



CLINICAL CORRELATION BETWEEN DIABETES MELLITUS TYPE 2 AND VITAMIN D3 (25 OH- CHOLECALCIFEROL) LEVEL

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ABSTRACT

25(OH) Vitamin D is the circulating form of vitamin D which is measurable in the blood. Vitamin D insufficiency has been defined as serum 25-hydroxyvitamin D (25(OH) D) levels below 30 ng/mL and it is common among patients with type 2 diabetes mellitus (DM). Our aim was to investigate the clinically meaningful associations between serum levels of 25(OH) D and DM type 2. The serum 25(OH) D and the HbA1c levels were determined in 50 patients with DM type 2, along with their FBS, PPBS and HbA1c and other parameters which were required to assess the diabetic control were also measured. The results of our study revealed a trend towards an inverse vitamin D - FBS (Pearson correlation, $r = -0.090$) and inverse vitamin D - PPBS (Pearson correlation, $r = -0.095$) association. The lower serum 25(OH) D levels were associated with the higher HbA1c levels (Pearson correlation, $r = -0.173$). This was a borderline association which may have probably occurred due to the small sample size. The association between the low serum 25(OH) D levels and elevated HbA1c in the study population may be in-scribed into a wider context, portraying vitamin D insufficiency as a poor prognostic factor, which may play a vital role in impairing the glycaemic control.

KEY WORDS: Vitamin D, HbA1c, type 2 DM

INTRODUCTION

Diabetes mellitus is a metabolic disease which is caused by absolute or relative insulin deficiency. About 10% of the Indian population suffers from this disease. Various factors play a role in the aetiopathogenesis and in the glycaemic control among the type 2 diabetic patients. Vitamin D is derived from 7 dehydro cholesterol or ergosterol by UV irradiation^[1]. Cholecalciferol is hydroxylated at the 25th position in the liver to form 25 hydroxy cholecalciferol. This is the major transport form of the vitamin. It then gets hydroxylated at the first position to form calcitriol, which is the active form of vitamin D. Interestingly, many studies have revealed that Vitamin D3 (calcitriol) has a role in the synthesis and the secretion of insulin^[2] by receptor mediated molecular mechanisms [3]. Various definitions for vitamin D insufficiency have appeared in the literature; the best established one pertains to serum levels which are below 30 ng/mL^[4]. A recent meta-analysis has demonstrated low vitamin D levels in the middle-aged and the elderly populations and these represent a risk factor for type 2 diabetes mellitus (DM), cardiovascular disease and metabolic syndrome^[5]. The deficiency of Vitamin D is associated with impairment of insulin synthesis and secretion and also an increase in the insulin resistance.

This study was done to find out the correlation between the vitamin D3 levels and the blood glucose levels, as well as the glycaemic control in already diagnosed type 2 diabetic patients.

MATERIALS & METHODS

Blood samples (5ml) were obtained from 50 DM type 2

patients of age (43 ± 7 years) with a disease duration of 5 years and without complications were recruited from the Medicine Department of our institute Gitanjali Medical college and hospital, Udaipur, Rajasthan, India, and all the participants were interviewed at the baseline by the same investigator (to assess the sunlight exposure) after obtaining informed consent.

Exclusion criteria: Those with hypercalcaemia, intake of vitamin D for osteoporosis in dietary supplements, other orthopaedic problems like rickets, osteomalacia or end-stage renal failure and pregnancy were excluded from the study.

All collected samples were centrifuged at 3000 RPM for a period of 10 minutes after giving unique ID to each sample and then the following investigations were performed:

1. Serum 25 (OH) Vitamin D- on cobas e 411 (Roche chemiluminescence)
2. Plasma blood glucose- Fasting and post prandial (GOD - POD method, Fully automated analyzer, Cobas C 311)
3. HbA1c (Immuno turbidimetry, direct technique, fully automated analyzer, Cobas C 311).

After obtaining Mean and SD of the above results, the association of 25(OH) D with FBS, PPBS and HbA1c is evaluated by using the Pearson's correlation coefficient. Correlation coefficient determines the degree to which two variable's movements are associated. The correlation coefficient will vary from -1 to +1. A -1 indicates perfect negative correlation, and +1 indicates perfect positive correlation.

RESULTS:**TABLE 1:** Correlations between Vit D and Glycemic Status

| Parameter | Mean±SD | Correlation coefficient r-value |
|-----------|--------------|---------------------------------|
| FBS | 146.22±45 | -0.090 |
| VIT D3 | 18.492±3.49 | |
| PP2BS | 275.28±66.40 | -0.095 |
| VIT D3 | 18.492±3.49 | |
| HBA1C | 8.32±1.15 | -0.173 |
| VIT D3 | 18.492±3.49 | |

The age of the participants ranged between 43 ±7 years with the 25(OH) D insufficiency (18.49 ±3.497 ng/ml) and the assessed glycaemic control with FBS(146.22 ± 45.007 mg/dl), PPBS (275.28 ± 66.400mg/dl) and HBA1C (8.326 ±1.15843) is shown in [Table-1]. The low serum vitamin D levels were negatively correlated with the fasting as well as the postprandial blood sugar levels. There was a trend towards an inverse 25(OH) D - HbA1C association, which did not show statistical significance, most probably due to the relatively small sample size.

DISCUSSION

The present study observed that the type 2 diabetic individuals with a vitamin D insufficiency showed a poor glycaemic control. According to various studies^[6], vitamin D has a potential influence on the glucose homeostasis, as was suggested by the following factors.

Effect of Vitamin D on Insulin Secretion:

Specific vitamin D cell receptors are present on the pancreatic cells^[7]. The pancreatic cells express 1 alpha hydroxylase which is responsible for an active vitamin D3 synthesis^[8] and also by increasing the insulin response to the glucose stimulation, but not affecting the basal insulin secretion^[9]. In some populations, type I diabetes is associated with certain polymorphisms within the VDR gene^[10] which is present in the human insulin gene promoter and also in the skeletal muscle and in adipose tissues^[11]. Pancreatic islets have both VDR and vitamin D-dependent calcium-binding proteins (CaBP)^[12,13], thus suggesting a role of vitamin D in insulin secretion. The insulin secretion and sensitivity is influenced by Vitamin D mediated intracellular calcium secretion. Raised intracellular calcium levels enhance the binding of the calcium binding protein to the IRS - 1 (Insulin receptor substrate 1), stimulating tyrosine phosphorylation and PI3 kinase activation and thus promoting insulin secretion^[11]. Vitamin D deficiency may also impair the insulin secretion through its associated increase in the PTH levels. It was proposed that vitamin D deficiency-associated hyperparathyroidism may actually cause a paradoxical increase in the intracellular calcium levels^[12,13]. This PTH-induced increase in calcium may in turn impair the calcium signal which is needed for glucose-induced insulin secretion^[14]. Of significance is the finding, that the vitamin D potentiation of glucose-induced insulin secretion is seen in normal individuals but not in patients with established type-2 DM^[15]. This could be because type-2 diabetes by itself may be a condition of impaired intracellular calcium homeostasis^[16]. Whether the insulin secretion is influenced by the direct action of Vitamin D or through its receptor or through changes in calcium, or PTH, is a matter of ongoing studies. It is also possible that

the insulin secretion may be influenced by a combination of different mechanisms.

Effect of vitamin D on insulin Sensitivity

Type-2 DM is a state of chronic systemic inflammation and it has been found to increase the insulin resistance^[17]. Type-2 DM was found to be associated with an increase in the levels of the tumour necrosis factor-α and β, the C reactive protein, the plasminogen activator inhibitor-1 (PAI-1), and interleukin-6 (IL-6)^[18-20]. The increase in these inflammatory mediators may precede and even predict the development of type-2 DM. In support of this concept, is the finding that VDR has been found on almost all the cells of the immune system^[21] and that vitamin D can repress the type 1 cytokines, inhibit dendritic cell maturation, and up regulate the regulatory T cells. Furthermore, immune cells such as macrophages contain 1-hydroxylase that can be upregulated by the inflammatory mediators and not by PTH^[22]. Vitamin D also suppresses the antigen-presenting capacity of the macrophages, it modulates the development of the CD4 lymphocytes and it inhibits the production of IFNγ (interferon γ) and IL-2 (interleukin 2)^[23], among other cytokines. These cytokines are known to activate the macrophages and the cytotoxic T cells, which in turn can lead to the destruction of the pancreatic islets. By the modulation of the immune and the inflammatory processes, vitamin D may also decrease insulin resistance and increase the insulin secretion in type-2 DM which is the two characteristic defects in this condition.

From the above discussion, it is clear that vitamin D has a significant role to play in the molecular mechanisms of the synthesis, secretion and the peripheral sensitivity of insulin. Hence, hypovitaminosis D may be associated with insulin resistance and beta cell dysfunction. A variety of limitations of this study need however to be addressed. The small sample size did not allow a multivariate approach for incorporating additional, potentially meaningful factors for modifying the levels of serum 25(OH) D, but it should be declared that from the evidence which was provided, that improving the vitamin D status will help in establishing a better glycaemic control in people with DM type 2. Nevertheless, it seems that the routine screening for vitamin D insufficiency may provide meaningful information and that it could be considered for diabetic care. Interventional studies are needed to evaluate whether the long-term supplementation of vitamin D could reduce the morbidity in a diabetic population, with an awareness of the side effects.

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