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The comparison of 25 (OH) vitamin D level in type 2 diabetes patients taking oral anti-diabetics and insulin.

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Abstract

Aim: The aim of this study was to compare the levels of 25(OH) Vitamin D in patients of type 2 diabetes, taking oral antidiabetics (OAD) medication and insulin.

Materials and Methods: This study is based on data collected at the time of admission from 126 patients of type 2 diabetes mellitus (DM) and 62 healthy patients in the control group, who were admitted to the Policlinic of Endocrinology in the Department of Internal Medicine and Policlinic of Family Medicine in the Education and Research Hospital of Faculty of Medicine, Eskişehir Osmangazi University between October 1, 2013 and April 30, 2014. For the purpose of this study, HbA1C, lipid profile and 25(OH) Vitamin D levels of the patients were determined simultaneously. Results: 25(OH) Vitamin D levels of participants in the control group (22.371 ± 13.888) were higher than the levels of patients in the OAD group. 25(OH) Vitamin D levels of participants in the control group (22.371 ± 13.888) were also higher than the levels of patients in the insulin group (10.177 ± 6.188). The level of 25(OH) Vitamin D was higher in the OAD group; however, the difference was not significant (p=0.189).

Discussion: 25(OH) Vitamin D levels of the insulin taking group were lower than the OAD taking and control group because of the increase in insulin resistance. Considering that diabetes plays a role in organ damage and dysfunction, the cost-effective and easy treatment of Vitamin D becomes more important.

Keywords: Type 2 DM, OAD medications, Insulin, 25(OH) Vitamin D.

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Introduction

Diabetes Mellitus (DM), a disease that develops due to absolute or relative insulin deficiency or insulin resistance, is manifest by hyperglycemia and characterized by carbohydrate, lipid and protein metabolism disorder [1].

The number of obese patients has been increasing rapidly due to fast growth of societies, unhealthy and irregular eating habits, increase in the prevalence of obesity and sedentary lifestyle, ageing and urbanization. In this connection, the International Diabetes Federation estimates that the number of people with type 2 DM will increase to 334 million in 2025 [2].

DM is the most common endocrine disease in the world. Chronic hyperglycemia in diabetes causes damage and dysfunction of various organs, including particularly eyes, kidneys, nerves, heart and blood vessels. Acute metabolic complications as well as chronic microvascular and macrovascular complications are the most significant causes of morbidity and early mortality associated with DM [3,4].

Vitamin D reduces insulin resistance, and thus decreases excessive insulin secretion which is a response to the increase in blood sugar due to insulin resistance and increases insulin sensitivity [5,6].

The aim of this study was to find out the relationship between the level of 25(OH) Vitamin D and type 2 DM, and as distinct from other similar studies, to compare – by means of metabolic parameters – the level of 25(OH) Vitamin D in type 2 DM patients taking oral antidiabetics (OAD) and taking insulin.

Materials and Methods

This study, approved by decision no.12 of May 14, 2013 of the Ethics Board of the Faculty of Medicine, Eskişehir Osmangazi University, is based on the findings collected at

the time of admission from 126 patients of type 2 DM and 62 healthy patients in the control group, who were admitted to the Policlinic of Endocrinology in the Department of Internal Medicine and Policlinic of Family Medicine in the Education and Research Hospital of Faculty of Medicine, Eskişehir Osmangazi University between October 1, 2013 and April 30, 2014. For the purpose of this study, HbA1C, lipid profile and 25(OH) Vitamin D levels of the patients were determined simultaneously. The sociodemographic data related to the patients were recorded. Of 126 type 2 DM patients, 64 were taking OAD medications and 62 were having insulin treatment. Patients with type 1 and other subgroups of diabetes, followed in the diabetes policlinic, were excluded from the study. Only type 2 DM patients taking OAD medications and insulin were included in the study. In the group of type 2 DM patients, patients with chronic liver disease, chronic kidney disease and parathyroid, i.e., diseases that are likely to affect the level of Vitamin D, were not taken into the study. (The patients' levels of ALT, AST, BUN, Cr, Parathormone were within the normal range.) The following factors were considered for the evaluation of patients: Body Mass Index (BMI=kg/m^2) calculated according to weight and height information obtained when patients were admitted; onset date of diabetes determined according to anamnesis obtained from patients; and levels of fasting blood glucose (FBG), HbA1C, ALT, AST, BUN, Cr (creatinine), Parathormone, Ca (calcium), P (phosphorus) and Albumin determined according to biochemical parameters.

The control group of healthy patients consisted of individuals aged over 35 with normal biochemical values, who did not have any additional disease and did not take any additional drugs.

The levels of 25(OH) Vitamin D were divided into four categories [7]:

- 0-20 ng/ml 25(OH) Vitamin D deficiency
- 21-29 ng/ml 25(OH) Vitamin D insufficiency
- 30-150 ng/ml 25(OH) Vitamin D normal level
- over 150 ng/ml 25(OH) Vitamin D excess

Statistical analysis

The statistical analysis of the data collected in this study was conducted in the Program in Biostatistics, Faculty of Medicine, Osmangazi University. The continuous data were presented in the form of mean ± standard deviation. The categorical data were presented in the form of percentage (%). The Shapiro-Wilk test was used to see whether the data showed normal distribution. In the comparison of groups that showed normal distribution, independent samples t-test was used for the cases where there were two groups, and one-way ANOVA was used for the cases where the number of groups was three and more. In the comparison of groups that did not show normal distribution, Kruskal-Wallis H test was used for the cases where the number of groups was three. Spearman's rank correlation coefficients were calculated to determine the level of correlation among variables. Pearson's chi-squared and Pearson's exact chi-squared tests were used for the analysis of cross tables. IBM SPSS Statistics 21.0 software was used for data analysis. The value of $p<0.05$ was considered to be statistically significant.

Findings

The total number of participants in this study was 188, and 65 (34.6%) of them were male while 123 (65.4%) were female. Among the participants, 62 (33.0%) were in the healthy control group, 64 (34.0%) were in the group of DM patients taking OAD, and 62 (33.0%) were DM patients taking insulin. Given the variable of Vitamin D level, 147 (78.2%) individuals had Vitamin D deficiency, 24 (12.8%) had Vitamin D insufficiency and 17 (9.0%) had Vitamin D at the normal level. The characteristics of participants in this study are summarized in Table-1.

When all participants were considered as a whole, there was no significant difference between genders with respect to the level of Vitamin D (χ^2=2.965; p=0.227). In the group of patients with Vitamin D deficiency, 48 (32.7%) were male and 99 (67.3%) were female; in the group of patients with Vitamin D insufficiency, 12 (50.0%) were male and 12 (50.0%) were female; and in the group of patients with a normal level of Vitamin D, 5 (29.4%) were male and 12 (70.6%) were female.

The average age of participants in the OAD group (57.328 ± 9.577) was higher than the average age of participants in the control group (48.016 ± 9.324). The average age of participants in the insulin group (60.516 ± 9.082) was higher than the average age of participants in the control group (48.016 ± 9.324). The difference with regard to the mean BMI was also significant (KW=7.415; p=0.025). The mean BMI of participants in the OAD group (28.389 ± 3.546) was higher than the mean BMI of participants in the control group (26.764 ± 4.317). The mean BMI of participants in the insulin group (28.816 ± 3.880) was

Table 1. *Summary of data related to the population.*

		N	Percentage (%)
Gender	Men	65	34.6%
	Women	123	65.4%
	Total	188	100.0%
Number of years with DM	5-10 years	62	49.2%
	10-20 years	51	40.5%
	20-25 years	8	6.3%
	Over 25 years	5	4.0%
	Total	126	100.0%
Group	Control	62	33.0%
	OAD	64	34.0%
	Insulin	62	33.0%
	Total	188	100.0%
Level of Vit. D	Deficiency	147	78.2%
	Insufficiency	24	12.8%
	Normal	17	9.0%
	Total	188	100.0%

higher than the mean BMI of participants in the control group (26.764 ± 4.317). The SBP level of participants in the OAD group (132.734 ± 16.059) was higher than the SBP level of participants in the control group (115.161 ± 17.902). The SBP level of participants in the insulin group (134.436 ± 15.892) was higher than the SBP level of participants in the control group (115.161 ± 17.902). The DBP level of participants in the OAD group (82.578 ± 8.451) was higher than the DBP level of participants in the control group (76.210 ± 6.382). The DBP level of participants in the insulin group (82.016 ± 7.760) was higher than the DBP level of participants in the control group (76.210 ± 6.382). The FBG level of participants in the insulin group (188.161 ± 81.966) was higher than the FBG level of participants in the OAD group (139.031 ± 48.957). The HbA1C level of participants in the insulin group (9.790 ± 2.295) was higher than the HbA1C level of participants in the OAD group (7.301 ± 1.699). In the group of patients taking OAD medications and insulin (i.e. the diabetic group), the difference in HbA1C level was not significant ($p>0.05$) between the patients with BMI 30 ≤ (8.9503 ± 2.69014) and the patients with BMI 30> (8.3626 ± 2.21934).

The tests indicated that the participants' levels of ALT, AST, BUN, Cr, PTH, Albumin, Ca and P serum were within the normal range. The 25(OH) Vitamin D level of participants in the control group (22.371 ± 13.888) was higher than the 25(OH) Vitamin D level of participants in the OAD group (12.390 ± 6.049). The 25 (OH) Vitamin D level of participants in the control group (22.371 ± 13.888) was higher than the 25(OH) Vitamin D level of participants in the insulin group (10.177 ± 6.188). The 25(OH) Vitamin D level of participants in the OAD group (12.390 ± 6.049) was higher than the 25(OH) Vitamin D level of participants in the insulin group (10.177 ± 6.188); however, the difference was not statistically significant. The findings are summarized in Table 2.

With regard to the level of 25(OH) Vitamin D, there was no statistically significant difference in the whole group between participants with BMI 30> and participants with BMI 30 ≤ ($p>0.05$).

The SBP level of participants with 25 (OH) Vitamin D deficiency (129.524 ± 16.700) was higher than the SBP level of participants with 25(OH) Vitamin D at the normal level (112.353 ± 30.929). According to the results of Kruskal-Wallis H test, conducted to see whether the mean DBP of participants had significant difference with regard to the variable of 25(OH) Vitamin D, provided no significant difference between the groups ($p>0.05$).

The FBG level of participants with 25(OH) Vitamin D deficiency (148.612 ± 72.441) was higher than the FBG level of participants with 25(OH) Vitamin D insufficiency (111.458 ± 37.584). The FBG level of participants with 25(OH) Vitamin D deficiency (148.612 ± 72.441) was higher than the FBG level of participants with normal 25(OH) Vitamin D level (89.177 ± 7.038).

In diabetic patients, the HbA1C level of participants with 25(OH) Vitamin D deficiency (7.891 ± 2.563) was higher than the HbA1C level of participants with 25(OH) Vitamin D insufficiency (6.385 ± 1.355).

Table 2. *The comparison of laboratory and measurable values in the study population.*

	Control	**OAD**	**Insulin**	**p value**
	Mean ± SD Median (Q1-Q3)	**Mean ± SD Median (Q1-Q3)**	**Mean ± SD Median (Q1-Q3)**	
Age*	48.016 ± 9.32 48.00 (39.75-55.25)	57.328 ± 9.577 57.50 (51.25-63.75)	60.516 ± 9.082 61.00 (55.00-67.00)	**<0.001**
Height*	165.145 ± 8.057 164.00 (159.00-170.00)	165.422 ± 8.745 163.50 (158.00 - 173.75)	166.048 ± 8.332 165.00 (159.00-174.00)	0.832
Weight*	73.073 ± 13.067 73.50 (63.50-81.25)	77.672 ± 10.918 77.00 (70.00-86.00)	79.397 ± 10.435 79.00 (72.00-87.00)	**0.008**
BMI*	26.764 ± 4.317 26.50 (24.05-29.73)	28.389 ± 3.546 28.10 (26.25-30.08)	28.816 ± 3.880 28.35 (26.80-30.15)	**0.025**
SBP*	115.161 ± 17.902 120.00 (110.00-120.00)	132.734 ± 16.059 130.00 (120.00-147.50)	134.436 ± 15.892 130.00 (120.00-150.00)	**<0.001**
DBP*	76.210 ± 6.382 80.00 (70.00-80.00)	82.578 ± 8.451 80.00 (80.00-90.00)	82.016 ± 7.760 80.00 (80.00-90.00)	**<0.001**
FBG*	88.274 ± 7.268 89.00 (81.75-94.00)	139.031 ± 48.957 120.50 (109.00-159.75)	188.161 ± 81.966 168.00 (128.25-231.75)	**<0.001**
HbA1C*	5.317 ± 0.396 5.21 (5.01-5.61)	7.301 ± 1.699 6.84 (6.43-7.47)	9.790 ± 2.295 9.18 (8.13-10.50)	**<0.001**
Vit D*	22.371 ± 13.888 18.65 (12.10-29.63)	12.390 ± 6.049 10.75 (7.57-16.30)	10.177 ± 6.188 8.10 (4.70-14.05)	**<0.001**

Mean ± SD: Mean ± Standard Deviation
*Kruskal Wallis H Test
**One-way Variance Analysis

When all participants were considered together, there was a significant reverse correlation at the level of 0.43 between HbA1C and 25(OH) Vitamin D ($p<0.001$). In patients taking OAD and insulin, there was a significant reverse correlation at the level of 0.25 between HbA1C and 25(OH) Vitamin D ($p=0.004$).

The difference between control, OAD and insulin groups was not significant with regard to 25(OH) Vitamin D deficiency (the rate of VD deficiency was respectively 82.3%, 71.9%, 72.6%) ($\chi^2=2.273$; $p=0.321$).

Discussion

DM is one of the most significant chronic health problems in the world. The world prevalence and incidence of DM vary considerably by regions. The difference in ethnic origin and race plays an important role in this variation [4].

It has long been known that Vitamin D deficiency constitutes a risk factor for impaired glucose tolerance. The level of Vitamin D was lower in type 2 diabetics than in non-diabetics. The research has also shown that there is a positive correlation between Vitamin D level and insulin sensitivity in normal-weight individuals with normal glucose tolerance, and that low level of Vitamin D constitutes an independent risk factor for metabolic syndrome in large populations [5]. The level of Vitamin D was lower in patients with the risk of DM than in patients without risk of DM. Vitamin D deficiency is associated with impaired insulin secretion, which is a high risk factor for diabetes [6].

In the present study, type 2 diabetic patients (those taking OAD medications and those taking insulin) and a healthy control group were compared with regard to gender, age, BMI, year of diabetes, HbA1C, FBG and 25(OH) Vitamin D. Furthermore, all participants' levels of ALT, AST, Ca, P, BUN, Cr, Albumin were determined for differential diagnosis of any other diseases (e.g., chronic liver disease, chronic kidney disease, hyperparathyroidism, etc.), which are likely to affect the level of Vitamin D. These values were within the normal range in the patients included in this study.

In the group of patients, 62 (49.2%) had DM for 5-9 years, 51 (40.5%) for 10-19 years, 8 (6.3%) for 20-24 years and 5 (4.0%) for 25 years or over. With respect to the variable of 25(OH) Vitamin D level, 147 (78.2%) had Vitamin D deficiency, 24 (12.8%) had Vitamin D insufficiency and 17 (9.0%) had Vitamin D at the normal level.

In recent years, there has been greater focus on the relationship between Vitamin D deficiency and type 2 diabetes. Vitamin D was significantly lower in type 2 diabetic patients taking OAD and insulin than participants in the control group. This indicates that Vitamin D deficiency is associated with diabetes and glucose intolerance [8].

Vitamin D plays an important role in the functions of beta cell, which is effective in the pathogenesis of insulin sensitivity, insulin resistance and type 2 DM. Vitamin D (400-1000 U/day) and calcium (600-1200 mg/day) support is important for the prevention of type 2 DM [9].

In their clinical study, Newton et al. found a negative correlation between fasting blood glucose and level of Vitamin D in a group of African-American women [5]. Similarly, NHANES III analysis was conducted to identify the relationship between serum 25(OH) Vitamin D, race and diabetes risk. It was found that insulin resistance was higher in non-Hispanic black people than in white people, and that the correlation between diabetes risk and Vitamin D level was reverse [10].

There is an increased risk of type 2 diabetes in obese and overweight people. Obesity and overweight increase relative risk of diabetes four times in individuals aged between 20 and 44 [11].

In a cohort study, the diabetes risk showed very strong correlation with BMI in over 50 thousand American male employees. The risk also applies to women. The relative risk of type 2 diabetes was high in the 90th percentile of BMI among 43,581 women registered in Nurses' Health Study [12]. High BMI is considered a dominant risk factor for type 2 diabetes. Haffner et al. observed 1734 individuals for 7 years in the San Antonio Heart Study. These researchers have recently found that 195 individuals who developed type 2 diabetes had higher BMI [13]. The results of many studies support that type 2 diabetes may mostly be prevented with the adoption of lifestyle characteristics and treatment methods that reduce obesity. As it was the case in a number of epidemiological studies, the frequency of obesity was high among type 2 diabetics in our study.

In the present study, the difference in mean HbA1C levels was significant between the groups ($KW=144.013$; $p<0.001$). The results indicate that the HbA1C level of patients was higher in the insulin group (9.790 ± 2.295) than in the OAD group (7.301 ± 1.699).

The first report related to the association between Vitamin D and type 2 DM was published 20 years ago. In 1988, Pietschmann et al. compared 25 (OH) Vitamin D levels of diabetic and non-diabetic patients and found that Vitamin D was lower in the diabetic group [14].

In recent years, Vitamin D deficiency has been reported to be a factor causing the development of type 2 DM. The results of our study has shown that Vitamin D level was lower in patients of type 2 diabetes than in healthy control patients, as it was suggested in many previous studies [15,16]. In patients of type 2 diabetes, the level of 25 (OH) Vitamin D has reverse correlation with the HbA1C level. This correlation was observed in our study as well as in the large community-based study of Tromsö and the study of Hutchinson et al. [17].

In brief, what distinguishes this study from other studies designed to disclose the relationship between 25 (OH) Vitamin D level and type 2 DM on the basis of metabolic parameters is that we compared 25 (OH) Vitamin D level in type 2 DM patients that take OAD and that take insulin. As a result, the level of 25(OH) Vitamin D was lower in the group of patients taking insulin, i.e., who had increased insulin resistance. Given that diabetes causes damage and dysfunction in various organs, including particularly eyes, kidneys, nerves, heart and blood vessels, the cost-effective and easy treatment related to Vitamin D becomes more important.

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