Effects of Vitamin-D Supplementation in Vitamin-D Deficient, Near Normal HbA1c Diabetic Patients

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ABSTRACT

Background: The study was conducted with aim to evaluate the effects of vitamin D supplementation on diabetic patients with subnormal serum vitamin D levels and minimally elevated HbA1c on their current regimen. Objective was to find association between vitamin D deficiency and type 2 diabetes.

Methods: Type 2 diabetic patients who were regular and compliant on their current prescription were investigated for their recent HbA1c level. Patients with HbA1c between 7.5 and 8.0 were further investigated for serum vitamin D level. Vitamin D deficient patients (serum vitamin D < 25ng/ml) were enrolled for the study and randomised one to one in two groups. Group 1 in whom oral vitamin D supplementation done at dose of 60.000IU weekly for 3 months. Group 2 in whom no vitamin D supplementation done. In both groups current medications and other advices were continued without any alteration for 3 months. HbA1c was estimated again at end of 3 month in both groups.

Results: 24 patients in each group completed the study period with regular compliance. Group 1; 15 female and 9 male, average age 54 years (SD 9.55), average HbA1c 7.7, average serum vitamin D was 16.8ng/ml (SD 4.51). Group 2; 10 female and 14 male, average age 50 years (SD 7.99), average HbA1c 7.8, average serum vitamin D was 17.3 ng/ml (SD 4.20). Group 1 average HbA1c after 3 months was 7.4 whereas in group 2 remain same 7.8. The difference was statistically significant (t-value is 3.51725. The p-value is 0.000497. The result is significant at p < 0.05)

Conclusion: A judicious supplementation of vitamin D among vitamin D deficient type 2 diabetic patients with near normal HbA1c can reduce the blood sugar level. HbA1c reduce to target levels if it is minimally elevated.

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Introduction

Diabetes mellitus is a complex, polygenic, and multifactorial disease. Both genetic predisposition and environmental factors contribute in the development and pathogenesis of T2DM. Several reports in literature have already shown that Vitamin D deficiency is a risk factor for glucose intolerance, causes decreased insulin secretion, and finally results in T2DM, suggesting the role for vitamin D in the pathogenesis of diabetes mellitus.

There are several mechanisms whereby vitamin D may influence insulin secretion and sensitivity. The three important mechanism are Impaired pancreatic β-cell function (Presence of vitamin D receptors in beta cells and vitamin D response element in human insulin gene support a direct effect of vitamin D on insulin synthesis and secretion), insulin resistance (vitamin D stimulate the expression of the insulin receptor in peripheral tissues and thereby increase glucose transport) and low-grade systemic inflammation. Vitamin D attenuates the expression of pro-inflammatory cytokines involved in insulin resistance such as interleukins, IL-1, IL-6, TNF-α, also down regulates NF-Kb (Nuclear factor) activity. Vitamin D appears to affect exclusively the insulin response to glucose stimulation, it does not appear to influence basal insulinemia. Diabetic patients have a higher incidence of hypovitaminosis D. The prevalence of Vitamin D deficiency in Diabetics ranged from 54% to 78%.

Material and Methods

Type 2 diabetic patients attending medicine OPD at SN Medical College, Agra were investigated for their recent HbA1c levels and serum vitamin D levels. The selection is done irrespective of their current treatment regimen and previous vitamin D supplementation. The patients who were having HbA1c between 7.5 and 8.0 and lower serum vitamin D level (serum vitamin level<25ng/ml) were enrolled for the study. Patients having diabetic nephropathy more than stage 2 were excluded. Besides this unwilling, poorly compliant patients, patient with hepatic diseases, severely sick patients requiring hospitalisation, patient having other comorbidity like tuberculosis or any other chronic infections, patients taking drugs that can alter vitamin D level were excluded from the study. Enrolled patients were divided into two groups, group 1 and group 2. 31 patients were selected in group 1 and 30 in group 2. Randomisation was done one to one. Oral vitamin D supplementation with dose of 60,000 international units per week as per prescribed instructions was done in patients of group 1 for 12 weeks. Besides this no changes is done in the current prescription and advices for diet and life style modification remains unchanged. Patient strictly advised to follow the instructions and avoid major changes in diet and physical activity. Patients further instructed to consult immediately, if appear any new symptom or complication or there is any major variation on SMBG. Similar instructions were given to patient in group 2 except the vitamin D supplementation. Patients were called every month for routine clinical examination and to check compliance. This is also done to monitor any untoward manifestation of vitamin D supplementation. After 12 weeks of regular follow up 24 patients form each group were selected for HbA1C testing. The selected patients were those who regular followed the instruction and were strict compliant to the treatment.

Observation and Results

24 patients in each group completed the study period with regular compliance. Characteristics of both groups summarized in table 1.

Group 1- 15 female and 9 male, average age 54 years (SD 9.55), average HbA1c 7.7, average serum vitamin D was 16.8ng/ml (SD 4.51).

Group 2- 10 female and 14 male, average age 50 years (SD 7.99), average HbA1c 7.8, average serum vitamin D was 17.3 ng/ml (SD 4.20).

After adjustment for age, sex, blood pressure, lifestyle, family history, seasonal change, parathyroid hormone, and high-sensitivity C-reactive protein, the participants with 25(OH) D deficiency had an increased risk of T2DM independent of BMI.
There is no static relationship between change in HbA1c levels and vitamin D supplementation. As depicted in figure 3 and figure 4 the difference in HbA1c is unpredictable after vitamin D supplementation.

The observation period remain uneventful and no new symptoms or complications developed with supplementation.

**Discussion**

Although the absolute difference in HbA1C due to Vitamin D supplementation may appear to be small (0.38%), such a difference could have a large effect at the population level, especially in individuals who are pre-diabetics. For example, in the Diabetes Prevention Program trial, which targeted a population very similar to our population, the difference in HbA1c between the active lifestyle intervention and placebo throughout the entire duration of the study was ≈0.15%, which was associated with a 58% decrease in incident diabetes.

Kositsawat et al.\(^6\) conducted cross-sectional analyses of data from 9,773 adults who participated in the 2003–2006 National Health and Nutrition Survey (NHANES), and found that Serum 25-hydroxyvitamin D concentration was inversely associated with Hba1c level in individuals 35–74 years old, but not among the younger or older adults. Lu L. et al.\(^7\) found Vitamin D deficiency and insufficiency is common (69.2 and 24.4%, respectively) in the middle-aged and elderly Gagnon C, Lu ZX, (the Australian Diabetes, Obesity and Lifestyle study)\(^8\) found that each 25 nm/ml increment in serum 25OHD was associated with a 24% reduced risk of diabetes. Dietary calcium intake was not associated with reduced diabetes risk. Parini PATEL et al.\(^9\) randomized Subjects with T2DM and serum 25-hydroxyvitamin D (25(OH) D) concentrations <25 ng/mL to receive 400 IU (Group 1) or 1200 IU (Group 2) cholecalciferol for 4 months. Mean 25(OH) D levels increased in both groups, but not to optimal levels.
In conclusion, our study showed that Vitamin D supplementation had a significant effect in glycemic control in diabetic patients especially among those deficient in vitamin D. The glycemic effect of vitamin D is more prominent in postprandial blood sugar control probably by decreasing insulin resistance. Patients with minimally elevated HbA1c and vitamin D deficiency, mare supplementation of vitamin D improves glycemic control without modification in present diabetic treatment.

**TABLE 1: Characteristics of Group 1 and Group 2**

<table>
<thead>
<tr>
<th>CHARACTERISTICS</th>
<th>Group 1</th>
<th>Group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex M/F</td>
<td>9/15</td>
<td>14/10</td>
</tr>
<tr>
<td>Average age in years (SD)</td>
<td>54 (9.55)</td>
<td>50 (7.99)</td>
</tr>
<tr>
<td>Vitamin D level</td>
<td>16.8 ng/ml</td>
<td>17.3 ng/ml</td>
</tr>
<tr>
<td>Average HbA1c before treatment</td>
<td>7.7</td>
<td>7.8</td>
</tr>
<tr>
<td>Average HbA1c after treatment</td>
<td>7.4</td>
<td>7.8</td>
</tr>
</tbody>
</table>

**Conclusion**

Judicious vitamin D supplementation among vitamin D deficient type 2 diabetic patients with minimally deranged HbA1c can promote better sugar control as evident with improved HbA1c levels. Placebo control trials with double blinding required to strengthen the present evidences.

**References**


8. Gagnon C1, Lu ZX, Magliano DJ, Dunstan DW, Shaw JE, Zimmet PZ, Sikaris K, Grantham N, Ebeling PR, Daly RM Serum 25-hydroxyvitamin D, calcium intake, and risk of type 2 diabetes after 5 years: results from a national, population-based prospective study (the Australian Diabetes, Obesity and Lifestyle study). Diabetes Care. 2011 May;34(5).