Effects of Vitamin D Supplementation on 25-Hydroxyvitamin D and Markers of Cardiovascular Disease Risk in Subjects with High Waist Circumferences

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Background

- Observational studies have shown an inverse relationship between circulating 25-hydroxyvitamin D [25(OH)D] concentration and the incidence of cardiovascular disease.
- We recently reported a strong positive relationship between serum 25(OH)D and high-density lipoprotein cholesterol (HDL-C) concentrations.

Objective

- The objective of this trial was to assess the effects of a multivitamin and mineral (MVM) supplement, with and without vitamin D (cholecalciferol), on serum 25(OH)D, HDL-C, and other cardiovascular disease risk markers in subjects with waist circumference ≥88 cm (women) or ≥102 cm (men). An extension study examined effects of incorporating low doses of omega-3 fatty acids and probiotics into the supplement.

Subjects

- Men and women 18-79 years of age, each with waist circumference ≥88 cm (women) or ≥102 cm (men).
- Participants agreed to avoid sunbathing and use of tanning beds throughout the study period.
- The 8 week trial was initiated in the summer months with the 8 week extension period ending in the fall.
- Participants refrained from supplemental vitamin D intake in functional foods or dietary supplements other than multivitamin supplements with no more than 200 IU of vitamin D.
- Exclusion criteria included coronary heart disease (CHD) or a CHD risk equivalent; abnormal laboratory test results of clinical significance; poorly controlled hypertension (≥160 mm Hg systolic or ≥100 mm Hg diastolic blood pressure); use of any medications, functional foods or dietary supplements known to alter lipid metabolism.

Methods

- Subjects were randomly assigned to receive a daily dose of either a MVM supplement (control) or a MVM supplement containing 1200 IU of vitamin D (MVM + D) for 8 weeks.
- Following the 8 week trial, the MVM + D group participated in an open-label extension period for an additional eight weeks during which bifidobacterium longum and lactobacillus acidophilus (500 million colony forming units/d total), eicosapentaenoic acid (280 mg/d), and docosahexaenoic acid (180 mg/d) were added to the supplement.
- Plasma 25(OH)D, serum lipids, and serum hs-CRP were assessed at baseline and the end of both the double-blind treatment period and the extension period.
- Analyses of covariance models were used to compare changes or percent changes from baseline to end-of-treatment for the double-blind treatment period.
- Analysis of variance models were used to compare baseline, end of double-blind treatment and end of extension period values. Pairwise comparisons were obtained using *t*-tests with Sidak corrections for multiple comparisons.

Results

Table 1. Subject characteristics for the double-blind treatment period.

Characteristic[1]	MVM (*n = 29*) n (%)	MVM + D (*n = 31*) n (%)
Gender		
Male	7 (24.1%)	8 (25.8%)
Female	22 (75.9%)	23 (74.2%)
Race/Ethnicity		
Non-Hispanic White	27 (93.1%)	30 (96.8%)
All Other	2 (6.9%)	1 (3.2%)
Smoking Status		
Non-Smoker	14 (48.3%)	15 (48.4%)
Current Smoker	15 (51.7%)	16 (51.6%)
	Mean (SEM)	
Age, *years*	54.3 (2.0)	50.3 (2.5)
Body Mass Index, *kg/m²*	31.7 (1.0)	31.7 (1.1)
Waist Circumference, *cm*	103.8 (2.1)	105.7 (2.2)

[1]There were no significant differences between groups. All P-values were >0.20.

Table 2. Indicators of cardiovascular disease risk for the double-blind treatment period.

Parameter[1]	MVM (*n = 29*)	MVM + D (*n = 31*)	P-value
	Mean (SEM) or Median (Interquartile Limits)[2]		
25-Hydroxyvitamin D, *ng/mL*			
Baseline	27.2 (1.5)	25.8 (1.5)	0.508
Change	–0.5 (1.0)	4.7 (1.2)	0.003
Total Cholesterol, *mg/dL*			
Baseline	213.9 (5.2)	202.2 (7.7)	0.220
% Change	–0.6 (1.9)	1.6 (1.5)	0.359
LDL-C, *mg/dL*			
Baseline	137.0 (5.1)	131.7 (6.0)	0.505
% Change	0.1 (2.6)	1.4 (1.9)	0.836
HDL-C, *mg/dL*			
Baseline	46.2 (1.9)	45.6 (2.4)	0.831
% Change	1.7 (1.4)	2.8 (2.0)	0.653
Non-HDL-C, *mg/dL*			
Baseline	167.5 (148.5, 186.0)	153.5 (126.5, 192.0)	0.237
% Change	0.3 (–6.2, 5.5)	0.0 (–3.6, 4.3)	0.650
TC/HDL-C Ratio			
Baseline	4.73 (3.83, 5.63)	4.36 (3.69, 5.58)	0.433
% Change	–2.11 (–4.40, 2.51)	–2.01 (–7.42, 5.60)	0.601
Triglycerides, *mg/dL*			
Baseline	149.0 (95.0, 200.0)	88.5 (72.0, 163.0)	0.044
% Change	–6.0 (–20.7, 1.8)	0.7 (–23.3, 18.6)	0.138
hs-CRP, *mg/dL*			
Baseline	1.9 (0.9, 4.1)	2.4 (0.9, 4.4)	0.731
Change	0.1 (–0.5, 0.6)	0.0 (–1.1, 1.4)	0.988
Body Weight, *kg*			
Baseline	85.4 (78.1, 95.7)	90.7 (77.1, 98.2)	0.496
Change	–0.1 (–1.0, 0.3)	0.6 (–0.4, 1.2)	0.009
Systolic Blood Pressure, *mm Hg*			
Baseline	120.3 (1.9)	115.8 (1.8)	0.090
Change	–3.5 (1.3)	–0.5 (1.1)	0.294
Diastolic Blood Pressure, *mm Hg*			
Baseline	74.1 (1.5)	71.9 (1.4)	0.227
Change	–1.8 (0.9)	0.1 (0.8)	0.244
Heart Rate, *bpm*			
Baseline	64.9 (60.0, 75.0)	69.6 (62.7, 74.2)	0.276
Change	3.1 (0.2, 4.3)	1.9 (–1.5, 3.3)	0.481

[1] Baseline was defined as average of visits 1 and 2 (weeks –1 and 0) and end of treatment was defined as average of visits 3 and 4 (weeks 7 and 8).

[2] Variables with results shown as median (interquartile limits) were not normally distributed and statistical modeling was completed after rank transformation.

Table 3. Indicators of cardiovascular disease risk for the extension period.

Parameter[1]	MVM + D Extension *n = 27*	
	Mean (SEM) or Median (Interquartile Limits)[3]	P-value[2]
25-Hydroxyvitamin D, *ng/mL*		
Baseline	25.6 (1.6)	
Change at End of Treatment	5.0 (1.3)	0.002
Change at End of Extension	2.9 (1.4)	0.095
Total Cholesterol, *mg/dL*		
Baseline	203.6 (8.4)	
% Change at End of Treatment	0.6 (1.4)	0.800
% Change at End of Extension	–2.9 (1.2)	0.048
LDL-C, *mg/dL*		
Baseline	131.4 (6.7)	
% Change at End of Treatment	–0.1 (1.9)	0.800
% Change at End of Extension	–4.3 (2.0)	0.072
HDL-C, *mg/dL*		
Baseline	46.7 (2.6)	
% Change at End of Treatment	2.2 (2.1)	0.638
% Change at End of Extension	7.2 (2.3)	0.008
Non-HDL-C, *mg/dL*		
Baseline	156.9 (8.1)	
% Change at End of Treatment	0.2 (1.6)	0.800
% Change at End of Extension	–5.7 (1.3)	0.001
TC/HDL-C Ratio		
Baseline	4.0 (3.6, 5.6)	
% Change at End of Treatment	–2.8 (–7.4, 5.5)	0.800
% Change at End of Extension	–7.3 (–14.3, –4.2)	0.001
Triglycerides, *mg/dL*		
Baseline	88.5 (75.0, 163.0)	
% Change at End of Treatment	2.3 (–22.9, 18.6)	0.677
% Change at End of Extension	–12.2 (–19.5, 8.4)	0.251
hs-CRP, *mg/dL*		
Baseline	2.3 (0.8, 4.2)	
Change at End of Treatment	0.0 (–1.1, 1.1)	0.800
Change at End of Extension	0.3 (–0.9, 0.7)	0.800
Body Weight, *kg*		
Baseline	91.1 (3.0)	
Change at End of Treatment	0.5 (0.3)	0.082
Change at End of Extension	1.0 (0.3)	0.006
Systolic Blood Pressure, *mm Hg*		
Baseline	115.7 (1.9)	
Change at End of Treatment	–0.2 (1.1)	0.800
Change at End of Extension	–0.9 (1.0)	0.715
Diastolic Blood Pressure, *mm Hg*		
Baseline	71.8 (68.1, 77.1)	
Change at End of Treatment	–0.5 (–2.0, 2.8)	0.800
Change at End of Extension	–0.7 (–5.5, 3.4)	0.781
Heart Rate, *bpm*		
Baseline	69.6 (62.7, 74.2)	
Change at End of Treatment	2.3 (–3.2, 5.1)	0.483
Change at End of Extension	1.9 (–2.2, 9.7)	0.164

[1] Baseline was defined as average of visits 1 and 2 (weeks –1 and 0); end of treatment was defined as average of visits 3 and 4 (weeks 7 and 8); end of extension was defined as an average of visits 5 and 6 (weeks 15 and 16). Change at End of Treatment = Change from Baseline to End of Treatment. Change at End of Extension = Change from Baseline to End of Extension.

[2] Treatment and Extension P-values were obtained from t-tests for changes different from zero. P-values are adjusted to correct for multiple comparisons.

[3] Variables with results shown as median (interquartile limits) were not normally distributed and statistical modeling was completed after rank transformation.

Table 4. Subjects with 25(OH)D levels ≥30 ng/mL.[1,2]

	MVM n = 29	MVM + D n = 31	MVM + D Extension n = 27	P-value
	n (%)			
Baseline	9 (31.0%)	11 (35.5%)	9 (33.3%)	0.720
End of Treatment	7 (24.1%)	12 (38.7%)	10 (37.0%)	0.232
End of Extension	NA	NA	9 (33.3%)	0.949

[1]NA = not applicable

[2]All comparisons were p > 0.200.

Abbreviations:

25(OH)D = 25-hydroxyvitamin D

CHD = coronary heart disease

HDL-C = high-density lipoprotein cholesterol

hs-CRP = high sensitivity C-reactive protein

IU = international units

LDL-C = low-density lipoprotein cholesterol

MVM = multivitamin mineral supplement

MVM + D = multivitamin mineral supplement + vitamin D

SEM = standard error of the mean

TC = total cholesterol.

Conclusions

- Although mean 25(OH)D levels increased from 25.8 ng/mL to 30.5 ng/mL, consuming a MVM supplement with 1200 IU/d of vitamin D for 8 weeks did not increase serum 25(OH)D concentrations to a desirable level in a majority of these predominantly overweight and obese participants, and did not significantly alter HDL-C or other markers of cardiovascular disease risk.
- Further research is warranted to assess the levels of supplemental vitamin D intakes required to raise 25(OH)D concentrations to sufficient levels in subjects with increased adiposity, which would be particularly relevant in the winter months when sun exposure is low.
- Preliminary evidence from the extension study suggests that adding low-dose probiotics and omega-3 fatty acids may favorably affect HDL-C and non-HDL-C concentrations.

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