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Original Research Article

Metabolic effects of oral vitamin D supplementation as an adjuvant therapy on subjects with type 2 diabetes

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ABSTRACT

Background: It is common for patients with type 2 diabetes mellitus (T2DM) to have vitamin D deficiency. Aim of the study is to determine the metabolic effects of oral vitamin D supplementation in a cohort of T2DM subjects.
Methods: Subjects with T2DM were divided into two groups. Group A (Control) included subjects who received the standard treatment (conventional antidiabetic drugs). Group B (Intervention), apart from the standard treatment (conventional antidiabetic drugs), was also supplemented with Vitamin D3. All the patients were followed up at baseline, 6 months, 12 months and 18 months.
Results: Vitamin D deficiency was noted down in all the study subjects. Even after 18 months of supplementation, all subjects remained vitamin D deficient. There was a significant improvement in the circulating levels of 25-hydroxyvitamin D. Improvement in the lipid profile of subjects was observed as evidenced by a decrease in total cholesterol (5.0±0.92 mmol/l) as compared to baseline (5.5±1.6 mmol/l). HOMA-IR changed significantly after 18 months of supplementation from baseline (7.0±1.06 vs 10.8±1.96 nmol/l).
Conclusions: Supplementation to achieve higher levels of vitamin D remains a promising adjuvant therapy for T2DM patients. Additionally, the intervention brought out a favourable change in HDL/LDL ratio among study subjects.

Keywords: Diabetes mellitus, Supplementation, Vitamin D

INTRODUCTION

Vitamin D is indispensable as well as vital for humans. Vitamin D can be obtained through a balanced die and is synthesized in the skin after sunlight exposure. Natural sources of vitamin D in foods are not sufficient to supply the normal body requirements. Thus, skin synthesis of vitamin D through exposure to sunlight is thought to

constitute the major source of vitamin D.[1] Vitamin D deficiency is rampant in tropical countries including India despite plenty of sunshine.[2] It is common for patients with type 2 diabetes mellitus (T2DM) to have vitamin D deficiency.[3]

Vitamin D has been established as a major factor influencing glucose and calcium metabolism, thus having bearing on diabetes mellitus.[4] Recently, T2DM is considered as one of the non-skeletal diseases associated with vitamin D deficiency.[5] Observational studies have indicated an association between vitamin D deficiency and the onset and progression of T2DM. Vitamin D correction, therefore, may increase insulin secretion and improve glucose homeostasis; however, its effects on healthy individuals or in those with impaired glucose tolerance remain unclear.[6,7] In this study, we wish to determine the metabolic effects of oral vitamin D supplementation in a cohort of T2DM subjects. This study may reveal whether oral vitamin D supplementation can be an adjunct therapy in T2DM patients, and on the importance of optimizing vitamin D levels in the prevention and improved management of T2DM. Keeping above facts in mind, we conducted this study with the aim of assessing the impact of vitamin D supplementation as an adjuvant therapy on subjects with type 2 diabetes.

METHODS

The present prospective interventional study was planned and executed by department of pharmacology in collaboration with the department of internal medicine of a tertiary care medical college and teaching hospital of northern India. A total of 226 participants diagnosed to have type 2 Diabetic Mellitus and seeking care at this study center formed the study population. This sample size was calculated using a statistical sample size calculator using mean Hb.A1C (%) values from previous study.[8]

Study subjects were divided into two groups. Group A (Control) included every alternate patient who received the standard treatment (conventional antidiabetic). Group B (Intervention), in addition to the standard treatment (conventional antidiabetic) was also supplemented with Vitamin D3.Subject demographics, duration of diabetes, antidiabetic medication, body mass index (BMI) was assessed. Laboratory measurements of serum vitamin D3 level, hemoglobin A1c (HbA1c), fasting plasma glucose (FPG), and lipid profile was measured for all patients. Homeostatic model assessment-insulin resistance (HOMA-IR) was calculated. Other laboratory parameters were also measured.

Subjects of intervention were started on cholecalciferol replacement-45,000 units once weekly for 8 weeks and then 22,500 units once weekly for 16 weeks. Measured variables were reassessed after 6 months of replacement therapy. All variables were measured before and after cholecalciferol supplementation. All the patients were followed up at baseline, 6 months, 12 months and 18 months. Written and informed consent was obtained from study subjects. Permission of ethical committee was obtained from the Institutional Ethics Committee.

All the questionnaires were manually checked and edited for completeness and consistency and were then coded for computer entry. After compilation of collected data, analysis was done using Statistical Package for Social Sciences (SPSS), version 21 (IBM, Chicago, USA). The results were expressed using appropriate statistical variables.

RESULTS

Vitamin D deficiency was noted down in all the study subjects. Even after 18 months of supplementation, all subjects remained vitamin D deficient 25-(OH)D=51.2±1.5 nmol/l. There was a significant improvement in the circulating levels of 25-hydroxyvitamin D from baseline to 6 months (31.2±1.6 vs 41.5±1.4 nmol/l), and these levels remained unchanged over the course of the supplementation period.

Table 1: Characteristics of study subjects with T2DM as per follow-up (Mean ± SD).

Variable	Baseline	6 Months	12 Months	18 Months	P Value
DMT2 Duration (years)	7.4±4.1				
25-(OH) D (nmol/l)	31.2±1.6	41.5±1.4	43.2±1.6	51.2±1.5	>0.05
BMI (kg/m^2)	28.0±5.2	28.2±5.3	28.6±5.3	28.9±5.8	>0.05
Glucose (mmol/l)	11.4±3.8	11.6±3.4	11.9±3.2	11.5±3.7	>0.05
T Cholesterol (mmol/l)	5.5±1.6	5.6±1.8	5.1±1.2	5.0±0.92	>0.05
Triglycerides (mmol/l)	1.5±0.38	1.8±0.40	2.1±0.45	1.7±0.40	>0.05
HDL-Chol (mmol/l)	1.7±0.30	1.6±0.32	1.2±0.29	1.0±0.26	>0.05
LDL-Chol (mmol/l)	5.0±1.62	5.1±1.65	4.8±1.53	5.0±1.52	>0.05
Insulin (IU/ml)	16.1±2.1	19.0±2.4	19.6±2.5	17.4±1.9	>0.05
HOMA-IR	7.0±1.06	7.3±1.17	9.5±1.36	10.8±1.96	<0.05*

*Statistically significant

An improvement in the lipid profile of subjects was observed as evidenced by a decrease in total cholesterol (5.0±0.92 mmol/l) as compared to baseline (5.5±1.6 mmol/l), as well as LDL-cholesterol (5.0±1.62 vs. 5.0±1.52 mmol/l) after 18 months. Non-significant increase in HDL- cholesterol was noted across time points. HOMA-IR changed significantly after 18 months of supplementation from baseline (7.0±1.06 vs 10.8±1.96 nmol/l) ($p<0.05$) (Table 1).

DISCUSSION

An important factor that links diabetes mellitus types 1 and 2 (T1DM and T2DM, respectively) is the expression of vitamin D receptors (VDRs) in more than 30 biological tissues, including the pancreatic islet cells.[9] On the other hand, it is common for patients with T1DM and T2DM to have vitamin D deficiency.[10] Furthermore, several longitudinal and observational studies have demonstrated that low levels of serum 25-hydroxyvitamin D predict T2DM risk in Europeans, African-Americans and South Asians.[11-13] Vitamin D correction, therefore, may increase insulin secretion and improve glucose homeostasis; however, its effects on healthy individuals or in those with impaired glucose tolerance remain unclear.

Observational studies have indicated an association between vitamin D deficiency and the onset and progression of T2D as well as future macrovascular events.[7,8] Moreover, in vivo and in vitro studies have proposed potential roles of vitamin D in glucose metabolism, e.g., stimulating insulin secretion via the vitamin D receptor on pancreatic β cells; modulating immune responses and lowering systematic inflammation; and reducing peripheral insulin resistance through vitamin D receptors in the muscles and liver.[11] However, evidence from interventional studies at a population level have been inconclusive. Recently, three meta-analyses observed no benefits of vitamin D supplementation on glycaemic indices and insulin resistance except for a modest reduction of hemoglobin A1c (HbA1c) (0.32-0.39%), although they did not separate intramuscular injections from oral supplementation, or fortified food from nutrient supplementation alone.[14]

In this study we observed that, Vitamin D deficiency was noted down in all the study subjects. Even after 18 months of supplementation, all subjects remained vitamin D deficient [25-(OH)D=51.2±1.5 nmol/l]. There was a significant improvement in the circulating levels of 25-hydroxyvitamin D from baseline to 6 months (31.2±1.6 vs 41.5±1.4 nmol/l), and these levels remained unchanged over the course of the supplementation period.

An improvement in the lipid profile of subjects was observed as evidenced by a decrease in total cholesterol (5.0±0.92 mmol/l) as compared to baseline (5.5±1.6 mmol/l), as well as LDL-cholesterol (5.0±1.62 vs. 5.0±1.52 mmol/l) after 18 months.

Another study from Egypt investigated the effects of vitamin D supplementation on glucose homeostasis and lipid profile in 125 T2DM subjects having vitamin D deficiency.[15] Vitamin D3 replacement was associated with a significant increase in its level (14.0±4.0 vs 31.0 vs 7.9 ng/mL, $P<0.001$). This was associated with a significant reduction of HbA1c (7.9±1.7 vs 7.4%±1.2%, $P=0.001$). Study concluded that Cholecalciferol helps improve blood glucose control and cholesterol profile in vitamin D3-deficient type 2 diabetic patients.

An author from Iran performed a double-blind randomized placebo-controlled trial among 70 subjects to study impact of treatment with oral calcitriol on glucose indices in T2DM patients.[8] One group received two capsules of calcitriol (0.25 µg 1,25-dihydroxy cholecalciferol per each capsule) per day. The second group received placebo tablets. At the end of the study, fasting plasma glucose increased in the control group ($p=0.038$), while it remained unchanged in calcitriol group. Level of insulin and HbA1c increased significantly in both groups (7.08±1.6 vs7.90±2.1, $p=0.013$ and 7.03±1.7 vs 8.59±2.5, 0.0004 in treatment and control group). Study concluded that Vitamin D supplementation attenuated the increase in glycemia, and increased insulin secretion, but had no effect on insulin resistance.

In this study, HOMA-IR changed significantly after 18 months of supplementation from baseline (7.0±1.06 vs 10.8±1.96 nmol/l) ($p<0.05$). Mirhosseini et al, found significant positive effects of vitamin D supplementation on fasting blood glucose (FBG), HbA1c and a homeostasis model assessment of insulin resistance (HOMA-IR), yet it calculated one study with considerable influence twice in the pooled analysis and combined results reported as median and interquartile range together with those reported as mean and standard deviation.[16]Soric et al, reported that significant improvements in glucose metabolism were only manifested in patients with poor glycaemic control at baseline.[17] While they used different cut-offs (HbA1c ≥8% and 9% respectively), applying alternative cut-offs did not change the results in this meta-analysis. Further investigations are required to clarify this association and explore the underlying explanation for it.

CONCLUSION

This study observed that in the study population receiving oral Vitamin D3 supplementation, circulating 25-hydroxyvitamin D levels remained suboptimal even after 18 months. But the intervention brought out a favourable change in HDL/LDL ratio. Thus, supplementation to achieve higher levels of vitamin D remains a promising adjuvant therapy for T2DM patients. Further studies are warranted to support our findings.

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Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Ardawi MS, Sibiany AM, Bakhsh TM, Qari MH, Maimani AA. High prevalence of vitamin D deficiency among healthy Saudi Arabian men: relationship to bone mineral density, parathyroid hormone, bone turnover markers, and lifestyle factors. Osteopor Int. 2012 Feb 1;23(2):675-86.
2. Bansal A, Singh AA, Goel S, Goel AK, Singh A, Chhoker VK et al. Evidence of vitamin d deficiency and its relation with possible cardiovascular risk among postmenopausal women. Healthline. 2014;5(2):41-5.
3. Gupta V, Singh A, Goel S. Correlation of Vitamin D Level with Biochemical Parameters in Healthy Indians Aged ≥50 Years. Sch J App Med Sci. 2017;5(7C):2655-8.
4. Qi D, Nie XL, Wu S, Cai J. Vitamin D and hypertension: Prospective study and meta-analysis. PLOS one. 2017 Mar 30;12(3):e0174298.
5. Vaidya A, Williams JS. The relationship between vitamin D and the renin-angiotensin system in the pathophysiology of hypertension, kidney disease, and diabetes. Metabolism. 2012 Apr 1;61(4):450-8.
6. Pereira-Santos M, Santos JY, Carvalho GQ, Santos DB, Oliveira AM. Epidemiology of vitamin D insufficiency and deficiency in a population in a sunny country: Geospatial meta-analysis in Brazil. Crit Rev Food Sci Nutr. 2018 Mar 6:1-8.
7. Makariou SE, Elisaf M, Challa A, Tentolouris N, Liberopoulos EN. No effect of vitamin D supplementation on cardiovascular risk factors in subjects with metabolic syndrome: a pilot randomised study. Archives of medical sciences. Atheroscle Dis. 2017;2:e52.
8. Eftekhari MH, Akbarzadeh M, Dabbaghmanesh MH, Hasanzadeh J. Impact of treatment with oral calcitriol on glucose indices in type 2 diabetes mellitus patients. Asia Pacific J Clin Nutr. 2011 Dec 1;20(4):521-6.
9. Mathieu C, Badenhoop K. Vitamin D and type 1 diabetes mellitus: state of the art. Trends Endocrinol Metab. 2005 Aug 1;16(6):261-6.
10. Di Cesar DJ, Ploutz-Snyder R, Weinstock RS, Moses AM. Vitamin D deficiency is more common in type 2 than in type 1 diabetes. Diabetes Care. 2006 Jan 1;29(1):174.
11. Deleskog A, Hilding A, Brismar K, Hamsten A, Efendic S, Östenson CG. Low serum 25-hydroxyvitamin D level predicts progression to type 2 diabetes in individuals with prediabetes but not with normal glucose tolerance. Diabetologia. 2012 Jun 1;55(6):1668-78.
12. Harris SS. Does vitamin D deficiency contribute to increased rates of cardiovascular disease and type 2 diabetes in African Americans?. Am J Clin Nutr. 2011 Mar 2;93(5):1175S-8S.
13. Boucher BJ: Hypovitaminosis D and risk of type 2 diabetes in British South Asians. Diabet Med 2006, 23(3):336.
14. Wu C, Qiu S, Zhu X, Li L. Vitamin D supplementation and glycemic control in type 2 diabetes patients: A systematic review and meta-analysis. Metabolism. 2017 Aug 1;73:67-76.
15. Nada AM, Shaheen DA. Cholecalciferol improves glycemic control in type 2 diabetic patients: a 6-month prospective interventional study. Therapeutics and clinical risk management. 2017;13:813.
16. Mirhosseini N, Vatanparast H, Mazidi M, Kimball SM. The effect of improved serum 25-hydroxyvitamin D status on glycemic control in diabetic patients: a meta-analysis. J Clin Endocrinol Metabol. 2017 Jul 3;102(9):3097-110.
17. Soric MM, Renner ET, Smith SR. Effect of daily vitamin D supplementation on HbA1c in patients with uncontrolled type 2 diabetes mellitus: a pilot study. J Diabetes. 2012 Mar 1;4(1):104-5.

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