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CLINICAL TRIAL REPORT

Effects of a Single Oral Megadose of Vitamin D3 on Inflammation and Oxidative Stress Markers in Overweight and Obese Women: A Randomized, Double-Blind, Placebo-Controlled Clinical Trial

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Aim: The study aimed to evaluate the effects of vitamin D3 (VD3) supplementation on inflammation and oxidative stress markers in overweight and obese women with deficiency or insufficiency of vitamin D.

Methods: Twenty-nine overweight or obese women who had a deficiency or insufficiency of vitamin D were placed into two groups according to VD3 intervention. Patients in the supplemented group received a single oral megadose of VD3 (VD3, n=14). Patients in placebo group received a single oral identical capsule without vitamin D (placebo, n = 15). Anthropometric and biochemical variables were assessed at baseline and after 4-weeks intervention.

Results: Anthropometric variables (waist circumference, waist–hip ratio, waist–height ratio and body mass index) were similar between groups ($p > 0.05$). VD3 supplementation increased the serum levels of 25-hydroxyvitamin D (p=0.000), malondialdehyde (p=0.021) and C-reactive protein (p=0.043) in overweight and obese women. Additionally, VD3 supplementation reduced the serum levels of aspartate aminotransferase (AST, p=0.035), alanine aminotransferase (ALT, p<0.0001) in overweight and obese women. Despite this, the serum levels of parathyroid hormone (PTH), fasting glucose (FG), and alpha-1- acid glycoprotein (A1GPA), total antioxidant capacity (TAC) were similar between groups.

Conclusion: In summary, a single oral megadose of VD3 increased 25-hydroxyvitamin D serum levels but did not improve oxidative stress and inflammation markers.

Keywords: vitamin D, obesity, inflammation, lipid peroxidation

Introduction

The prevalence of overweight and obesity has increased worldwide and is recognized as a chronic disease of complex management and increased risk of morbidity and mortality.[1,2] Early evidence has shown that serum levels of 25-hydroxyvitamin D [25(OH)D] are frequently reduced in obese subjects[3–6] and that adipose tissue serves as a reservoir for vitamin D, leading to less bioavailability and reduced serum levels.[6,7] An early study demonstrated that obese women have greater adipose stores of vitamin D in subcutaneous and omental comportments.[8] Obesity in these women has been associated with low-serum vitamin D levels, increased pro-inflammatory markers and oxidative stress, as demonstrated by increased measures of reactive oxygen species and reduced antioxidant defense.[4,6,9]

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Vitamin D is a lipid-soluble vitamin with steroid-like hormonal functions and with a broad spectrum of action in the body. The two major forms of vitamin D are vitamin D3, also called as cholecalciferol, which is synthesized in the skin from cholesterol upon sun exposure (UVB radiation), and vitamin D2 or ergocalciferol, which is mainly ingested from the diet. Vitamin D plays a fundamental role in mineral homeostasis and skeletal health by normalizing calcium and phosphorus metabolism. It has also been reported in the prevention of cardiovascular disease, diabetes mellitus, hypertension, autoimmune disease and cancer.[10,11] Additionally, vitamin D has been shown to downregulate pro-inflammatory markers, to have antioxidant properties[4,12] and to reduce the risk of liver cancer.[13]

A preclinical study demonstrated that vitamin D supplementation for 5 weeks of reduced adipose tissue oxidative stress and inflammatory makers in rats fed on a high-fat diet.[14] Even though this was a promising result in these rodents, the anti-inflammatory and anti-oxidant effects of vitamin D supplementation in obese subjects remain uncertain. Recognizing the high prevalence of vitamin D deficiency in obese subjects[6] and considering the potential anti-inflammatory and antioxidant role of vitamin D and lack of clinical evidence concerning the potential role of vitamin D in attenuating obesity-induced oxidative stress and inflammation, we aimed to evaluate the impact of the vitamin D3 supplementation on the inflammation and oxidative stress markers in overweight and obese women with deficiency or insufficiency of vitamin D.

Methods

Ethical Aspects

This study was approved by the Ethics Committee for Human Research of the Lauro Wanderley University Hospital of the Federal University of Paraíba, João Pessoa, Brazil (Protocol number 2.455.892). All procedures were in accordance with the institution's ethical standards, conducted in compliance with Resolution 466/2012 of the National Health Council and International Declaration of Helsinki. After the subjects had given written informed consent, they underwent screening procedures. At the request of the ClinicalTrial.gov, this study was registered with the Brazilian registry of clinical studies under the number, ID RBR-39srtp.

Subjects

Women were recruited from the Food and Nutrition Unit in the Lauro Wanderley University Hospital of the Federal University of Paraiba. The randomization adopted was of the simple type with the participants being randomly assigned to a given group. The eligibility criteria were as follows: women aged 18–59 years with vitamin D deficiency (≤20 ng/mL) or insufficiency (21–29 ng/mL) and with body mass index ≥25 kg/m^2. Exclusion criteria were as follows: intake of vitamin D supplements, intake of anticonvulsants or medications to treat the human immunodeficiency virus (HIV) or acquired immunodeficiency syndrome (AIDS), diagnosis of type I diabetes mellitus, nephrotic syndrome, acute or chronic renal disease, liver diseases, hypothyroidism, hyperthyroidism, history of cerebrovascular accident (CVA) or acute myocardial infarction (AMI) within the last 6 months, smoking and alcohol consumption. The flowchart of the study is shown in Figure 1.

Sample Size Calculation

Based on the prevalence of 25(OH)D serum level deficiency and insufficiency in a previous study, the sample size calculation considered an α error (Zα) of 5% and a β error (Zβ) of 10%. A standard deviation (δ) of 8 ng/mL was adopted for the concentrations of 25(OH)D[15] and a mean difference before and after the impact of the supplementation of 10 ng/mL. Considering the difference between the values, for a coefficient of 95% and test power of 80%, the sample size was estimated at a minimum of 11 participants per group.

In the present study, the screening for 25(OH)D serum levels was administered to 69 participants (men and women), of whom, 39 had a vitamin D insufficiency or deficiency (56.5%). Among the participants with vitamin D deficiency or insufficiency, 9 were men and 30 were women. In agreement with the minimum sample size calculation for the establishment of groups, it was no expedient to test the effects of vitamin D supplementation in the male participants. Among women, one had normal body weight and so was not included in the study. After the initial screening, 29 overweight or obese women with vitamin D deficiency or insufficiency were block randomized and divided into two groups: women receiving placebo (placebo, n=14) or women that received a single oral megadose of vitamin D3 (VD3, n=15).

Study Design

This study was designed as a double-blinded, randomized, placebo-controlled trial. At the first visit, a questionnaire was applied in order to record information regarding age, physical activity, smoking, skin phototype, time of sunlight exposure,

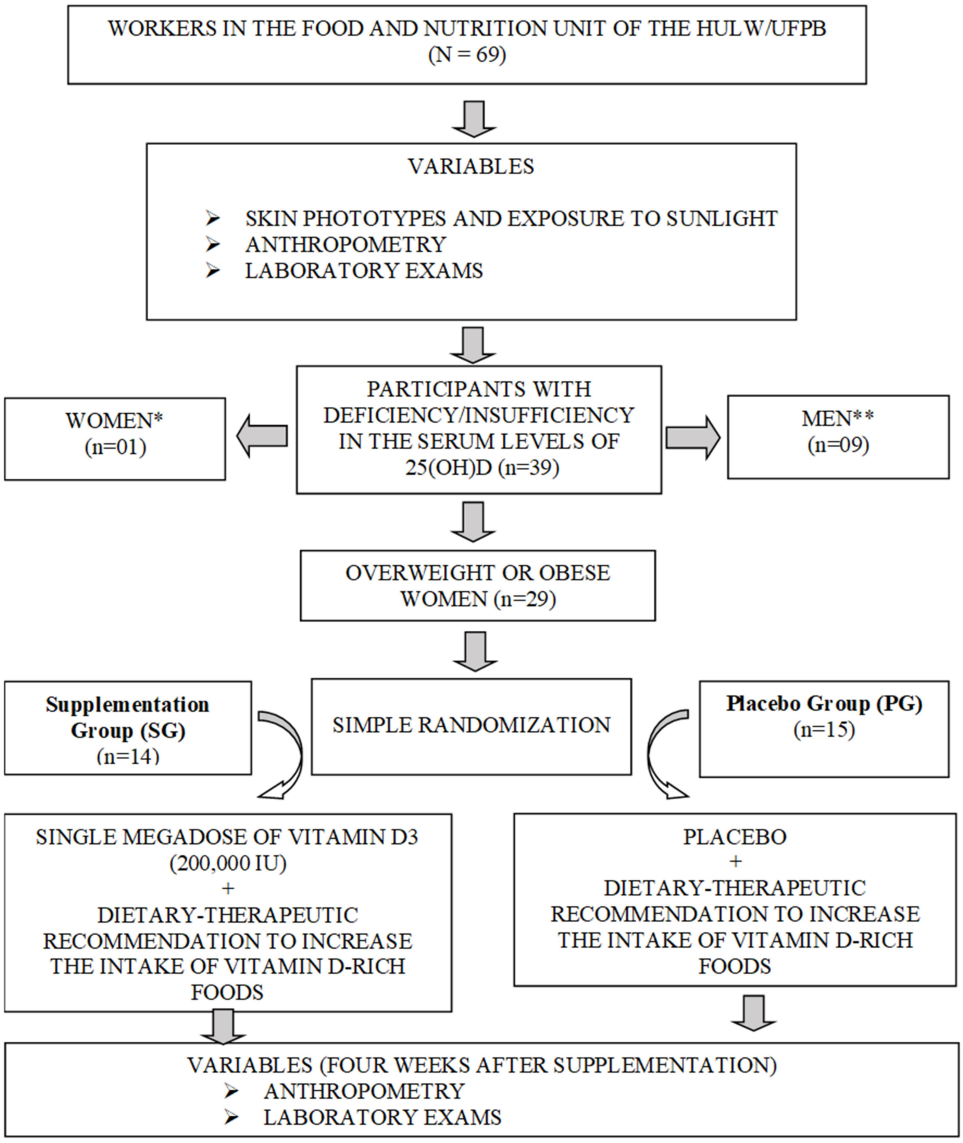

Figure 1 Double-blind, controlled trial flow chart. *One woman with normal weight was removed of trial. **Men were not included in the study.

use of sunscreen, method of sunscreen use, physical activity when exposed to sunlight, and anthropometric measures.

After the randomization of the overweight and obese women with 25(OH)D deficiency or insufficiency, VD3 supplementation or the placebo was administered. The placebo group (n=14) received a capsule (1g) containing sunflower oil. In the vitamin D group, the women received a single oral megadose of 200.000 IU of vitamin D3 (lots 1877) in oleaginous capsules with identical appearances to the placebo.[15] The placebo and VD3 were provided by Leviale (Vila Olímpica, São Paulo, Brazil).

All participants received diet therapy assistance and were instructed to increase foods rich in vitamin D intake (fish, milk, egg yolk, liver, and butter, among others). After 4 weeks of intervention, all participants were asked to return to be revaluated concerning anthropometric variables and fasting blood. Participants and statistician were all blind to which came from the vitamin D and which from the placebo groups.

Skin Phototypes and Exposure to Sunlight

The skin phototypes were classified according to the Fitzpatrick classification, with a variation of one to six types, based on the individual ability to tan as well as on skin sensitivity and redness when exposed to sunlight. Sunlight exposure was defined as the average

time of exposure per day without considering seasonal variations.

Anthropometric Parameters

Nutritional status was determined through the Body Mass Index (BMI), obtained from the weight/height^2 (kg/m^2) ratio, with the following cutoff points being adopted: less than 18.5 kg/m^2 (underweight); between 18.5 and 24.9 kg/m^2 (normal weight); between 25 and 29.9 kg/m^2 (overweight); between 30 and 34.9 kg/m^2 (class I obesity); between 35 and 39.9 kg/m^2 (class II obesity); and greater than or equal to 40 kg/m^2 (class III obesity).

The waist circumference (WC) was measured at the midpoint between the outer side of the last rib and the iliac crest, and classified as level 1 for the WC values ≥80 cm and <88 cm (high risk), and level 2 for WC ≥88 cm (very high risk), considering the metabolic complications associated with obesity in women.[16]

The waist-to-height ratio (WHtR) is a simple measure for assessing the risk associated with excess weight in adults, with a cutoff point of 0.5 (the waist must be less than half the height) according to the Brazilian Guidelines for obesity in 2016. The waist-hip ratio (WHR) was analyzed to assess peripheral obesity, with the cut-off points to classify individuals or groups being 0.75–0.85 cm for moderate risk and >0.85 cm for high risk.[17]

Blood Sample and Biochemical Measurements

Blood samples were collected from individuals after a 12-h fasting. Fasting glucose (FPG), aspartate aminotransferase (AST), alanine aminotransferase (ALT) and creatinine were measured with specific commercial kits (Labtest, Minas Gerais, Brazil) in an automated analyzer (Labmax 240 Premium; Labtest, Minas Gerais, Brazil) according to the manufacturer's instructions. The 25-hydroxyvitamin D serum concentrations were measured through chemiluminescent immunoassay. The classification of 25(OH)D levels was done based on the reference values established by the Endocrine Society, as follows: serum levels of 25 (OH)D less than or equal to 20 ng/mL as deficient, 21–29 ng/mL as insufficient and between 30 and 100 ng/mL as sufficient.[18] The serum levels of parathyroid hormone (PTH) were assessed through chemiluminescent immunoassay and the serum concentrations of calcium (Ca) were measured through the colorimetric technique. The oxidant activity of malondialdehyde (MDA) was quantified in plasma by the reaction of thiobarbituric acid with the products of decomposition of hydroperoxides.[19] Total antioxidant capacity (TAC) was quantified in the plasma by measuring the scavenging activity of the free radical 2.2-diphenyl-1-picrylhydrazyl.[20] Plasma concentrations of high-sensitivity C-reactive protein (hs-CRP) and alpha-1-acid glycoprotein (A1GPA) was quantified by immunoturbidimetry using specific commercial kits (Labtest) and an automatic analyzer (LabMax 240 Premium; Labtest) according to the manufacturer's instructions.

Statistical Analyses

Statistical analyses were performed according to a previous study.[21] Values were reported as mean (95% confidence interval) for parametric data or median (maximum − minimum) for nonparametric data. All the data were checked for normal distribution using the Kolmogorov Smirnov test. Data were reported as mean (95% confidence interval) and median (maximum − minimum) since some variables were not normally distributed. Comparison between VD3 and placebo groups at baseline was tested using the unpaired Student's *t* test or Mann–Whitney test. The paired Student's *t* test or Wilcoxon-matched pairs signed-rank test was used to analyze the differences between the baseline and the endpoint values. The categorical data were analyzed by the chi-square test when the expected minimum was not reached, the Fisher exact test was used. The differences were considered significant when the p value was ≤0.05. Statistical analysis was performed using the computational software Stata Statistical version 14 or Prism 6 (GraphPad Software, San Diego, CA, USA).

Results

Baseline characteristics of participants in each group are shown in Table 1. Before the intervention period, age, skin phototype, time of sunlight exposure and use of sunscreen, practice of physical activity and nutritional status were similar between groups (Table 1). Anthropometric variables (weight, waist circumference; waist–hip ratio, waist–height ratio and body mass index) were similar between the two groups at baseline and after the 8-week intervention ($p \geq 0.05$, Table 2).

Regarding the biochemical variables, overweight or obese women had similar serum levels of 25(OH)D before VD3 supplementation (placebo: 24.2 (22.6–25.7) vs VD3: 23.8 (22.0–25.7) ng/mL, p=0.755, Figure 2A). Subjects that received a single oral megadose of VD3 had a significant increase in serum levels of 25(OH)D after 4 weeks of

Table 1 Characteristics of the Sample at the Beginning of the Study

Variables	VD3		Placebo		Total		*P*-value
	n	%	n	%	n	%	
Age							
Less than or equal to 45 years	8	50.0	8	50.0	16	100	0.837*
More than 45 years	6	46.2	7	50.0	13	100	
Skin phototype							
Phototypes: I, II, III, IV	12	44.4	15	55.6	27	100	0.224#
Phototype V	2	100	0	0.0	2	100	
Time of exposure to sunlight							
Less than or equal to 15 minutes	10	52.6	9	47.4	19	100	0.700#
More than 15 minutes	4	40.0	6	60.0	10	100	
Use of sunscreen							
No	5	50.0	5	50.0	10	100	0.893*
Yes	9	47.4	10	52.6	19	100	
Use of sunscreen							
Daily	1	14.3	6	85.7	7	100	0.081#
When being exposed to sunlight	5	71.4	2	28.6	7	100	
Other	3	60.0	2	40.0	5	100	
Does not use	5	50.0	5	50.0	10	100	
Physical activity							
No	12	50.0	12	50.0	24	100	1.000#
Yes	2	40.0	3	60.0	5	100	
Physical activity with exposure to sunlight							
No	13	50.0	13	50.0	26	100	1.000#
Yes	1	33.3	2	66.7	3	100	
Nutritional status							
Overweight	6	66.7	3	33.3	9	100	0.177#
Obese	8	40.0	12	60.0	20	100	

Notes: *Chi-square test; #Fisher's exact test; p-value shows a non-significant difference (p>0.05).

intervention (before: 23.8 (22.0–25.7) vs week 4: 31.7 (26.-2–44.5) ng/mL, p = 0.0004, Figure 2A). Serum levels of calcium, PTH glucose, ALT, AST and creatinine were similar between the two groups at baseline period (p-value ≥0.05, Table 3). The serum levels of calcium augmented after placebo (p=0.0003) or VD3 (p=0.002) supplementation (Table 3). Subjects of placebo group displayed increased PTH serum levels after 4-week intervention (p=0.035), but not after VD3 supplementation (p=0.501, Table 3).

The VD3 supplementation reduced serum levels of ALT (before: 21.6 (19.0–24.1) vs week 4: 16.1 (14.2–18.1) mg/dL, p<0.0001, Table 3) and AST (before: 22.4 (11.0–46.0) vs week 4: 17.7 (11.0–31.0) mg/dL, p=0.035, Table 3) in overweight or obese women. Regarding creatinine serum levels, a reduction was found after placebo (p<0.0001) or VD3 (p=0.001) supplementation (Table 3). Lastly, placebo or VD3 supplementation did not impact on serum levels of fasting glucose (Table 3).

Concerning oxidative status, total antioxidant capacity (placebo: 26.9 (21.8–32.0) vs VD3: 20.9 (14.6–27.2) %, p=0.116, Figure 2B) and MDA serum levels (placebo: 2.8 (2.4–3.2) vs VD3: 2.7 (2.4–3.0) µmol/L, p=0.556, Figure 2C) were similar between the two groups at baseline period. Following the four-week intervention, it was observed that VD3 group had increased MDA concentration in comparison to baseline condition (before: 2.72 (2.43–3.00) vs week 4: 3.52 (2.50–5.80) µmol/L, p=0.006, Figure 2C), but not in TAC (p=0.378, Figure 2B).

Regarding inflammatory markers, C-reactive protein (placebo: 5.25 (0.40–16.70) vs VD3: 4.27 (0.10 −14.30) mg/dL,

Table 2 Anthropometric Characteristics Among Women Receiving a Single Oral Megadose of VD3 Supplementation (n=14) or a Placebo (n=15) Before and After 4-Week Intervention

Variables	Placebo	VD3	*p*-value
WC (cm)			
Before	93.7 (88.2–99.1)	88.6 (83.1–94.1)	0.171
Week 4	95.0 (89.0–101.1)	88.9 (83.9–93.4)	0.106
WHR			
Before	0.84 (0.79–0.90)	0.81 (0.77–0.84)	0.248
Week 4	0.85 (0.80–0.89)	0.81 (0.78–0.85)	0.263
WHtR			
Before	0.59 (0.55–0.63)	0.56 (0.52–0.59)	0.138
Week 4	0.60 (0.56–0.64)	0.56 (0.53–0.59)	0.070
BMI (kg/m^2)			
Before	33.3 (30.6–35.9)	30.8 (27.9–33.7)	0.179
Week 4	33.4 (30.7–36.1)	30.7 (27.8–33.4)	0.133

Abbreviations: WC, waist circumference; WHR, waist-hip ratio; WHtR, waist-height ratio; BMI, body mass index.

p=0.739, Figure 2D) and alpha glycoprotein (placebo: 96.5 (84.5–108.6) vs VD3: 96.2 (84.3–108.1) mg/dL, *p*=0.967, Figure 2E) were similar between the two groups at baseline period. Following the 4-week intervention, it was observed that VD3 group had increased C-reactive protein in comparison to baseline condition (before: 4.27 (0.10 −14.30) vs week 4: 6.03 (0.40–17.70) µmol/L, p=0.043, Figure 2D), but not in alpha glycoprotein (*p*=0.285, Figure 2E).

Discussion

In the present study, a single oral megadose of VD3 increased the serum levels of 25(OH)D in overweight and obese women with insufficiency or deficiency of vitamin D. However, the results demonstrated that VD3 supplementation was not effective to improve pro-inflammatory markers, anti-oxidant activity. Further, VD3 augmented plasma concentration of lipid peroxidation, as evidenced by increase in MDA measurement, as well as increased the C-reactive protein serum levels.

Regarding the risk factors associated with the deficiency/insufficiency of 25(OH)D,[22] it was found that more than half of the women had a daily exposure to sunlight equal or less than 15 minutes. In our understanding, the low sun exposure combined with overweight be the main cause or contribute to of insufficiency or deficiency of vitamin D in these women.[23]

In agreement with previous studies, vitamin D supplementation increased serum levels of vitamin D. Different doses of vitamin D supplementation have been used in clinical trials to recover vitamin D deficiency. For example, 1.25-di-dihydroxycholecalciferol, at 50,000 IU/week for 8 weeks is able to recover vitamin D deficiency in patients with diabetic nephropathy.[24] Using VD3 supplementation in a daily dose of 5000 IU for 12 weeks, increased 25 (OH)D serum levels in patients with type 2 diabetes.[25] Lastly, a randomized, double-blind, placebo-controlled trial, carried with 40 elderly women with vitamin D insufficiency, demonstrated that a single oral megadose of 200,000 UI of vitamin D significantly increased serum levels of 25(OH)D.[15] Taken together, the studies demonstrated that daily, weekly or a single megadose of vitamin D may be effective to increase serum levels of vitamin D.

Vitamin D deficiency may lead to an increase in serum levels of PTH in order to adjust the calcium serum concentrations.[26] Previous studies, however, have demonstrated that vitamin D supplementation decreased parathyroid hormone levels in obese[27] and elderly women with vitamin D insufficiency.[15] The results from our study showed that vitamin D supplementation neither decreased nor increased parathyroid hormone levels in overweight obese women with vitamin D insufficiency or deficiency.

Table 3 Biochemical Variables Among Women Receiving a Single Oral Megadose of VD3 Supplementation (n=14) or the Placebo (n=15) in the Moments Before and After 4-Week Intervention

Variables	Placebo	VD3	*p*-value
Calcium (mg/dL)			
Before	9.0 (8.8–9.2)	8.9 (8.7–9.1)	0.715
Week 4	9.5 (9.3–9.7)*	9.4 (9.2–9.6)*	0.506
PTH (pg/mL)			
Before	43.9 (29.7–78.9)	43.9 (35.2–52.6)	0.898
Week 4	54.8 (45.2–64.4)*	42.4 (16.7–90.6)	0.049
AST (IU/L)			
Before	21.5 (18.2–24.7)	21.6 (19.0–24.1)	0.957
Week 4	18.9 (12.0–48.0)	16.1 (14.2–18.1)*	0.441
ALT (IU/L)#			
Before	25.0 (16.0–42.0)	19.5 (11.0–46.0)	0.099
Week 4	24.0 (12.0–72.0)	16.0 (11.0–31.0)*	0.013
Creatinine (mg/dL)			
Before	0.82 (0.75–0.89)	0.79 (0.73–0.85)	0.465
Week 4	0.64 (0.59–0.69)*	0.69 (0.64–0.74)*	0.179
FG (mg/dL)#			
Before	95 (82–157)	89.5 (77–179)	0.690
Week 4	96 (89–170)	94 (83–167)	0.370

Notes: *p-value shows a significant difference between moments (p<0.05). #Non-parametric data

Abbreviations: AST, aspartate aminotransferase; ALT, alanine aminotransferase; FG, fasting glucose. PTH, parathyroid hormone.

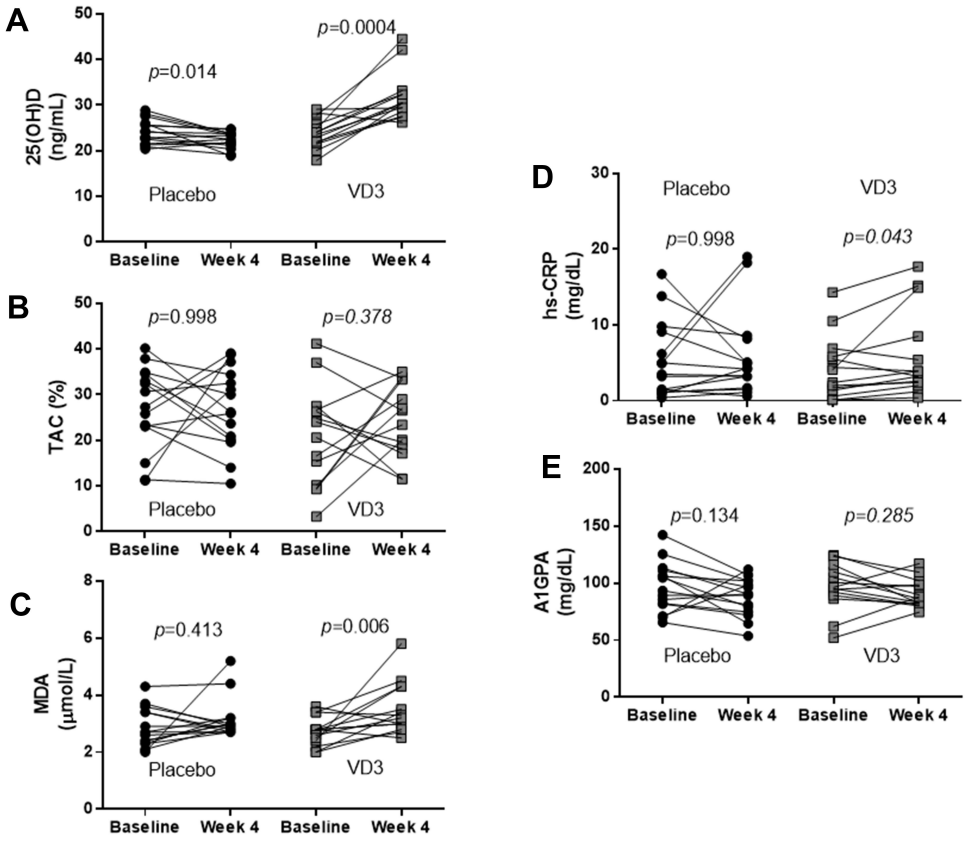

Figure 2 Effects of a single oral megadose of VD3 supplementation on 25 hydroxy-vitamin D and oxidative stress and inflammation variables in overweight and obese women with insufficiency or deficiency of vitamin D. Assessment of the serum levels of hydroxy-vitamin D (**A**), total antioxidant capacity (**B**), malondialdehyde (**C**), high-sensitivity C-reactive protein (**D**) and alpha glycoprotein (**E**) in overweight and obese women with insufficiency or deficiency of vitamin D who received a single oral megadose of VD3. Baseline and intervention data were compared by paired t-tests or the Wilcoxon rank-sum test according to the data distribution.

As a safety measure for the VD3 supplementation, a biochemical monitoring of total serum calcium, hepatic and renal biomarkers was performed with both groups at the beginning of the study and after the 4-week supplementation. Although the serum creatinine level was reduced in placebo group after 4-week intervention, the creatinine values remained within range of standard parameters. Hepatic transaminases were reduced in the VD3 group after 4-weeks, suggesting that liver function may be improved by VD3 supplementation in overweight or obese women. The results of vitamin D supplementation on hepatic variables are conflicting. For example, daily supplementation of 2800 IU vitamin D3 for 8 weeks did not reduce ALT and AST serum levels in cirrhotic patients.[28] Similarly, an early study demonstrated that a single oral megadose of VD3 did not alter kidney or liver markers in elderly women.[15] On the other hand, daily supplementation of vitamin D 3200 IU for 3 months reduced hepatic transaminases in women with polycystic ovary syndrome.[29] A future challenge is to evaluate with wider and longer studies whether vitamin D supplementation in obese subjects exerts beneficial effects on hepatic variables.

The results of this clinical trial demonstrated that a single oral megadose of VD3 increased the serum levels of hs-CRP. In fact, the effects of vitamin D supplementation on inflammatory markers are conflicting and inconclusive. For example, it has been demonstrated that vitamin D supplementation did not improve the hs-CRP level in patients with inflammatory bowel disease.[30] A meta-analysis of seven randomized controlled trials carried out in patients with heart failure demonstrated that vitamin D supplementation could lower concentrations of tumor necrosis factor-alpha (TNF-α), but was not effective in reducing hs-CRP, interleukin (IL)-10 or IL-6.[31] Another meta-analysis of 13 randomized controlled trials carried with type 2 diabetes mellitus subjects demonstrated that vitamin D supplementation is beneficial for the reduction of hs-CRP but does not have a significant influence on TNF-α and IL-6.[32] Lastly, a meta-analysis of 13 randomized controlled trials carried out with overweight and obese subjects demonstrated that vitamin D supplementation did not have a significant influence on changes in the concentration of hs-CRP, TNF-α and IL-6.[33]

Early study has demonstrated that oxidative stress markers are augmented in obese subjects than healthy controls.[34] This suggests that anti-oxidant therapies should be recommended for subjects with an obesity condition. Regarding the effects of vitamin D supplementation on oxidative stress markers, the results of the present study demonstrated that a single oral megadose of VD3 did not affect TAC, but significantly increased lipid peroxidation through the determination of MDA concentrations in overweight and obese women. A recent meta-analysis carried out in 17 randomized clinical trials found that oral vitamin D supplementation had beneficial effects on oxidative stress parameters by significantly decreasing circulating MDA levels as well as significantly enhancing antioxidant defense systems compared to placebo.[12] However, no study has been carried on obese subjects for these meta-analyses.

Other antioxidant strategies with the potential to down-regulate oxidative stress, inflammation, obesity indices and metabolic dysfunction have been related in early studies. For example, systematic reviews and meta-analysis of randomized controlled trials have demonstrated that berberine supplementation may ameliorate the state of chronic inflammation[35] and reduces obesity indices.[36] Another systematic review and meta-analysis of randomized controlled trials found that phytosterols supplementation at 1–2 g/day could effectively lower fasting blood sugar and glycosylated hemoglobin.[37] Additionally, green tea supplementation associated with a balanced and healthy diet and regular physical exercise has been suggested to improve anthropometric indices in obese subjects.[38] Lastly, a systematic review and meta-analysis of randomized controlled trials found that probiotic/symbiotic supplementation can significantly increase serum TAC, glutathione and NO, as well as reduce MDA levels in adults.[39]

In present study, we highlight that vitamin D supplementation in obese or overweight women who have an insufficiency or deficiency of vitamin D did not improve obesity indices and metabolic variables, indicating that this treatment must be proceeded with caution and following oxidative stress and inflammatory parameters.

Potential limitations:

This was a clinical trial performed with small samples size of women only, due to the fact that males were not recruited for the study. Additionally, the lack of a wash-out or recovery time point could be considered also as potential limitation of study.

Conclusion

The results of this randomized, double-blind, placebo-controlled clinical trial showed that a single oral megadose of VD3 significantly increased the serum levels of 25(OH)D, but did not improve inflammatory and oxidative stress markers.

Data Sharing Statement

After publication, the authors intend to share individual de-identified participant data, for 1 year, when requested for e-mail.

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Disclosure

The authors report no conflicts of interest for this work and declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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