ORIGINAL RESEARCH

Effect of Intermittent Vit D3 supplements in postmenopausal women with diabetes

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ABSTRACT

Background: Vitamin deficiencies can lead to a number of physiological and metabolic issues as well as increase the risk of developing diabetes mellitus.Restoring normal serum vitamin D levels may help a number of postmenopausal women's common diseases that are linked to low levels of the hormone including muscle strength.

Objective: The aim of this study was to evaluate the effect of weekly vitamin D3 supplementation on metabolic parameters and muscle strength of postmenopausal women with type 2 diabetes.

Methods: Type 2 diabetic postmenopausal women were recruited from an outpatient clinic and were divided into 2 groups to receive vehicle versus vitamin D3 supplements along with their regular antidiabetic therapy. Handgrip strength was measured both before and after the intervention. Secondary parameters were related to blood glucose, lipid profle and blood pressure and vitamin D3 level. Comparison was made between 12-week post intervention versus baseline level.

Results: Baseline characteristics were not different for the patients in the intervention and control groups. All patients were above the age of 60 years and duration of diabetes was>10 years. At the end of treatment period, the intervention group exhibited notable elevations in blood vitamin D3 levels but it was not seen in the control group. The intervention group exhibited a significant improvement in handgrip strength, as evidenced by the increase in kilograms for both the right arm. Effect was visible in both the hands. Other parameters were not significantly different between intervention and control group.

Conclusion: In postmenopausal women with long-standing type 2 diabetes, vitamin D3 supplementation at levels similar to 942 IU/day increased isometric handgrip strength but had no effect on glycaemic management.

Keywords: Type 2 Diabetes., Vitamin D3 supplements, Muscle strength, Postmenopausal, Glycemic control

INTRODUCTION

Hyperglycemia, or elevated blood glucose, is a hallmark of many different metabolic illnesses together referred to as diabetes mellitus (DM). Type 2 diabetes mellitus (T2DM) is caused by inadequate insulin or insulin resistance, a condition in which the body cells fail to use insulin. Type 1 diabetes mellitus (T1DM) starts when the immune system malfunctions and kills the pancreatic β-cells [1,2]. Numerous etiologies, such as genetic and epigenetic predispositions, environmental variables, and lifestyle modifications, have been associated with diabetes mellitus [3]. Antioxidant deficits, encompassing both antioxidant and other vitamins, have lately been associated with an increase in the disease load [4]. According to studies, diabetics produce unusually high levels of reactive oxygen species and have low levels of antioxidant activity, which increases oxidative damage [5].Vitamin deficiencies can lead to a number of physiological and metabolic issues as well as increase the risk of developing diabetes mellitus. Among these physiological abnormalities include oxidative stress, decreased islet cell populations, B-cell mortality, impaired tyrosine kinase activity, and dysfunctional pancreatic β-cells [6]. Reduced lean body mass, an impaired insulin

signaling pathway, and elevated protein kinase C activity are a few more [6]. The body cannot operate correctly without all vitamins in the proper quantities, which is necessary for a healthy existence [3]. However, a number of research, including a systematic review and meta-analysis by Balbi et al. [7], demonstrate that the vitamins B-vitamins, C, D, E, and A are primarily important in the pathophysiology of diabetes mellitus. Numerous investigations on the role of vitamin D in diabetes have revealed a link between low vitamin D levels and a higher risk of type 2 diabetes and its complications. Through altering several critical processes in the development of diabetes and its complications, including peripheral insulin resistance, down-regulation of the insulin receptor gene, systemic "sterile" inflammation, immune activation, and pancreatic insulin secretion, vitamin D deficiency may play a significant role in the pathogenesis of type 2 diabetes [8]. Based on some experimental investigations, vitamin D has been found to possess antioxidant properties that may block the production of free radicals, hence causing lipid peroxidation and oxidative modification of other biomolecules [9]. Owing to the aforementioned benefits, vitamin D supplementation has been suggested as a potential treatment strategy for type 2 diabetes in order to improve glycaemic control and avert complications [10]. Restoring normal serum vitamin D levels may help a number of postmenopausal women's common diseases that are linked to low levels of the hormone. Low vitamin D levels in postmenopausal women are linked to hypersecretion of PTH, which is linked to higher cortical bone porosity [11]. Postmenopausal women who have inadequate or deficient levels of 25(OH)D are more likely to develop metabolic syndrome, and vitamin D treatment dramatically lowers triglyceride, insulin, and HOMA-IR levels. Supplementing with vitamin D may help women with prediabetes and low 25(OH)D levels become more insulin-sensitive [12]. It is uncertain, nonetheless, if vitamin D treatment will improve the metabolic regulation and muscular strength of individuals with diabetes mellitus type 2 or if there is a causative association between vitamin and diabetic problems. A 6-month follow-up randomized controlled trial was conducted to ascertain if vitamin D supplementation in T2DM patients was beneficial.

MATERIALS AND METHODS

STUDY POPULATION

74 postmenopausal type 2 diabetic women were recruited consecutively from an outpatient clinic. The women had serum vitamin D levels less than 30 ng/ml and hand strength less than 20 kg. They were randomly assigned to receive either 2cc olive oil preparation or oral vitamin D3 (6600 IU, or 943 IU per day) once a week for three months. All subjects received the study medication under supervision. The Institute of Medicine's guideline [13] was followed while choosing the vitamin dosage.

CRITERIA FOR EXCLUSION

Patients diagnosed with type 1 diabetes; those taking drugs known to disrupt bone metabolism, including bisphosphonates, hormonal therapy, anabolic steroids, calcium and vitamin D supplements, and glucocorticoids; primary hyperparathyroidism, uncontrolled hyper- and hypothyroidism, Paget's disease of the bone; cancer; chronic kidney and liver disease; severe vitamin D deficiency (serum 25(OH)D <15 ng/ml); neurological disorders that impair muscle function, such as dementia, Parkinson's disease, and multiple sclerosis; rheumatoid arthritis; congestive heart failure; HIV infection; and malabsorption syndromes?

DRUG INTERVENTION AND RANDOMIZATION

The statistical program research randomizer carried out the randomization. Extra virgin olive oil infused with vitamin D3 was provided to the intervention group (n=38), whereas the control group (n=36) was given the identical extra virgin olive oil used for the group intervention. For a period of 12 weeks, the doses for the control and intervention groups were administered once a week under supervision. The vitamin D3 intervention dose was in compliance with American and European guidelines, which equate to 6600 IU per week or 942 IU per day [13].

STUDY OUTCOMES

Using the dynamometer approach, handgrip strength was measured both before and after the intervention (JAMAR dynamometer; Lafayette Instrument Company, IN, USA). The amounts of serum 25(OH)D were determined by the chemiluminometric assay (LIAISON, DiaSorin, USA). 1.8 ng/ml was the assay sensitivity, which is the lowest value that deviates from zero; the interassay coefficient of variation was 5%. Creatinine, triglycerides, calcium, total cholesterol and fractions, glycated haemoglobin (HbA1c), and glucose level in serum were measured using autoanalyzer.

STATISTICAL ANALYSIS

The statistical analysis employed the Student's t-test for independent samples or the Mann-Whitney test to compare the groups in each assessment for continuous variables. Additionally, the paired Student's t-test or Wilcoxon test was used for paired data to compare two assessments within each group. The F test (analysis of variance) was employed for repeated measurements to compare several evaluations within each group, with further multiple comparisons conducted using the Bonferroni method.

RESULTS

DEMOGRAPHIC CHARACTERISTICS

All recruited diabetic patients were divided into two groups according to baseline characteristics. These characteristics were not different for the patients in the intervention and control groups. Age of the patients in intervention groups was age 61.23 ± 6.41 versus 62.81 ± 7.14 years in control group; duration of diabetes was 12.56 ± 4.56 versus 11.56 ± 5.97 years;BMI 28.2 ± 4.5 versus 28.8 ± 4.9 kg/m2;HbA1c 9.31 ± 1.21 versus 9.43 ± 1.34 %; serum 25(OH)D 23.1 ± 2.37 versus 23.34 ± 2.42 ng/ml, serum total cholesterol 232.45 ± 19.21 versus 228.34 ± 17.57 mg/dl; serum triglycerides 178.61 ± 21.59 versus 186.42 ± 21.86 mg/dl;serum high-density lipoprotein cholesterol (HDL-C) 52.83 ± 6.34 versus 53.78 ± 7.34 mg/dl and serum low-density lipoprotein cholesterol (LDL-C) 134.41 ± 12.21 versus 132.74 ± 11.45 mg/dl in intervention and control group, respectively (Table 1).

Table 1: Baseline characteristics of study subjects.

Variable	Control	Intervention	*p* value
Age (years)	62.81 ± 7.14	61.23 ± 6.41	0.95
Duration of diabetes (years)	11.56 ± 5.97	12.56 ± 4.56	0.36
BMI (kg/m^2)	28.8 ± 4.9	28.2 ± 4.5	0.61
SBP (mm Hg)	138 ± 13.23	139.56 ± 14.32	0.65
DBP (mm Hg)	86.67 ± 7.32	83.58 ± 6.17	0.23
25(OH)D (ng/ml)	23.34 ± 2.42	23.1 ± 2.37	0.62
RAHS (kg)	17.67 ± 2.79	16.31 ± 1.88	0.63
LAHS (kg)	15.83 ± 1.89	15.73 ± 1.86	0.87
HbA1c (%)	9.43 ± 1.34	9.31 ± 1.21	0.15
Total cholesterol (mg/dl)	228.34 ± 17.57	232.45 ± 19.21	0.38
HDL-C (mg/dl)	53.78 ± 7.34	52.83 ± 6.34	0.87
LDL-C (mg/dl)	132.74 ± 11.45	134.41 ± 12.21	0.23
Triglycerides (mg/dl)	186.42 ± 21.86	178.61 ± 21.59	0.98

Vit D3 supplements increased serum Vit D3 level

At the end of treatment period, the intervention group exhibited notable elevations in blood vitamin D3 levels, which rose from a baseline value of 23.1 ± 2.37 ng/ml to 28.46 ± 2.51 ng/ml. The control group had a tatistically insignificant reduction, with levels decreasing from 23.34 ± 2.42 ng/ml at baseline to 22.95 ± 2.31 ng/ml (Table 2).

Table 2: Effect of treatment on serum vitamin D level

Variable	Control		Intervention	
	Baseline	12-weeks post treatment	Baseline	12-weeks post treatment
Vit D3 (ng/ml)	23.34 ± 2.42	22.95 ± 2.31	23.1 ± 2.37	28.46 ± 2.51*

*P<0.05 vs baseline, Student's t-test.

EFFECT ON HAND GRIP STRENGTH

The intervention group exhibited a significant improvement in handgrip strength, as evidenced by the increase in kilograms for both the right arm (from 16.31 ± 1.88 to 22.91 ± 2.47 kg, P<0.01) and the left arm (from 15.73 ± 1.86 to 20.95 ± 2.07 kg, P<0.01) (Figure 1A and Figure 1B, respectively). In contrast, the control group did not experience a significant change in handgrip strength, with the right arm measurements showing a change from 17.67 ± 2.79 to 19.61 ± 2.78 kg, P>0.05, and the left arm measurements showing a change from 15.83 ± 1.89 to 16.46 ± 1.98 kg, P>0.05.

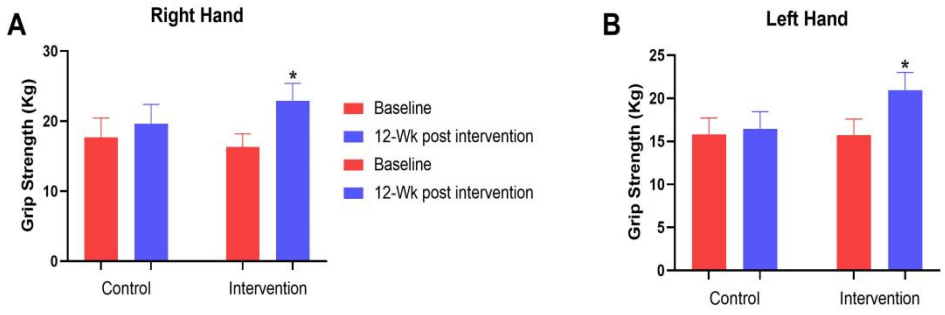

Figure 1: Handgrip strength in the right (A) and left (B) arm before and after vitamin D supplementation.

There were no statistically significant disparities seen in the initial distribution of body mass index (BMI) among the study participants. However, it is noteworthy that a greater proportion of individuals in the control group exhibited obesity towards the conclusion of the study period, as compared to those in the Vitamin D3 group (Control: 32.2 ± 3.9 vs. Vitamin D3: 27.5 ± 3.9; P<0.05). There were no statistically significant alterations seen in the average levels of fasting plasma glucose (FPG) (154.3 ± 46.3 to 162.1 ± 56.1 mg/dl, P>0.05), postprandial glucose (PPG) (221.6 ± 42.4 to 234.5 ± 38.9 mg/dl, P>0.05), and HbA1c (9.31 ± 1.21 to 8.56 ± 1.34 %, P>0.05). Furthermore, the administration of vitamin D3 supplements did not have any impact on the blood levels of triglycerides, cholesterol, HDL, and LDL. Nevertheless, the vitamin D3 therapy effectively maintained these values, in contrast to the control group of diabetic women who had elevated levels in the absence of vitamin supplementation. Vitamin D supplementation was shown to effectively control and maintain both systolic blood pressure (SBP) and diastolic blood pressure (DBP). The systolic blood pressure (SBP) exhibited a notable rise within the control group, rising from an initial mean value of 138 ± 13.23 mmHg to a final mean value of 142.5 ± 13.6 mmHg (P<0.05).

DISCUSSION

Our study demonstrated a substantial increase in handgrip strength with vitamin D3 supplementation in postmenopausal women with T2DM but no effect on blood glucose management. Clinically and biochemically, our patients matched well, and neither group had any anomalies related to hand joints. Other authors have not seen improvement in glycaemic indices with vitamin D administration, which is consistent with our findings. When Jorde and Figenschau compared the weekly dosage of 40,000 IU of cholecalciferol to a placebo over a 6-month period, they found that there was no increase in insulin secretion or a decrease in HbA1c in DM2 individuals [14]. However, Mitri and colleagues assessed the effects of supplementing with 800 mg of calcium and 2000 IU of cholecalciferol per day, alone or in combination, on insulin sensitivity, glucose tolerance, and pancreatic β-cell function in adults with a high-risk of developing DM2, and found no significant effect [15].

Additionally, vitamin D3 treatment did not enhance the lipid profile in the current trial. In a 5-year study, 1259 postmenopausal women were compared to a placebo-controlled daily dose of 400 IU of vitamin D3 and 1 g of calcium. The study found no significant changes in the levels of triglycerides, total cholesterol, HDL-C, and LDL-C in the serum [16]. Nevertheless, throughout the intervention period, our data showed that vitamin D had a positive impact on handgrip strength. Research has examined the connection between diabetes mellitus and handgrip strength, demonstrating a decrease in those with diabetes. 76 individuals with DM2 had substantially reduced handgrip strength values using the Jamar dynamometer in research conducted by Cetinus and colleagues [17]. Savas et al. (2007) found that the handgrip and pinch strength of diabetes patients were lower in both hands than those of nondiabetic patients [18]. Janssen et al. (2010) conducted a study involving 70 female geriatric patients who were over 65 years of age. The results showed that baseline serum 25(OH)D concentrations were significantly correlated with knee extension strength, handgrip strength, and leg extension power. However, after six months, there were no significant differences in strength or functional mobility between the groups receiving 400 IU of cholecalciferol plus 500 mg of calcium supplementation daily and the placebo plus calcium group [19]. Our study is unique in that it was conducted on female patients with diabetes and utilized a somewhat larger dosage. High dosage vitamin D3 supplementation (60,000 IU/week for 8 weeks, then 60,000 IU twice a month for 4 months) did not enhance handgrip strength or quality of life in a trial conducted on young, healthy females. Cholecalciferol dosing at 2000 IU and 5000 IU daily for 3 months showed beneficial benefits on muscular strength. Longer periods between vitamin D3 dosage delivery would not be functionally beneficial in this regard. While it is impossible to completely rule out the impact of weight increase on blood pressure in the control group, newer research suggests that vitamin D and blood pressure have an inverse connection. According to research by Forman and colleagues, the risk of hypertension was negatively correlated with plasma 25(OH)D levels [20]. There is no correlation between a high vitamin D consumption and an increased risk of developing arterial hypertension [20]. The prevalence of hypovitaminosis D and found a significant negative correlation between blood 25(OH)D and both SBP and DBP.In the current investigation, supplementing with vitamin D3 did not significantly alter SBP; nevertheless, the control group had considerable increases. In general, there were non-significant decreases in measures taken every 24 hours. The baseline mean blood 25(OH)D concentrations were comparable to the results of our investigation (23 ng/ml); however, the treatment period was extended to five months and the cholecalciferol dosage was increased to three thousand IU/day. The current study discovered that the intervention group's serum 25(OH)D levels increased significantly, while the control group's levels decreased at the end of the treatment period. This is consistent with other previously published research, which demonstrates that vitamin D3 administration may raise 25(OH)D in diabetic patients and yet produce a satisfying clinical response without producing an effective laboratory response. Despite having poor dietary vitamin D consumption, our patients did not exhibit extremely low blood 25(OH)D

levels (22.2 ng/ml) as a result of frequent sun exposure. This might possibly be the reason that there were no appreciable increases in serum 25(OH)D at the supplementation dosage that was utilized. A greater dosage of supplements could make this feasible. In conclusion, postmenopausal individuals with long-standing DM2 showed better isometric handgrip strength with vitamin D3 supplementation at dosages similar to 942 IU/day, but no change in glycaemic management.

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