = 0.007). Додаткове призначення вітаміну D у хворих на ЦД типу 2 справляло позитивний вплив на інсулінорезистентність (зменшення вмісту інсуліну та індексу HOMA). Не встановлено взаємозв'язку між вмістом вітаміну D та індексом маси тіла та об'ємом талії.

Висновки. Подальші дослідження з більшими вибірками хворих необхідні для встановлення достовірного ефекту додаткового призначення вітаміну D на перебіг ЦД.

Ключові слова: цукровий діабет типу 2, холекальциферол, інсулінорезистентність.

РЕЗЮМЕ

Эффективность витамина D на инсулинорезистентность и антропометрические параметры у больных сахарным диабетом типа 2

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Вступление. Заболеваемость сахарным диабетом (СД) типа 2 увеличивается во всем мире. На сегодня необходимы эффективные программы профилактики для уменьшения риска возникновения СД и его прогрессирования. К одной из стратегий принадлежит применение витаминов, в частности витамина D.

Цель работы — установить эффективность дополнительного назначения витамина D на инсулинорезистентность и антропометрические параметры у больных СД типа 2.

Материалы и методы. В рандомизированное клиническое исследование были включены 52 пациенты с СД типа 2, распределенных на две группы — контрольную и интервенционную. Больные интервенционной группы дополнительно получали 28000 международных единиц (МЕ) холекальциферола. После установления демографических и антропометрических факторов (объем талии, артериальное давление и индекс массы тела) дважды проводился забор крови для определения гликемии натощак, 25-гидроксивитамина D [25(OH)D], инсулина, гликированного гемоглобина (HbA1c) и индекса инсулинорезистентности (HOMA): в начале исследования и через три месяца.

Результаты и обсуждение. Больные двух групп (по 26 человек) не отличались по основным показателям в начале исследования. Через три месяца после лечения холекальциферолом показатель HbA1c, антропометрические данные в интервенционной группе не изменялись, однако установлено достоверное увеличение концентрации 25(OH)D в сыворотке крови (p = 0,007). Дополнительное назначение витамина D у больных СД типа 2 оказывало положительное влияние на инсулинорезистентность (уменьшение концентрации инсулина и индекса HOMA). Не установлено взаимосвязи между содержанием витамина D и индексом массы тела и объемом талии.

Выводы. Дальнейшие исследования с большими выборками больных необходимы для установления достоверного эффекта дополнительного назначения витамина D на течение СД.

Ключевые слова: сахарный диабет типа 2, холекальциферол, инсулинорезистентность.

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