Impact of vitamin D supplementation on adiposity in African-Americans

P D. Chandler  
Harvard Medical School

J B. Scott  
Michigan State University

B F. Drake  
Washington University School of Medicine in St. Louis

K Ng  
Harvard Medical School

A T. Chan  
Harvard Medical School

See next page for additional authors

Follow this and additional works at: https://digitalcommons.wustl.edu/open_access_pubs

Please let us know how this document benefits you.

Recommended Citation

https://digitalcommons.wustl.edu/open_access_pubs/4284
BACKGROUND: African-Americans have higher rates of obesity-associated chronic diseases. Serum 25-hydroxyvitamin D (25(OH)D) shows an inverse association with obesity status. We investigated whether vitamin D supplementation changes body mass index (BMI).

SUBJECTS: In total, 328 overweight African-Americans were enrolled over three consecutive winter periods (2007–2010) into a randomized, double-blind, placebo-controlled trial to receive cholecalciferol supplementation (0, 1000 international units (IU), 2000 IU or 4000 IU per day) for 3 months. Plasma concentrations of 25(OH)D and anthropometric measurements were done at baseline, 3 and 6 months.

RESULTS: At 3 months, vitamin D supplementation in three dose groups (1000 IU, 2000 IU or 4000 IU per day) did not cause any significant changes in BMI as compared with placebo group 3-month change in BMI per 1000 IU per day estimate (SE): 0.01 (0.039); P = 0.78.

CONCLUSIONS: In overweight African-Americans, short-term high-dose vitamin D supplementation did not alter BMI.

INTRODUCTION
An urgent need exists to identify modifiable dietary risk factors for obesity in African-Americans. Human observations since the 1980’s of lower levels of 25-hydroxyvitamin D25(OH)D in obese than in nonobese individuals highlight a possible inverse relation between vitamin D and obesity.1

African-Americans have consistent associations of vitamin D deficiency with obesity and obesity-associated chronic diseases, such as hypertension, coronary heart disease, diabetes and certain cancers,2 although of potentially lower magnitude than Whites.3,4 Furthermore, African-Americans have lower vitamin D and calcium dietary intake.5 The mechanisms underlying this association may include a role for 25(OH)D in regulating lipid metabolism in adipose cells. In vivo studies suggest that vitamin D and calcium administration increase fatty-acid oxidation and decrease lipogenesis.6,7

Results from clinical trials measuring the effect of vitamin D supplementation on obesity are limited and mixed. Some trials show no association of vitamin D supplementation with weight loss.8–10 Other trials show that vitamin D supplementation may be significantly associated with less weight gain but that this association may depend on adjunctive calcium supplementation and a particular region of fat.11,12 A recent meta-analysis showed no significant effect of vitamin D supplementation on body mass index (BMI), weight or other adiposity measures.13 This meta-analysis did not assess potential ethnic/racial differences in the effect of vitamin D supplementation on adiposity measures. Studies evaluating the effect of vitamin D supplementation on measures such as insulin resistance in African-Americans14 have not reported on changes in adiposity measures. Thus, this ancillary analysis was undertaken to test the hypothesis that supplementation with vitamin D3 (cholecalciferol) leads to weight loss in African-Americans.

MATERIALS AND METHODS
Study design and participants
This is a prospective, randomized, double-blind, placebo-controlled clinical trial of oral cholecalciferol (vitamin D3) in a community-based overweight African-American population (ClinicalTrials.gov NCT00585637). The protocol has been described in detail elsewhere.15 The primary goal of the trial was to examine the effect of daily supplementation of 1000 international units (IU) of vitamin D3, 2000 IU of vitamin D3 and 4000 IU of vitamin D3 and placebo on plasma 25(OH)D levels. All participants provided written informed consent. This trial focused on African-Americans because African-Americans have higher rates of vitamin D deficiency compared with Whites6 or Africans.16 The project was approved by the Institutional Review Boards of Harvard School of Public Health and Dana-Farber Cancer Institute. All procedures were followed in accordance with institutional guidelines.

Recruitment and randomization. Participants in Open Doors to Health, a colorectal cancer prevention intervention study conducted in 12 public housing communities in the Boston metropolitan area,17 were invited to participate if they were 30–80 years old, understood written and spoken English, self-identified as Black18–20 and had permission from their primary care doctors. We also recruited participants from community and faith-based organizations and refer-a-friend program. A total of 328 individuals participating in the main trial were randomized to receive cholecalciferol or placebo treatment at baseline.

PD Chandler1,2, JB Scott3, BF Drake4, K Ng5,6, AT Chan2,5, BW Hollis7, KM Emmons2,8, EL Giovannucci2,9,10, CS Fuchs2,5 and GG Bennett11

Impact of vitamin D supplementation on adiposity in African-Americans

Original Article
Impact of vitamin D supplementation on adiposity in African-Americans

ORCID
PD Chandler: http://orcid.org/0000-0002-1211-6781
JB Scott: http://orcid.org/0000-0002-5279-9400
BF Drake: http://orcid.org/0000-0002-2043-3577
K Ng: http://orcid.org/0000-0002-4932-581X
AT Chan: http://orcid.org/0000-0002-0802-390X
BW Hollis: http://orcid.org/0000-0002-6722-9585
KM Emmons: http://orcid.org/0000-0002-7024-7306
EL Giovannucci: http://orcid.org/0000-0003-4168-872X
CS Fuchs: http://orcid.org/0000-0002-9929-0934
GG Bennett: http://orcid.org/0000-0002-8892-7380

Received 29 May 2014; revised 28 September 2014; accepted 15 November 2014

Citation: Nutrition & Diabetes (2015) 5, e147; doi:10.1038/nutd.2014.44; published online 19 January 2015

www.nature.com/nutd
were enrolled into the parent trial (Figure 1). Exclusion criteria included pregnancy, renal disease, pre-existing parathyroid, thyroid, or calcium metabolism disorders, sarcoidosis, requirement for calcium channel blockers, type 1 diabetes and active malignancies (other than non-melanoma skin cancer). Those taking vitamin D supplementation were enrolled if they agreed to discontinue these medications for 6 months prior to enrollment and during the study.

Treatment. Participants were assigned to four arms consisting of placebo, 1000 IU per day, 2000 IU per day or 4000 IU per day of vitamin D3 for 3 months in a 1:1:1:1 ratio using block randomization stratified by age, sex and enrollment month. Study statisticians generated the random allocation sequence and subjects were enrolled by research assistants. All capsules also contained 200 mg of calcium carbonate (Pharmavite LLC, Mission Hill, CA, USA). Calcium was included because prior studies have shown that African-Americans have low calcium intake.21 All capsules were indistinguishable, and both participants and research staff were blinded to treatment assignment. Study medications were started in early winter (November or December) and were taken orally once daily for 3 months (completed in February or March).

Compliance and safety. All participants were assessed for adverse events by study staff over the phone at week 2 of each month and in-person at the beginning of each month when the next month’s supply of vitamins was provided. Participants were educated on the warning signs and symptoms of hypercalcemia. Serum calcium was measured in subjects taking hydrochlorothiazide at 1 and 3 months. An additional subset of 44 ‘control’ participants not taking hydrochlorothiazide also underwent calcium assays at 3 months. Electronic pill dispenser systems and pill counts were used to track compliance with study supplementation in addition to biweekly phone calls. Any subject found to have calcium

Figure 1. Consort diagram.
Association of baseline 25(OH)D and BMI and weight
There was no significant association between BMI or weight and 25(OH)D at the beginning of the study. Baseline weight and baseline BMI were not significantly associated with 25(OH)D (estimate (SE), P-value: BMI, −0.04 (0.07), P = 0.55; weight, −0.02 (0.01), P = 0.06). Baseline 25(OH)D was not significantly associated with baseline BMI or baseline weight (BMI, −0.03 (0.05), P = 0.55; weight, −0.56 (0.30), P = 0.06).

Impact of vitamin D supplementation on BMI and weight
The primary efficacy analyses of vitamin D3 supplementation on weight and BMI are shown in Table 2. In linear regression with the dose of vitamin D3 (per 1000 IU per day) as the independent variable and the 3-month change in weight (or 3-month change in BMI) as the dependent variable, no effect of vitamin D3 on change in BMI or weight was observed. For each additional 1000 IU per day of vitamin D3, BMI increased by estimate (SE): 0.01 (0.039); P = 0.78 and weight increased by estimate (SE):0.06 (0.24); P = 0.81. At 6 months, no significant change in BMI or weight was observed (Table 2).

Adverse events
There were five isolated incidences of mild hypercalcemia that were in the reference range on repeated sampling. Vitamin D supplements were discontinued in the four participants with mild hypercalcemia at 1 month. Vitamin D supplementation was discontinued in the participant who had hypercalcemia at month 3. There were no episodes of nephrolithiasis.

DISCUSSION
On the basis of evidence showing that vitamin D deficiency is associated with obesity, we tested the hypothesis that vitamin D supplementation could reduce BMI in a randomized, placebo-controlled trial of African-Americans. Although circulating 25(OH)D increased with vitamin D supplementation, we found that vitamin D supplementation did not lower BMI or weight among healthy African-Americans. Numerous cross-sectional studies have assessed the relationship between vitamin D status and different measures of adiposity. These studies found an inverse relationship between vitamin D and total body fat and regional adipose tissue. Others have shown an inverse relationship between vitamin D levels and components of metabolic syndrome, including abdominal obesity, which is a known risk factor for several chronic conditions. Furthermore, a recent meta-analysis evaluating the effect of vitamin D supplementation on adiposity biomarkers in randomized controlled trials found no significant reduction in adiposity measures in the absence of calorie restriction.

The lack of effect of vitamin D supplementation on weight may be due to low dietary calcium intake. Heaney et al. concluded that vitamin D status and benefits associated with vitamin D supplementation appear to be dependent on calcium intakes at or above recommended amounts. The doses of vitamin D tested in this study, as well as the dosing schedule (once per day, rather than intermittent large boluses), may provide an optimal balance of efficacy and safety based on current evidence and the recommended daily allowance and tolerable upper limit set by the Institute of Medicine.

Although there have been some trials including Whites that suggest that vitamin D supplementation prevents weight gain or promotes weight loss, little is known about African-Americans. Some have shown positive effects on weight but these effects may have been due to the adjunctive calcium supplementation. For example, in the Women’s Health Initiative Study, women who were randomly assigned to calcium and vitamin D...
supplementation arm had significantly less weight gain. Although the overall mean weight change difference between groups was small (−0.13 kg), women in the active intervention who had inadequate baseline calcium intakes (<1200 mg per day) had 11% lower risks for substantial weight gain (1–3 kg or >3 kg), whereas those who had calcium intakes >1200 mg per day were unaffected by treatment (P for interaction = 0.008).

The vitamin D/calcium trial was imbedded in the other Women’s Health Initiative randomized controlled trials, including a diet modification trial that may have led to weight loss, thus influencing the effects of combined vitamin D/calcium supplementation. It was not possible to differentiate between the effect of calcium and vitamin D supplementation. Major et al.,29 showed that among women with calcium intake <800 mg per day, calcium and vitamin D supplementation enhanced the beneficial effect of body weight loss on lipids and lipoprotein profile in overweight and obese women.

In our study, vitamin D supplementation was not associated with any significant adverse effects. This confirms the
Table 2. Effect of vitamin D supplementation on BMI and weight during the treatment (baseline to 3 months, mean (SE)) and 6 months after treatment

<table>
<thead>
<tr>
<th>Parameter, mean (SE)</th>
<th>Placebo</th>
<th>1000</th>
<th>2000</th>
<th>4000</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (at baseline)</td>
<td>81</td>
<td>81</td>
<td>83</td>
<td>83</td>
</tr>
<tr>
<td>BMI, kg m⁻²</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline BMI</td>
<td>31.85 (0.9)</td>
<td>32.46 (0.91)</td>
<td>32.96 (0.96)</td>
<td>32.15 (0.81)</td>
</tr>
<tr>
<td>3 month BMI</td>
<td>32.00 (0.9)</td>
<td>32.41 (0.93)</td>
<td>33.11 (0.96)</td>
<td>32.28 (0.83)</td>
</tr>
<tr>
<td>6 month BMI</td>
<td>32.14 (0.92)</td>
<td>32.50 (0.96)</td>
<td>32.54 (0.96)</td>
<td>32.02 (0.84)</td>
</tr>
<tr>
<td>Difference BMI (0–3)</td>
<td>0.15 (0.09)</td>
<td>–0.04 (0.11)</td>
<td>0.15 (0.13)</td>
<td>0.13 (0.12)</td>
</tr>
<tr>
<td>Difference BMI (3–6)</td>
<td>–0.18 (0.10)</td>
<td>–0.19 (0.10)</td>
<td>0.01 (0.11)</td>
<td>–0.14 (0.12)</td>
</tr>
<tr>
<td>Difference BMI (0–6)</td>
<td>0 (0.11)</td>
<td>–0.17 (0.16)</td>
<td>0.02 (0.16)</td>
<td>–0.02 (0.15)</td>
</tr>
<tr>
<td>Weight (wt), kg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline weight</td>
<td>89.63 (2.44)</td>
<td>89.40 (2.43)</td>
<td>92.73 (2.73)</td>
<td>89.54 (2.44)</td>
</tr>
<tr>
<td>3 month weight</td>
<td>90.03 (2.50)</td>
<td>89.29 (2.50)</td>
<td>93.13 (2.71)</td>
<td>89.90 (2.49)</td>
</tr>
<tr>
<td>6 month weight</td>
<td>201.22 (5.63)</td>
<td>200.02 (5.62)</td>
<td>203.23 (6.22)</td>
<td>198.48 (5.71)</td>
</tr>
<tr>
<td>Difference weight (0–3)</td>
<td>0.41 (0.27)</td>
<td>–0.11 (0.30)</td>
<td>0.39 (0.38)</td>
<td>0.36 (0.36)</td>
</tr>
<tr>
<td>Difference weight (3–6)</td>
<td>–1.05 (0.62)</td>
<td>–1.37 (0.60)</td>
<td>0.02 (0.70)</td>
<td>–0.78 (0.73)</td>
</tr>
<tr>
<td>Difference weight (0–6)</td>
<td>0.07 (0.67)</td>
<td>–1.37 (0.60)</td>
<td>0.01 (0.96)</td>
<td>–0.02 (0.94)</td>
</tr>
<tr>
<td>25(OH)D, ng ml⁻¹</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline 25(OH)D</td>
<td>17.07 (1.03)</td>
<td>17.33 (1.00)</td>
<td>16.12 (0.98)</td>
<td>17.79 (0.98)</td>
</tr>
<tr>
<td>3 month 25(OH)D</td>
<td>14.23 (0.96)</td>
<td>28.12 (1.11)</td>
<td>35.48 (1.21)</td>
<td>47.30 (1.22)</td>
</tr>
<tr>
<td>6 month 25(OH)D</td>
<td>19.07 (1.0)</td>
<td>22.26 (0.96)</td>
<td>26.77 (1.02)</td>
<td>31.48 (0.81)</td>
</tr>
<tr>
<td>Difference 25(OH)D (0–3)</td>
<td>–2.58 (0.66)</td>
<td>11.01 (1.22)</td>
<td>19.21 (1.21)</td>
<td>29.79 (1.29)</td>
</tr>
<tr>
<td>Difference 25(OH)D (3–6)</td>
<td>4.78 (0.77)</td>
<td>–5.80 (1.10)</td>
<td>–9.20 (0.91)</td>
<td>–15.71 (0.93)</td>
</tr>
<tr>
<td>Difference 25(OH)D (0–6)</td>
<td>1.83 (0.86)</td>
<td>5.02 (0.87)</td>
<td>10.29 (0.95)</td>
<td>13.81 (0.99)</td>
</tr>
</tbody>
</table>

Difference BMI (0–3) = month 3 BMI kg m⁻² – month 0 BMI kg m⁻²; mean (SE). Difference BMI (3–6) = month 6 BMI kg m⁻² – month 3 BMI kg m⁻²; mean (SE). Difference BMI (0–6) = month 6 BMI kg m⁻² – month 0 BMI kg m⁻²; mean (SE). Difference weight (0–3) = month 3 weight, kg – month 0 weight, kg; mean (SE). Difference weight (3–6) = month 6 weight, kg – month 3 weight, kg; mean (SE). Difference weight (0–6) = month 6 weight, kg – month 0 weight, kg; mean (SE). Difference 25(OH)D (0–3) = month 3, 25(OH)D – month 0, 25(OH)D; mean (SE). Difference 25(OH)D (3–6) = month 6, 25(OH)D – month 3, 25(OH)D; mean (SE). Difference 25(OH)D (0–6) = month 6, 25(OH)D – month 0, 25(OH)D; mean (SE). 0–3 month change in weight, BMI or 25(OH)D per 1000 IU per day of vitamin D supplementation. 3–6 month change in weight, BMI or 25(OH)D per 1000 IU per day of vitamin D supplementation. 0–6 month change in weight, BMI or 25(OH)D per 1000 IU per day of vitamin D supplementation. 25(OH)D conversion is 2.49 nmol l⁻¹ for each ng ml⁻¹.
documented by others that even higher doses of vitamin D3 supplements are safe. \(^{30} \) Strengths of our study include its prospective design, the use of a double-blind, randomized placebo-controlled intervention and our adjustment for season. Another strength is the similarity of living environments of these placebo-controlled intervention and our adjustment for season.

Prospective design, the use of a double-blind, randomized speci- our results. This study is unique in that it evaluates vitamin D recognition that low dietary calcium intake may have contributed to 25(OH)D status may be related to other hormones that change in weight and BMI. These are weaker measures of adiposity than direct measures. Thus, we may be underestimating the association between vitamin D supplementation and adiposity. \(^{21} \) Yet, our finding agree with other published null findings of the effects of vitamin D supplementation on adiposity biomarkers. \(^{13} \) We also recognize that low dietary calcium intake may have contributed to our results. This study is unique in that it evaluates vitamin D supplementation effects in African-Americans with a low intake of calcium.

Other limitations of the trial compared with some trials specifically designed for obesity is the lack of records of energy intake and detailed measurements of physical activity. Small changes in BMI may not be detected because of the small sample size and the measurements of adiposity may not be sufficiently sensitive. BMI includes fat mass, lean mass and bone mass. Furthermore, a variety of hormones including gonadal, thyroidal, adrenal and growth hormones influence adiposity. These hormones are under the influence of the hypothalamic-pituitary axis and have circadian and circannual rhythms in adults. \(^{20} \) Thus, the association between obesity and serum 25(OH)D status may be related to other hormones that change by season.

In conclusion, supplementation with vitamin D did not significantly alter the weight or the BMI over a relatively short duration in a cohort of overweight or obese African-Americans. It is not known whether the low serum 25(OH)D in African-Americans is due to vitamin D deficiency secondary to the increase in fat mass or to other factors such as genotype variation in vitamin D binding protein or enzymes involved in vitamin D metabolism. Future trials of longer vitamin D supplementation in African-Americans are needed to examine the biological contributions to the interaction between vitamin D deficiency, obesity, health disparities and obesity-related chronic diseases.

CONFLICT OF INTEREST

Hollis has support from DiaSorin S.p.A for serving as an academic consultant. The remaining authors declare no conflict of interest.

ACKNOWLEDGEMENTS

We would like to thank Cara Marcus, MSLIS, AHP, Director of Library Services, Brigham and Women’s Faulkner Hospital for facilitating access to reference articles and Harvard Catalyst for statistical support. The authors’ responsibilities as follows—CSF, ELG, KME, BFD, GGB: conceived and designed the study; PDC, CSF, ELG: analyzed the study; and all authors contributed to the manuscript. This trial was funded by the National Cancer Institute (P50CA127003; K07CA148894 (Ng); K22CA126992; SK05CA124415 [Emmons]; U01CA138962 [Chandler]), the Department of Defense Prostate Cancer Research Program (PC081669 [Drake]), the American Society of Clinical Oncology Career Development Award (Ng) and Pharmavite LLC. The sponsor had no role in designing, developing the protocol, or conducting the trial; in data collection, analysis, management, or interpretation of the data; or in preparing the manuscript.

REFERENCES


25 Martini LA, Wood RJ. Vitamin D status and the metabolic syndrome. *Nutr Rev* 2006; **64**: 479–486.


This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivs 4.0 International License. The images or other third party material in this article are included in the article’s Creative Commons license, unless indicated otherwise in the credit line; if the material is not included under the Creative Commons license, users will need to obtain permission from the license holder to reproduce the material. To view a copy of this license, visit http://creativecommons.org/licenses/by-nc-nd/4.0/