



ORIGINAL RESEARCH ARTICLE

The Effect of Vitamin D Supplementation on Blood Lipids in Minorities with Type 2 Diabetes

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Abstract

Introduction: Vitamin D deficiency and type 2 diabetes are common among Hispanics and African Americans in the US. The aim of the study was to determine the effect of supplemental vitamin D intake (4000 IU/day or 6000 IU/day of vitamin D3 over a 6-month period) on blood lipids in a sample of African Americans and Hispanics with type 2 diabetes and vitamin D insufficiency.

Materials and methods: Participants (n = 75) were recruited by community outreach. Participants in both groups were required to take either 4000 IU or 6000 IU of vitamin D (Cholecalciferol) per day given in the form of a pill in a single daily dose. Mixed model was used to compare treatment effects (4000 IU vs. 6000 IU) on the outcome variables. Bonferroni multiple comparison test was used to detect significant changes from baseline, 3 months, and 6 months.

Results: A significant decrease in total cholesterol (from 193.88 ± 41.03 to 180.48 ± 27.53 mg/dl, P = 0.040) and triglycerides (from 201.44 ± 91.35 to 172.92 ± 76.87 mg/dl, P = 0.037) was found for the 6000 IU group at 6 months. The significance was lost after adjusting for confounders.

Conclusion: Our results suggest that the positive effect of vitamin D supplementation on lipid profile may be mediated by other cofactors related to vitamin D metabolism among Hispanic and African American participants with type 2 diabetes.

Keywords

Vitamin D, Blood lipids, Hispanics, African Americans, Type 2 diabetes

Introduction

Low levels of vitamin D are prevalent in the US. According to data from the National Health and Nutrition Examination Surveys (NHANES) in 2001-2006, 33% of the general US population had serum 25(OH)D below 50 nmol/L. In addition, low vitamin D levels are common among minorities. For instance, 41% of African Americans and 33% of Mexican Americans had serum 25(OH)D below 50 nmol/L compared to 18% of non-Hispanic Whites [1].

Vitamin D is produced in the skin by the action of ultraviolet light. Even with similar levels of sun exposure, the skin color is a key determinant in vitamin D production. African Americans and Hispanics are at a particularly high risk for vitamin D deficiency because their darker skin color limits the amount of ultraviolet light that penetrates, thereby reducing cutaneous synthesis of vitamin D₃ [2]. Vitamin D can also be obtained from the diet with consumption of vegetable and animal products. Vitamin D needs to be activated by hydroxylation in the liver and kidney to form its metabolically active form: 1,25(OH)₂D₃. This metabolite produces its effects by activating the vitamin D receptor (VDR) in the cells [2].

The VDR is present in vascular and myocardial cells

which suggest an involvement of vitamin D mediated effects in the development of cardiovascular disease (CVD) [3]. Cardiovascular risk factors such as type 2 diabetes (T2D) and dyslipidemia are the major causes of death in the US, especially among minorities [4]. Therefore, it is of crucial importance to determine the role of vitamin D supplementation on the prevention of CVD.

Associations among vitamin D insufficiency and lower high density lipoprotein (HDL), higher triglycerides, and hypercholesterolemia have been reported [5-7]. However, randomized clinical trials evaluating the effects of vitamin D repletion on lipid panel have reported conflicting results [8-10].

Patients with T2D are more likely to develop hypertension, dyslipidemia, arteriosclerosis and all of the complications related to myocardial infarction and stroke [11]. Since finding new strategies to decrease diabetes complications and cardiovascular risk among patients with T2D is a major public health goal, testing the direct benefit of vitamin D repletion on blood lipids is warranted. In addition, most of the current studies have been conducted in Caucasian populations. Since African Americans and Hispanics are more prone to both vitamin D insufficiency and T2D compared to Caucasians, it is important to test the effect of vitamin D repletion on these high risk populations.

The aim of the present study was to determine the effect of supplemental vitamin D intake (4000 IU/day or 6000 IU/day of vitamin D₃ over a 6-month period) on blood lipids in a sample of African Americans and Hispanics with T2D and vitamin D insufficiency (25(OH)D < 30 ng/ml) living in South Florida.

Methods

Subject recruitment

An intervention study to assess the effects of vitamin D supplementation (4000 IU/day and 6000 IU/day) over six months on cardiovascular disease markers among a sample of African Americans and Hispanics with T2D was conducted (clinicaltrials.gov NCT 01412710). The present study analyzed the data collected at screening (serum 25(OH)D), baseline (blood lipids), 3 months (serum 25(OH)D and blood lipids), and 6 months (serum 25(OH)D and blood lipids).

The study consisted of two phases: phase one included the screening of individuals, phase two included the recruitment of individuals who met inclusion criteria and beginning of the vitamin D intervention trial. Inclusion criteria were vitamin D insufficiency (25(OH)D < 30 ng/ml), 30-70 years of age, African American or Hispanic with confirmed T2D. Exclusion criteria were taking vitamin D supplements other than standard daily multivitamin formula, receiving insulin therapy, being pregnant or lactating, having thyroid, hepatic, renal dysfunction, cancer, HIV, or major psychiatric disorders. Renal fail-

ure was defined as currently on dialysis or glomerular filtration rate lower than 15 ml/min/1.73 m² (stage 5) confirmed by primary care physician.

Flyers explaining the purpose of the study, inclusion/exclusion criteria and the investigators' emails and phone numbers were distributed in highly visited community areas such as churches, supermarkets, and clinics. Two clinics were visited every week for recruitment purposes: Borinquen Health Care Center and Clinical Care Medical Center. When volunteer participants called the investigators back, purposes of the study were explained and specific questions were asked to assure compliance with inclusion criteria. All qualified participants were invited to take part in a morning session at the Human Nutrition Laboratory at Florida International University (FIU) for fasting blood sampling to screen for vitamin D insufficiency. The study was approved by IRB at FIU. All participants were asked to sign an informed consent form previous to screening data collection. Only participants with confirmed T2D diagnosis by a physician were eligible for the study. Exclusion criteria were self-reported and confirmed by primary care physician. All participants were screened for vitamin D insufficiency in phase one. They were contacted either to continue in the study or to inform them that they were disqualified based on their vitamin D levels.

Participants in both groups were required to take either 4000 IU or 6000 IU of vitamin D (Cholecalciferol) per day given in the form of a pill in a single daily dose. For safety reasons, the group receiving the higher dosage was proportionally half the size of the group receiving 4000 IU per day. Therefore, less patients were exposed to possible toxic effects. Subjects were included in a first come, first served basis and assigned in a 2:1 proportion to the 4000 IU or 6000 IU group until minimum sample size needed was achieved. For example, the first and second subjects that qualified for the study were assigned to the 4000 IU group, the third subject to the 6000 IU group. The study was not blinded. Compliance was determined by returned pill count at follow ups. When less than 80% of the pills were taken, the subject was classified as non-compliant. Adverse events were recorded at each visit. Each participant was seen 4 times; at screening, baseline, 3 months, and 6 months. Serum 25(OH)D was measured at screening, 3 months, and 6 months. Blood lipids were measured at baseline, 3 months, and 6 months. The time span between screening and baseline was one week.

Total study lasted for 25 weeks for each participant from screening to final assessment. The study was conducted across all seasons. The study started in June 2011 and was completed on September 2013. In addition, located in a tropical area, sunlight is plentiful in South Florida all year round. Therefore, all subjects had similar sun exposure potential. Ninety-two participants were screened. Seventy-five participants met the study's in-

clusion (n = 50 for 4000 IU/day treatment and n = 25 for 6000 IU/day treatment). Three participants qualified for the study based on their vitamin D status but did not attend the 3 month and 6 month follow ups (all in the 4000 IU group). Eight participants attended the 3 month but not the 6 month follow up (5 in the 4000 IU and 3 in the 6000 IU group, respectively). Five participants completed the study but were non-compliant (3 in the 4000 IU and 2 in the 6000 IU treatment, respectively). Since an intent to treat approach was followed, all 75 participants were included in the present study.

Blood collection

Venous blood (15 ml) was collected from each subject by a certified phlebotomist using standard laboratory methods at each study point. After coagulation, blood was centrifuged at 2500 RPM for 30 minutes. Plasma total cholesterol, triglycerides, LDL, and HDL cholesterol were assayed by enzymatic methods (Cobas Mira, Roche Diagnostics, Indianapolis, IN). Serum vitamin D concentrations were measured with an enzyme-immunoassay kit by absorbance (Immunodiagnostic Systems Scottsdale, AZ). Vitamin D values were tested at screening, 3-month and 6-month visits. Total cholesterol, triglycerides, LDL, and HDL cholesterol were tested at baseline, 3-month, and 6-month visits.

Socio-demographic questionnaire

Participants were asked to complete the standard questionnaire on site. Trained bilingual interviewers (English and Spanish) administered the questionnaires in the subjects' language of preference. Data were collected using a socio-demographic questionnaire which included questions related to gender, age, education level, years with diabetes, smoking, and medication use.

Anthropometric measurements

Height and weight were measured using a SECA clinical balance scale (Seca Corp, Columbia, MD). Body mass index (BMI) was calculated as weight in kg/height in m². BMI was calculated at baseline, 3-month, and at 6-month visits. Only baseline values were used for the analysis due to the lack of significant changes in BMI at 3 months and 6 months.

Sun exposure questionnaire

The sun exposure questionnaire developed by Hanwell, et al. [12] was applied following the original rubric. Time spent outdoors during the previous week (0 ≤ 5 minutes, 1 = 5-30 minutes and 2 ≥ 30 min) was self-reported. Four options for skin exposed while outdoors were offered (1 = face and hands, 2 = face, hands and arms, 3 = face, hands and legs and 4 = bathing suit). The daily sun exposure score for each day was calculated by multiplying the time spent outdoors score times the skin exposed while outdoors score. The scale for each day ranged from 0 to 8. The weekly sun exposure was calculated by adding

the daily scores (min = 0, max = 56). The questionnaire was administered at baseline, 3 months, and 6 months, but because sun exposure scores did not change significantly, only baseline values were used in the analysis.

Skin color

In order to have an objective measure of sun exposure, skin color was determined by reflectance colorimetry using the SmartProbe 400 (IMS Inc. USA). This instrument uses the International Commission on Illumination Scale which ranges from 0 (black) to 100 (white) for skin color. Two readings at each measurement site for each participant were taken: two on the dorsal aspect of the wrist of the right hand (area most exposed to sun), two on the inside of the right upper arm (area less exposed to the sun). The mean values of the two readings at each measurement site were used for analysis. Data were collected at baseline, 3 months, and 6 months, but because it did not change significantly, only baseline values were used in the present analysis. Since participants with darker skin color tend to have lower levels of serum 25(OH)D, skin color may have an effect on lipid profile.

Assessment of dietary intake

Dietary intake was determined using the long food frequency questionnaire (FFQ) developed by Walter Willett [13]. This FFQ has been validated in different ethnic groups and, also, specifically in Cuban-Americans in South Florida [14]. Participants self-reported the average consumption of specific amount of foods over the past 12 months. Frequencies ranged from "never" to "six or more servings per day". The FFQ also assessed the frequency use of multivitamin/mineral supplements, salt, sugar, alcohol and vitamin D intake. The questionnaire was administered at baseline.

Statistical analysis

Descriptive statistics were used for baseline characteristics. Numerical normally distributed data and categorical data were compared using independent t-test and Chi-Squared test, respectively. Intent to treat analysis was used to analyze the effect of vitamin D on the outcome variables.

Main variables of the study were: plasma total cholesterol, triglycerides, LDL, and HDL cholesterol. All variables were input as continuous in the analysis. Control variables included: BMI, gender, age, smoking, years with diabetes, sun exposure score, vitamin D intake, fasting plasma glucose, lipid lowering medication use, and skin color.

Mixed model was used to compare treatment effects (4000 IU vs. 6000 IU) on the outcome variables. Bonferroni multiple comparison test was used to detect significant changes from baseline, 3 months, and 6 months on the outcome variables with and without adjustment for age, gender, years with diabetes, smoking, BMI, vitamin D intake, sun exposure score, upper arm skin color, forearm skin color, fasting plasma glucose, and li-

Table 1: Baseline characteristics of participants prior to vitamin D repletion treatments.

Characteristic	Treatment		P-value
	4000 IU (n = 50)	6000 IU (n = 25)	
25(OH)D (ng/ml)	22.25 ± 7.19	23.74 ± 5.09	0.302
FGP (mg/dl)	188.76 ± 87.19	168.16 ± 55.94	0.220
Age (years)	54.76 ± 8.56	54.17 ± 10.99	0.999
Gender (Female %)	48%	52%	0.809
Years with T2D	6.48 ± 5.18	5.48 ± 5.93	0.478
Smoking (yes %)	10%	28%	0.091
BMI (kg/m ²)	34.72 ± 6.98	30.74 ± 4.93	0.013
Total Cholesterol (mg/dl)	213.08 ± 42.30	193.88 ± 41.03	0.065
Triglycerides (mg/dl)	182.98 ± 110.11	201.44 ± 91.35	0.445
LDL cholesterol (mg/dl)	128.34 ± 40.54	115.56 ± 34.53	0.160
HDL cholesterol (mg/dl)	50.64 ± 12.20	42.44 ± 10.40	0.004
Vitamin D intake (IU/day)	316.82 ± 251.70	301.97 ± 225.49	0.797
Sun exposure score	20.06 ± 14.92	18.68 ± 15.52	0.715
Upper arm skin color	58.67 ± 9.54	62.09 ± 5.65	0.056
Forearm skin color	54.82 ± 8.51	54.37 ± 4.37	0.099
Lipid lowering meds	64%	68%	0.215

Continuous variables are presented as mean ± SD and categorical variables as %.

25(OH)D: serum vitamin D; FPG: fasting plasma glucose; T2D: type 2 diabetes; BMI: body mass index; LDL: low density lipoprotein; HDL: high density lipoprotein.

Table 2: Group comparisons of metabolic parameters at different time points without adjusting for covariates.

	4000 IU (n = 50)	6000 IU (n = 25)
25(OH)D (ng/ml)		
Baseline	22.25 ± 7.19	23.74 ± 5.09
3 months	37.34 ± 12.31*	43.20 ± 15.94*
6 months	37.99 ± 13.22*	40.62 ± 19.39*
P-value groups = 0.225	P-value time = 0.006	P-value interaction = 0.238
Total Cholesterol (mg/dl)		
Baseline	213.08 ± 42.30	193.88 ± 41.03
3 months	209.26 ± 43.62	184.68 ± 50.89
6 months	199.84 ± 32.79	180.48 ± 27.53*
P-value groups = 0.027	P-value time = 0.044	P-value interaction = 0.653
Triglycerides (mg/dl)		
Baseline	182.98 ± 110.11	201.44 ± 91.35
3 months	174.62 ± 109.83	192.20 ± 94.49
6 months	187.08 ± 151.26	172.92 ± 76.87*
P-value groups = 0.221	P-value time = 0.117	P-value interaction = 0.227
LDL Cholesterol		
Baseline	128.34 ± 40.54	115.56 ± 34.53
3 months	125.88 ± 40.90	120.00 ± 35.37
6 months	120.76 ± 30.35	121.96 ± 40.60
P-value groups = 0.542	P-value time = 0.685	P-value interaction = 0.354
HDL Cholesterol		
Baseline	50.64 ± 12.20	42.44 ± 10.40
3 months	48.92 ± 11.12	42.12 ± 12.35
6 months	46.98 ± 10.37	42.12 ± 12.76
P-value groups = 0.072	P-value time = 0.214	P-value interaction = 0.351

Data represented by mean ± standard error; *Represents significant differences from baseline; Level of significance is at $P < 0.05$. 25(OH)D: serum vitamin D; LDL: low density lipoprotein; HDL: high density lipoprotein.

lipid lowering medication use. Significance was set at $p < 0.05$ and all analyses were two sided. Statistical analysis was conducted using SPSS 18.0 (Chicago).

Results

Groups were different at baseline on BMI (34.72 ±

6.98 kg/m² vs. 30.74 ± 4.93 kg/m², $P = 0.013$ for 4000 IU and 6000 IU; respectively) and HDL cholesterol (50.64 ± 12.20 mg/dl vs. 42.44 ± 10.40 mg/dl, $P = 0.004$ for 4000 IU and 6000 IU; respectively) (Table 1).

There was no significant difference between groups

regarding serum 25(OH)D ($P = 0.225$). However, significant improvements in serum 25(OH)D levels were seen from baseline to 3 months and 6 months, respectively in both treatments (from 22.25 ± 7.19 to 37.34 ± 12.31 and 37.99 ± 13.22 , $P < 0.05$ in the 4000 IU group; from 23.74 ± 5.09 to 43.20 ± 15.94 and 40.62 ± 19.39 , $P < 0.05$ in the 6000 IU group) (Table 2).

Differences between 3 months and 6 months' levels for serum 25(OH)D were not significant in both treatments ($P > 0.05$). In the 6000 IU group, the value showed a non-significant decline at 6 months compared to the 3 months follow up.

In the unadjusted model, the difference between and within groups was significant for total cholesterol ($P = 0.027$ and $P = 0.044$, respectively). However, the interaction between time and treatment was not significant ($P = 0.653$) (Table 2). The multiple comparisons analysis showed a borderline not significant decrease in total cholesterol for the 4000 IU group at 6 months (from 213.08 ± 42.30 to 199.84 ± 32.79 mg/dl, $P = 0.052$) and a significant decrease for the 6000 IU group at 6 months (from 193.88 ± 41.03 to 180.48 ± 27.53 mg/dl, $P = 0.040$). However, when the model was adjusted for confounders, significance was lost (Table 3).

Similarly, in the unadjusted model (Table 2), a significant change for triglycerides was observed at 6 months

in the 6000 IU group (from 201.44 ± 91.35 to 172.92 ± 76.87 mg/dl, $P = 0.037$). The significance was lost after adjusting for confounders (Table 3).

In the adjusted model, only serum 25(OH)D changed significantly over time (Table 3). Adherence defined as consumption of more than 80% of supplied vitamin D pills was 94% for the 4000 IU group and 92% for the 6000 IU group without any differences between groups. No adverse events were reported during the course of the study.

Three participants stopped taking lipid lowering medication during the course of the study due to lack of money to buy the refills (2 in the 4000 IU group and 1 in the 6000 IU group). No other changes in medication dosage were reported.

Discussion

In the current study, vitamin D₃ supplementation at 6000 IU/day significantly reduced total cholesterol, and triglycerides in a sample of Hispanics and African Americans with T2D and vitamin D insufficiency. However, the significance was lost after adjusting for confounders.

In fact, vitamin D insufficiency is related to other cardiovascular risk factors such as obesity, smoking, and unhealthy diet [15,16]. Regarding the strong association between obesity and vitamin D insufficiency, it has been

Table 3: Group comparisons of metabolic parameters at different time points adjusting for covariates.

	4000 IU (n = 50)	6000 IU (n = 25)
25(OH)D (ng/ml)		
Baseline	22.25 ± 7.19	23.74 ± 5.09
3 months	37.34 ± 12.31*	43.20 ± 15.94*
6 months	37.99 ± 13.22*	40.62 ± 19.39*
P-value groups = 0.232	P-value time = 0.019	P-value interaction = 0.352
Total Cholesterol (mg/dl)		
Baseline	213.08 ± 42.30	193.88 ± 41.03
3 months	209.26 ± 43.62	184.68 ± 50.89
6 months	199.84 ± 32.79	180.48 ± 27.53
P-value groups = 0.204	P-value time = 0.954	P-value interaction = 0.605
Triglycerides (mg/dl)		
Baseline	182.98 ± 110.11	201.44 ± 91.35
3 months	174.62 ± 109.83	192.20 ± 94.49
6 months	187.08 ± 151.26	172.92 ± 76.87
P-value groups = 0.962	P-value time = 0.250	P-value interaction = 0.167
LDL Cholesterol		
Baseline	128.34 ± 40.54	115.56 ± 34.53
3 months	125.88 ± 40.90	120.00 ± 35.37
6 months	120.76 ± 30.35	121.96 ± 40.60
P-value groups = 0.969	P-value time = 0.872	P-value interaction = 0.423
HDL Cholesterol		
Baseline	50.64 ± 12.20	42.44 ± 10.40
3 months	48.92 ± 11.12	42.12 ± 12.35
6 months	46.98 ± 10.37	42.12 ± 12.76
P-value groups = 0.088	P-value time = 0.188	P-value interaction = 0.118

Data represented by mean ± standard error. *Represents significant differences from baseline. Level of significance is at $P < 0.05$. 25(OH)D: serum vitamin D; LDL: low density lipoprotein; HDL: high density lipoprotein; Analysis was adjusted for age, gender, years with diabetes, smoking, BMI, vitamin D intake, sun exposure score, fasting plasma glucose, upper arm skin color, forearm skin color, and lipid lowering medication use.

hypothesized that vitamin D is stored in the fat tissue and is not bioavailable in obese participants resulting in low levels of serum vitamin D despite sufficient intake [15]. In this context, if obesity is corrected we may see improvements in both serum vitamin D levels and lipid profile. Our results support this hypothesis. The participants were obese based on BMI classification. The positive effect of vitamin D supplementation on total cholesterol and triglycerides observed in the 6000 IU/day group disappeared when the model was adjusted for covariates such as smoking, age, gender, skin color, sun exposure, lipid lowering medication, years with diabetes, and BMI. Therefore, our results suggest that the association between vitamin D insufficiency and dyslipidemia may be mediated by other cardiovascular risk factors.

Recent clinical trials examining the effect of vitamin D supplementation on lipid profile among individuals with and without T2D and vitamin D insufficiency have been inconsistent [8,9,17]. Some studies have found significant improvements in lipid profile after vitamin D supplementation. However, none of them adjusted for covariates in the analysis. Alkharfy, et al. [9], randomly assigned 499 participants with T2D to 8 groups: control (n = 151), rosiglitazone alone (n = 49), diet (n = 15), insulin alone (n = 55), insulin + orals (n = 12), metformin alone (n = 121), oral agents combination (n = 37), and sulphonylurea alone (n = 59). Participants received 2000 IU/day of vitamin D₃ for 12 months. In the insulin alone group, total cholesterol decreased significantly in women. In the insulin + orals group, triglycerides and total cholesterol decreased significantly after 12 months. This study provides a view of how vitamin D supplementation can interact with certain drugs commonly used in patients with T2D regarding lipid lowering benefits. In contrast, Ponda, et al. [8], randomly assigned 151 vitamin D deficient participants at high risk for CVD to either 50,000 IU of vitamin D₃ weekly or placebo. Vitamin D failed to improve lipid profile. In addition, a significant increase in LDL was noted which significantly correlated with a decrease in parathyroid hormone (PTH) levels. Similarly, Salehpour, et al. [17], randomly distributed 77 healthy premenopausal overweight and obese women to either 25 µg/day of vitamin D₃ or placebo for 12 weeks. Significant increases in total cholesterol, LDL and HDL were reported. This study excluded participants taking any antihypertensive and lipid lowering medication. Since it is difficult to evaluate the effect of vitamin D supplementation on lipid profile when participants are already taking lipid lowering medication, this study provided a new insight into the raw metabolic effects of vitamin D. Authors from the last two studies warned that vitamin D may have both positive and negative effects on different cholesterol particles. Therefore, it should be monitored and used with caution among participants at risk of CVD. Conflicting results may be a consequence of different dosages used, different populations, different duration

of treatment, and lack of control for obesity, physical activity, sun exposure, vitamin D intake, and medication usage.

In a meta-analysis of 10 randomized controlled trials conducted by Wang, et al. [18], obesity was a strong confounding variable. When subjects were classified according to BMI > 30 kg/m², supplementation with vitamin D showed a negative effect on lipid profile compared to non-obese subjects. For instance, total cholesterol increased 3.22 mg/dl in the obese group compared with a reduction of 0.68 mg/dl in the non-obese group. Even though, these results were not statistically significant, a trend was observed. Authors concluded that none of the 10 studies reviewed in the meta-analysis were specifically designed to detect changes in lipid profile and, therefore, were lacking power. Also, all the studies used low dosages of vitamin D (from 300 IU to 3332 IU daily), and hyperlipemia and vitamin D deficiency were not inclusion criteria which decreases the probabilities of finding significant changes at the end of the treatments. Similarly, none of the 10 studies included were conducted on Hispanics or African Americans.

Another meta-analysis of 12 randomized controlled trials conducted by Swart, et al. [19], found significant changes in LDL only in participants with the lowest baseline serum vitamin D. Total cholesterol also decreased but the change was not statistically significant due to lack of power. However, the authors remarked that the change was clinically significant. Authors concluded that none of the studies recruited participants based on their vitamin D status, resulting in low number of subjects with vitamin D deficiency, leading to negative effects of vitamin D supplementation on lipid profile. Also, all the studies were conducted among healthy Caucasian populations.

Regarding lipid metabolism, studies have shown that vitamin D can reduce hepatic triglyceride synthesis and increase uptake by peripheral tissues due to increased intestinal calcium absorption [20,21]. Similarly, vitamin D promotes the formation of large HDL particles due to an increase in apolipoprotein A1, which increases reverse cholesterol transport [22]. Vitamin D also increases the lipolytic activity of heparin and reduces VLDL-cholesterol synthesis [20].

In our study, the positive effect of vitamin D supplementation on total cholesterol and triglycerides was observed only in the 6000 IU group despite both groups reaching similar serum vitamin D levels. It may be that sufficient vitamin D status was achieved sooner in the 6000 IU/group. Therefore, participants were exposed to sufficient vitamin D for a longer period of time. The half-life of vitamin D₃ is about 2 months. Therefore, maintaining a plateau of sufficient 25(OH)D levels for more than 20 weeks is needed in order to see improvements on tissues not related to calcium metabolism [23].

Our study has several strengths. First, to our knowl-

edge this is the first study that analyzed vitamin D supplementation effects on Hispanics and African Americans with T2D living in a tropical area like South Florida. Second, the dosages used were large enough to raise serum vitamin D to normal levels in a population that was insufficient at baseline. Third, analysis was adjusted for a wide range of covariates related to vitamin D metabolism. Fourth, only participants with vitamin D insufficiency and confirmed T2D were included. Lastly, compliance in our study was high with 94% for the 4000 IU group and 92% for the 6000 IU group without any differences between groups. No adverse events were reported during the course of the study.

Limitations of our study included. First, participants were not randomly distributed among groups as evidenced by differences in BMI and HDL cholesterol at baseline. Second, a longer duration of treatment may be needed to see more drastic effects on lipid profile. In addition, the number of African American participants was not large enough to analyze data by ethnicity. Lastly, 64% and 68% of participants were taking lipid lowering medication in the 4000 IU and 6000 IU groups, respectively. Medication use may mask the effect of vitamin D supplementation. We tried to control for it by advising participants to keep their medication use constant during the study. However, this panorama reflects common clinical practice among patients with T2D.

Finally, our results suggest that the positive effect of vitamin D supplementation on lipid profile may be mediated by other cofactors related to vitamin D metabolism among Hispanic and African American participants with T2D. Longer, well designed randomized clinical trials are needed to confirm these results.

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Disclosure

No potential conflict of interest relevant to this article was reported.

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