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ROLE OF SERUM 25 HYDROXY CHOLECALCIFEROL IN TYPE 2 DIABETES MELLITUS IN RELATION WITH GLYCEMIC STATUS

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ABSTRACT The extraskeletal effects of vitamin D have attracted considerable interest. Vitamin D deficiency appears to be related to the development of Type 2 Diabetes mellitus. Vitamin D may affect glucose homeostasis, found to be inversely related to Glycated hemoglobin levels. It appears to protect from the development of Type 2 diabetes mellitus. Glycated hemoglobin (HbA1c) and 25(OH)D3 levels were measured in Type 2 Diabetes mellitus patients. 25(OH)D3 was measured by radioimmunoassay and HbA1c was measured by HPLC. 25(OH)D3 levels were lower in the Type 2 Diabetes mellitus patients group, being 19.26 ± 0.95 ng/ml ($p < 0.001$, Student's t-test). 25(OH)D3 levels were found to be inversely associated with HbA1c levels in the diabetic patients ($p = 0.008$, $r2 = 0.058$, linear regression). These findings may have therapeutic implications as cautious vitamin D supplementation may improve glycemic control in Type 2 Diabetes mellitus patients.

KEYWORDS : Type 2 Diabetes mellitus patients, HbA1C levels , 25(OH)D3 levels (vitamin D)

INTRODUCTION

Type 2 Diabetes Mellitus is a non communicable disease caused by increased insulin resistance and beta cell dysfunction. Inflammatory factors, reactive oxygen species and autoimmune reactions are the major pathogenic effectors for diabetes. Recently vitamin D has sparked interest in pathogenesis of diabetes by playing a role in Insulin resistance.

Vitamin D receptors identified in pancreatic islets and vitamin D dependent calcium binding protein in pancreatic tissue. As a major regulator of homeostasis of calcium, Vitamin D directly or indirectly improves insulin exocytosis and glucose tolerance. Assessment of the serum vitamin D level in Type 2 Diabetes mellitus patients will help in preventing further complications.

Vitamin D is a hormone related to skeletal integrity[1] .Vitamin D deficiency appears to be related to the development of Type 2 Diabetes mellitus .Mild to moderate vitamin D insufficiency has been proposed as a risk factor for Type 2 Diabetes mellitus. Higher plasma vitamin D has been shown to be related with a lower risk for the development of diabetes mellitus in high risk patients .Vitamin D deficiency has been described in the metabolic syndrome , specific vitamin D receptor gene polymorphisms having been found to be related to components of the metabolic syndrome. Moreover, vitamin D seems to affect glucose homeostasis, vitamin D levels having been found to be inversely related to glycated hemoglobin levels in Type 2 Diabetes mellitus .

The aim was to study levels of 25-hydroxy vitamin D3 [25(OH)D3] and the relationship between 25(OH)D3 levels and glycemic control in patients with Type 2 Diabetes mellitus.

MATERIALS AND METHODS

This is an observational study done in Coimbatore medical college hospital in south india 120 patients attending Diabetology OPD with Type 2 DM were selected for this study.After getting Institutional ethics committee approval blood samples were collected and analysed for 25(OH)D3 and HbA1c levels. Levels of 25(OH)D3 were measured by chemiluminescence immunoassay (CLIA). Levels of HbA1c were measured by high-performance liquid chromatography (HPLC).

Statistical evaluation of the results was performed using the statistical package SPSS 20.. Regression analysis was performed to analyse the relationship between HbA1c and 25(OH)D3 levels. In order to test normality of the parameters involved in regression analysis, histograms of regression standardized residuals and p–p plots of regression standardized residuals were performed. A chi-squared test was performed to compare the number of subjects with vitamin D deficiency and insufficiency within the patient groups.

RESULTS

Table 1. 25(OH)D3 (ng/ml) (mean ± SEM), HbA1c (%) (mean ± SEM) in the diabetes mellitus type 2 patients (n = 120) and statistical significance (Student's t-test), number and percentage of subjects with 25(OH)D3 deficiency and insufficiency [25(OH)D3 ≤ 10 ng/ml and < 20 ng/ml] in the patient groups and statistical significance (chi-squared test)

Subjects	HbA1C[%]	25[OH]D ng/ml	<10 ng/ml	<20ng/ml
Patients	7.2 ±0.18	19.26. ±0.94	21	76
Statistical significance	p<0.001	p<0.001	P=0.0088	p<0.001

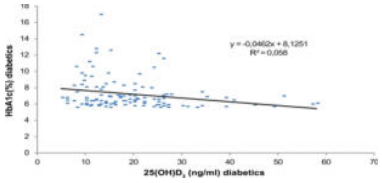

Figure 1.
Inverse association between 25(OH)D_3 (ng/ml) and HbA1c (%) in diabetes mellitus type 2 patients, ($p = 0.008$, $r^2 = 0.058$, linear regression analysis).

25(OH)D_3, 25-hydroxy vitamin D3; HbA1c, Glycated haemoglobin.

HbA1c levels were higher in the group of Type 2 Diabetes mellitus patients than in the control group, HbA1c levels being 7.2 ± 0.18 % in the patient groups ($p < 0.001$, Student's t-test) (Table 1).

In the group of Type 2 Diabetes mellitus patients, 25(OH)D3 levels were lower , 25(OH)D3 levels being 19.26 ± 0.94 ng/ml in the patients($p < 0.001$) (Table 1).

In the group of diabetes mellitus type 2 patients, 21 of 120 (17.5%) (5.8%) had vitamin D deficiency, 25(OH)D3 levels ≤ 10 ng/ml (chi-squared test, $p = 0.0089$). In the group of diabetes mellitus type 2 patients, 76 of 120 (63.3%) had vitamin D insufficiency, 25(OH)D3 levels < 20 ng/ml (chi-squared test, $p < 0.0001$) (Table 1).

25(OH)D3 levels were found to be inversely associated with HbA1c levels in the group of Type 2 Diabetes mellitus patients ($p = 0.008$, $r = 0.058$, linear regression analysis) (Figure 1).

DISCUSSION

In the present study, lower 25(OH)D3 levels were observed in Type 2

Diabetes mellitus patients and an inverse relationship was observed between Glycated hemoglobin levels and 25(OH)D3 levels in the patient group, implying that 25(OH)D3 levels may affect glucose control in Type 2 Diabetes mellitus. In addition, statistically significantly more Type 2 Diabetes mellitus had vitamin D deficiency and insufficiency.

Vitamin D is related to bone metabolism, being a secosteroid synthesized in the skin by the action of ultraviolet irradiation from the sun. The extraskeletal effects of vitamin D are currently the focus of research .The relationship of vitamin D with the immune system is being intensely discussed. It has been shown that vitamin D induces immune tolerance [3].Vitamin D has been shown to be related to glucose metabolism and the development of Type 2 Diabetes mellitus and the metabolic syndrome [4,5].

In a longitudinal study of the determinants of insulin resistance and the metabolic syndrome, a significant inverse association of baseline 25(OH)D3 with fasting glucose at follow up was observed [5]. Previous studies have shown that low vitamin D ingestion may be related with a higher risk for the development of Type 2 Diabetes mellitus and the metabolic syndrome [6].

In the present study, lower 25(OH)D3 levels were observed in Type 2 Diabetes mellitus patients. vitamin D levels were found to be negatively correlated with Glycated hemoglobin levels. The correlation persisted even after outliers were excluded. In addition, it has been suggested that adequate vitamin D intake may be related with a lower risk for the development of diabetes mellitus.

Vitamin D receptors have been found in pancreatic beta cells, which additionally have been found to express the enzyme 1-α-hydroxylase. Vitamin D facilitates the secretion of insulin from pancreatic beta cells, thus appearing to regulate insulin secretion[7]. Therefore vitamin D deficiency may be related to impaired insulin secretion in Type 2 Diabetes mellitus. Based on these results it would be physiologically correct to recommend vitamin D supplementation to improve glucose control in Type 2 Diabetes mellitus [8]. At a molecular level vitamin D appears to reduce oxidative stress [9].

The present study has several limitations. It is an observational study and therefore no conclusion can be made as far as any cause and effect relationship is concerned between vitamin D deficiency and Type 2 Diabetes mellitus. In addition, 25(OH)D3 was chosen as a marker of vitamin D deficiency, as currently recommended. However, vitamin D circulates in several forms in the blood and its active form is 1,25(OH)2D3. More studies are also needed with vitamin D supplementation and long-term observation of glucose control in Type 2 Diabetes mellitus.

CONCLUSION

The findings presented in our study have therapeutic implications. In patients with Type 2 Diabetes mellitus, normal levels of vitamin D in the blood may facilitate glucose control. In addition, in people with a tendency to develop Type 2 Diabetes mellitus, optimal levels of vitamin D within the blood may retard the clinical development of Type 2 Diabetes mellitus.

Conflict of interest : Nil

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