Vitamin D supplementation during Antarctic winter[1–3]

Scott M Smith, Keri K Gardner, James Locke, and Sara R Zwart

ABSTRACT

Background: Persons with limited exposure to ultraviolet B light, including space travelers, may not receive enough vitamin D. Recent studies indicate that optimal serum 25-hydroxyvitamin D [25(OH)D] should be ≥80 nmol/L.

Objective: This study was designed to evaluate the effectiveness of 3 doses of vitamin D to raise and maintain 25(OH)D to a concentration >80 nmol/L in persons with limited ultraviolet B light exposure.

Design: This was a 5-mo, prospective, randomized, double-blind study of vitamin D supplementation. It was conducted during winter in Antarctica at the McMurdo Station, when ultraviolet B radiation levels are essentially zero. The 55 subjects were randomly divided into 3 groups for vitamin D supplementation: 2000 IU/d ($n = 18$), 1000 IU/d ($n = 19$), and 400 IU/d ($n = 18$). An additional 7 subjects did not take supplements or took supplements of their own choosing. Blood samples were collected about every 2 mo during the winter.

Results: About 5 mo after supplementation started, 25(OH)D increased to 71 ± 23 nmol/L in the 2000-IU/d group, 63 ± 25 nmol/L in the 1000-IU/d group, and 57 ± 15 nmol/L in the 400-IU/d group and decreased to 34 ± 12 nmol/L in the group not taking supplements.

Conclusions: These data will enable us to provide space crews with evidence-based recommendations for vitamin D supplementation. The findings also have implications for other persons with limited ultraviolet light exposure, including polar workers and the elderly. *Am J Clin Nutr* 2009;89:1092–8.

INTRODUCTION

Vitamin D has long been known to play an important role in calcium metabolism, and, more recently, it has been found to have noncalcitropic functions (1–5). Functionally relevant measures from several recent studies suggest that the lower limit of serum 25-hydroxyvitamin D (the functional indicator of vitamin D status) should be greater than the current 25 nmol/L. It is generally agreed that the optimal concentration should be defined as ≥75 or 80 nmol/L (6–9). The 2005 *Dietary Guidelines for Americans* recommends that persons in high-risk groups (such as those who are elderly, have dark skin, or are exposed to little sunlight) need to have substantially higher intakes of vitamin D (25 μg, or 1000 IU/d) to maintain their serum 25-hydroxyvitamin D values at ≈80 nmol/L—the concentration at which serum parathyroid hormone (PTH) concentrations are

maximally suppressed in several studies (10–12). Increasing serum 25-hydroxyvitamin D concentrations to 75–80 nmol/L from <50 nmol/L is associated with the suppression of serum PTH, a two-thirds greater calcium absorption efficiency, a one-third decrease in osteoporotic fracture risk, greater bone mineral density, and reduced rates of bone resorption and loss (13, 14).

Supplemental vitamin D is critical for space travelers because spacecraft shielding prevents them from being exposed to ultraviolet light and because the space food systems provide an insufficient dietary supply of vitamin D (15). Despite the provision of daily vitamin D supplements (400 IU) to International Space Station (ISS) and Skylab crew members, the vitamin D status of these astronauts was consistently lower after flight than before, and, in several crew members, it has decreased to concentrations considered clinically significant (16, 17). As reported in 2005, the mean serum 25-hydroxyvitamin D concentration for a group of US ISS crew members before flight was 63 ± 16 nmol/L; after a 4- to 6-mo space flight, it decreased 25–30% despite the provision of vitamin D (400 IU/d) supplements (16).

Providing an evidence-based recommendation for vitamin D supplementation to maintain serum 25-hydroxyvitamin D at optimal concentrations (≥75–80 nmol/L) is important for long-duration crew members on the ISS (6-mo flights) and is critical for exploration-class missions on the Moon or Mars that could be years in duration. Ground-based models of spaceflight in which subjects receive limited sunlight exposure are valuable for performing vitamin D supplementation trials. One of these models is subjects spending the winter in Antarctica, where ultraviolet B light (UVB) radiation is essentially zero during the winter months. The main objective of this study was to determine the effectiveness of 3 different doses of supplemental vitamin D_3 in enabling subjects with no sunlight exposure to reach and

maintain optimal vitamin D status (serum 25-hydroxyvitamin D concentration of 80 nmol/L).

SUBJECTS AND METHODS

Subjects

This study was conducted at McMurdo Station, Antarctica, during the winter months (March to August) of 2007. The protocol was approved by the Johnson Space Center Committee for the Protection of Human Subjects. The procedures followed were in accordance with the Helsinki Declaration of 1975 as revised in 1983. The subjects provided written informed consent before they participated in the study. No adverse events were reported.

Study design

This was a 5-mo prospective, randomized, double-blind study of vitamin D supplementation that consisted of 3 data collection sessions, each including a 7-d diet record, a blood draw, and body weight determination. Baseline data (session 1) were collected at week 5 of the South Polar winter (the end of March and beginning of April); session 2 was at week 18 (the end of June and beginning of July), and session 3 was at week 25 (the middle of August). Fifty-two percent of the population wintering over in McMurdo, Antarctica, was recruited for the study. The health and physical requirements for this assignment at McMurdo were used as inclusion criteria (except for vitamin D supplementation, as described below).

After the first blood draw, 55 subjects (41 men and 14 women, all white) were randomly divided into 3 groups in a double-blind fashion. The groups received 2000 IU/d ($n = 18$), 1000 IU/d ($n = 19$), or 400 IU/d ($n = 18$) vitamin D. Seven additional subjects (3 men and 4 women) agreed to participate in the blood draws and diet logging, but they either did not want to take study supplements or were taking their own vitamin D supplements. Those taking supplements of vitamin D >400 IU/d or of calcium >500 mg/d were excluded. A placebo control group was considered in the original design of the study, but was not included because of ethical concerns. Three subjects dropped out after the first blood draw, and one subject dropped out after the second blood draw for unknown reasons. The sample sizes listed above are the number of subjects in each group who completed the entire study.

The vitamin D_3 supplements used (Douglas Laboratories, Pittsburgh, PA) provided 0, 400, or 1000 IU per pill (verified as <20 IU for the placebo, 416 IU for the 400-IU pill, and 1380 IU for the 1000-IU pill by Covance, Madison, WI). The subjects were given 2 bottles, each with a known number of pills, and were instructed to take 1 pill from each bottle daily. Each bottle was labeled with a single letter code; there were 12 possible combinations (4 possible combinations for each study dose) to ensure blinding of both the subjects and the on-site medical staff who conducted the study. The 2 bottles would provide either one placebo and one 400-IU pill (the 400-IU dose group), one placebo and one 1000-IU pill (the 1000-IU dose group), or two 1000-IU pills (the 2000-IU dose group). The subjects were asked to return the bottles at the end of the study so that pill counts could be conducted to estimate compliance. Thirty-one of the 55 subjects returned the pill bottles at the end of the study. Repeat analysis of the pills at that time verified that neither time nor transit to Antarctica had a significant effect on the vitamin D content.

Dietary vitamin D food log

For 7 d before each of the 3 blood draws, each subject completed a diet questionnaire. The subjects were provided a log book that contained a sheet for each diet collection day, which listed foods known to contain vitamin D. Information was obtained from the staff at the McMurdo Station regarding food sources of vitamin D, including foods fortified with vitamin D, that were available to the subjects. The subjects were asked to record the amount of each of these food items that they consumed that day and any vitamin D–containing supplements that they took. Nutrient intake was calculated from the food logs by using the Nutrition Data System for Research (2007 version) developed by the Nutrition Coordinating Center, University of Minnesota, Minneapolis, MN (18). Seven-day averages ($\pm$SD) were calculated for each session.

Blood collection and biochemical analyses

Blood was collected into serum separator tubes (Becton Dickinson, Franklin Lakes, NJ) after an 8-h fast and was centrifuged to separate the cells from the serum. The centrifuged tubes were stored upright at $-80°C$ until they were received at the Johnson Space Center (in October 2007), where they were thawed, separated into aliquots, and analyzed. For tests (such as the one for PTH) sensitive to cycles of freezing and thawing, analyses were performed on the day the samples were thawed. On thawing, samples were logged into the Nutritional Biochemistry Laboratory information management system and assigned 6-digit tracking numbers. The aliquot labels did not provide dose or session information; therefore, the analyses were blinded as well.

Two 5-mL blood tubes were filled for each subject at each session. On receipt of the tubes in Houston, it was found that many of them had inadvertently not been centrifuged before they were frozen. This affected 27–29 data points, depending on whether one or both of the tubes were affected and whether hemolysis affected the tests. Accordingly, data are reported with the n for each test.

PTH was assayed for the intact peptide by radioimmunoassay (RIA; DSL, Webster, TX). Serum 1,25-dihydroxyvitamin D was measured by RIA (DiaSorin, Stillwater, MN) after the samples were extracted with acetonitrile and purified on $C_{18}OH$ cartridges. Serum 25-hydroxyvitamin D was measured by RIA after extraction with acetonitrile (DiaSorin). Our laboratory participates in the DEQAS quality-assessment program (19) for 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D, and our data are in good agreement with data from other laboratories around the world that use the DiaSorin RIA. Vitamin D–binding protein was measured by using a commercially available enzyme-linked immunosorbent assay (ELISA) kit (Alpco Diagnostics, Windham, NH). Serum N-telopeptide was measured by ELISA (Osteomark; Ostex International, Seattle, WA). Serum calcium was measured by atomic absorption spectrometry, and serum phosphorus and magnesium were measured spectrophotometrically.

TABLE 1
Demographic characteristics of subjects[1]

Supplementation group	Age	Height	Race	Sex	Body weight S1	S2	S3	BMI at S1
	y	*cm*			*kg*			*kg/m²*
400 IU/d (*n* = 18)	42 ± 12	178 ± 8	White	13 M/5 F	91 ± 22	93 ± 26	93 ± 25	29 ± 6
1000 IU/d (*n* = 19)	44 ± 8	175 ± 12	White	13 M/6 F	95 ± 22	95 ± 22	95 ± 23	31 ± 7
2000 IU/d (*n* = 18)	43 ± 10	177 ± 9	White	15 M/3 F	89 ± 18	89 ± 19	89 ± 19	28 ± 6
No pills (*n* = 7)	39 ± 12	170 ± 8	White	3 M/4 F	78 ± 22	79 ± 24	78 ± 23	28 ± 7

[1] All values are means ± SDs. S1, S2, and S3, data collection sessions 1, 2, and 3. The data were analyzed with a repeated-measures 2-factor ANOVA, and no significant differences were found.

Free 25-hydroxyvitamin D was calculated as described by Al-oanzi et al (20). Briefly, they found that the concentration of free 25-hydroxyvitamin D was approximately equal to the concentration of total 25-hydroxyvitamin D divided by the concentration of vitamin D–binding protein.

The body weight of each subject was measured at the time of each blood draw, and height was recorded at the beginning of the study. Height and weight were determined by using a standard physician's office Health-O-Meter (Continental Scale Corporation, Bridgeview, IL).

Statistical analyses

Data were analyzed by using repeated-measures analysis of variance. A Bonferroni post hoc *t* test was used to identify differences between sessions. Statistical analyses were performed by using Sigma Stat 3.11 (Systat Software Inc, Chicago, IL). Statistical significance was defined as $P < 0.05$. For 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D, statistical analyses were performed once with all data and again with data from the hemolyzed samples excluded (described above). For all other tests, all available data were included, because hemolyzed samples were not analyzed. Outliers were determined by using Grubbs' test.

RESULTS

Age, height, body weight, and body mass index for each group are presented in **Table 1**. The groups did not differ significantly in body weight at the beginning of the study, and there was no significant effect of time (different data collection sessions) on body weight for any group.

The mean 7-d vitamin D intake (not including study supplements) before each blood collection session is presented in **Table 2**. In the group that did not take supplements, vitamin D intake was greater in session 1 than in the other 2 sessions. One subject in that group was an outlier, and, when that subject was excluded from the analyses, there was no interaction between group and time. Vitamin D intake from the diet was not significantly different between supplement groups.

There were no significant differences between groups at baseline for any of the serum analytes measured. In sessions 2 and 3, the serum concentration of 25-hydroxyvitamin D was higher in the 2000-IU/d group than in the group that did not take study supplements (**Table 3**). When hemolyzed samples were excluded, similar results were obtained, except that 25-hydroxyvitamin D was higher in the 1000-IU/d group and in the 2000-IU/d group than in the group not taking supplements in

session 3. In all groups that took study supplements, serum 25-hydroxyvitamin D was greater in sessions 2 and 3 than in session 1. The average changes per 100 IU supplement/d (based on actual vitamin D analysis in the supplements) were 2.5 ± 4.0, 1.4 ± 0.87, and 0.95 ± 0.61 for the 400-, 1000-, and 2000-IU/d groups, respectively. Vitamin D–binding protein showed no significant effect of group. Calculated free 25-hydroxyvitamin D (20) showed a significant effect of time, being greater in sessions 2 and 3 than in session 1; it showed no significant effect of group. Likewise, 1,25-dihydroxyvitamin D was greater in sessions 2 and 3 than in session 1, showing a significant effect of time but not group. Similar results were obtained when hemolyzed samples were excluded from the analysis.

PTH was not significantly affected by group or time (Table 3). In **Figure 1**, PTH is graphed against 25-hydroxyvitamin D for all subjects at all time points. Serum calcium showed a significant effect of time but not group, being greater in session 3 than in session 2. Bone-specific alkaline phosphatase was greater in session 3 than in session 1, showing a significant effect of time but not group; however, the data were not normally distributed and could not be normalized by transformation. Serum phosphorus showed a significant interaction between group and time, but serum magnesium was not significantly affected by either group or time.

Body weight did not change over the course of the study, but serum 25-hydroxyvitamin D status did change. To determine whether the expected relation between body weight and 25-hydroxyvitamin D was present at baseline and after 5 mo of supplementation, body

TABLE 2
Average vitamin D intakes on the 7 d before each blood draw session[1]

Vitamin D intake	Supplementation group 400 IU/d (*n* = 18)	1000 IU/d (*n* = 19)	2000 IU/d (*n* = 18)	No pills (*n* = 7)
Session 1 (IU)	302 ± 201	329 ± 231	356 ± 231	626 ± 931
Session 2 (IU)	241 ± 217	352 ± 237	283 ± 188	302 ± 343[2]
Session 3 (IU)	234 ± 207	346 ± 259	276 ± 218	334 ± 370[2]

[1] All values are means ± SDs. Data include total dietary vitamin D_2 and vitamin D_3 and all nonstudy supplements. The data were analyzed with a repeated-measures 2-factor ANOVA.

[2] Significantly different from session 1 for the group that took no pills, $P < 0.05$. One subject in this group was an outlier; when the data for this subject were excluded from the analyses, there was no interaction between group and time and no difference between groups.

TABLE 3
Concentrations of serum vitamin D and markers of bone metabolism[1]

	Supplementation group			
	400 IU/d	1000 IU/d	2000 IU/d	No pills
25-Hydroxyvitamin D (nmol/L)[2]				
Session 1	44 ± 18[3]	44 ± 19[3]	45 ± 14[3]	36 ± 17
Session 2	55 ± 19[a,b]	63 ± 20[a,b]	71 ± 20[b]	38 ± 17[a]
Session 3	57 ± 15[a,b]	63 ± 25[a,b]	71 ± 23[b]	34 ± 12[a]
1,25-Dihydroxyvitamin D (pmol/L)[4]				
Session 1	81 ± 36[3]	89 ± 36[3]	87 ± 29[3]	84 ± 21[3]
Session 2	96 ± 35	114 ± 39	101 ± 29	82 ± 25
Session 3	108 ± 36	114 ± 33	103 ± 36	89 ± 17
Parathyroid hormone (pg/mL)				
Session 1	46 ± 30	42 ± 33	47 ± 22	35 ± 18
Session 2	35 ± 24	30 ± 20	39 ± 36	53 ± 35
Session 3	37 ± 19	33 ± 19	38 ± 25	45 ± 21
Calcium (mmol/L)[5]				
Session 1	2.20 ± 0.15	2.26 ± 0.09	2.30 ± 0.11	2.27 ± 0.14
Session 2	2.21 ± 0.09[6]	2.27 ± 0.10[6]	2.27 ± 0.07[6]	2.16 ± 0.19[6]
Session 3	2.27 ± 0.10	2.28 ± 0.10	2.32 ± 0.10	2.34 ± 0.20
N-Telopeptide (nmol/L)[7]				
Session 1	13 ± 3	13 ± 5	14 ± 4	13 ± 3
Session 2	13 ± 3[6]	14 ± 6[6]	14 ± 5[6]	14 ± 2[6]
Session 3	13 ± 2	14 ± 5	14 ± 5	12 ± 3
Bone-specific alkaline phosphatase (U/L)[7]				
Session 1	24 ± 6[6]	22 ± 6[6]	24 ± 7[6]	25 ± 4[6]
Session 2	23 ± 6	23 ± 6	26 ± 7	28 ± 9
Session 3	24 ± 6	26 ± 9	26 ± 8	29 ± 14
Vitamin D–binding protein (nmol/L)				
Session 1	5203 ± 2038	5771 ± 1168	5201 ± 1035	4859 ± 840
Session 2	5163 ± 1010	5789 ± 1673	5115 ± 1063	5591 ± 1650
Session 3	5642 ± 1453	5599 ± 1977	5201 ± 746	5493 ± 1475
Calculated free 25-hydroxyvitamin D (pmol/L)[5]				
Session 1	15.5 ± 6.7[3]	13.2 ± 6.2[3]	15.6 ± 8.2[3]	12.4 ± 4.5[3]
Session 2	18.2 ± 7.1	20.0 ± 10.0	24.8 ± 10.6	11.4 ± 4.2
Session 3	17.8 ± 5.5	23.3 ± 17.4	23.1 ± 8.2	10.4 ± 3.5
Phosphorus (mmol/L)[8]				
Session 1	1.21 ± 0.19	1.15 ± 0.19	1.06 ± 0.21	1.14 ± 0.13
Session 2	1.06 ± 0.15[6]	1.18 ± 0.18	1.06 ± 0.20	1.24 ± 0.14
Session 3	1.17 ± 0.20	1.18 ± 0.24	1.10 ± 0.24	1.06 ± 0.14
Magnesium (mmol/L)				
Session 1	0.82 ± 0.06	0.78 ± 0.06	0.80 ± 0.06	0.81 ± 0.07
Session 2	0.81 ± 0.06	0.81 ± 0.06	0.83 ± 0.09	0.88 ± 0.09
Session 3	0.81 ± 0.08	0.82 ± 0.08	0.84 ± 0.12	0.84 ± 0.12

[1] All values are means ± SDs. Samples for the 3 sessions ($\approx$2.5 mo apart during the Antarctic winter) were batched and analyzed at the end of the study. Only data from subjects who completed the study are represented. For 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D, $n = 18$, 19, 18, and 7 for the 400-, 1000-, and 2000-IU/d and no-pill groups, respectively. For all other analytes, the respective values are $n = 15$, 17, 15, and 5 in session 1; $n = 13$, 15, 16, and 6 in session 2; and $n = 16$, 15, 18, and 7 in session 3 for the 400-, 1000-, and 2000-IU/d and no-pill groups, respectively. The data were analyzed with a repeated-measures 2-factor ANOVA. Values in a row with different superscript letters are significantly different, $P < 0.05$ (post hoc Bonferroni t test).

[2,8] Significant interaction between group and time: [2]$P < 0.001$, [8]$P < 0.05$.

[3] Significantly different from sessions 2 and 3, $P < 0.05$ (post hoc Bonferroni t test).

[4,5,7] Significant effect of time: [4]$P < 0.001$, [5]$P < 0.01$, [7]$P < 0.05$.

[6] Significantly different from session 3, $P < 0.05$ (post hoc Bonferroni t test).

weight was graphed against 25-hydroxyvitamin D at both of these time points in **Figure 2**. There was a negative correlation between body weight and 25-hydroxyvitamin D at baseline ($r = -0.36$, $P < 0.01$) and after 5 mo of supplementation ($r = -0.26$, $P < 0.05$). No adverse events were reported from subjects or the medical staff during or after the study.

DISCUSSION

To our knowledge, this is the first intervention study in which 3 different doses of vitamin D supplements were compared with respect to their effectiveness at raising and maintaining 25-hydroxyvitamin D status in an environment where subjects are not exposed to ultraviolet light. Other studies conducted in
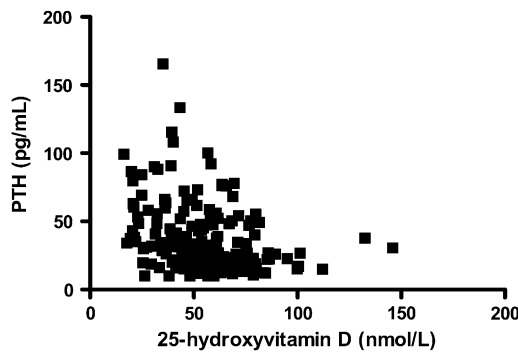
FIGURE 1. Correlation between serum 25-hydroxyvitamin D and serum parathyroid hormone (PTH) concentrations. Data are from all subjects and sessions ($n = 197$).

Antarctica were mostly observational and showed a decrease in 25-hydroxyvitamin D status, as expected (21–26). A shorter study (49 d) in submariners documented the inability of 400-IU doses to improve 25-hydroxyvitamin D concentrations (27). In our study, none of the treatment groups had a decrease in status; in fact, serum 25-hydroxyvitamin D increased after 3 and 5 mo of supplementation in subjects taking 400, 1000, or 2000 IU/d. The untreated group had essentially no change in vitamin D status over the course of the winter.

Although the average serum 25-hydroxyvitamin D did not reach the optimal concentration of 75–80 nmol/L, nevertheless, a significant increase in vitamin D status occurred with all levels of supplementation. Changes of similar magnitude have been noted in other studies providing similar doses (1000 IU/d) (28). The average dietary intake of vitamin D during the study was 295 ± 224 IU/d (average for all subjects except one outlier). Whereas this intake maintained vitamin D concentrations in the nonsupplemented subjects, it did not raise serum 25-hydroxyvitamin D concentrations to >40 nmol/L. Regardless of the exact concentration for optimal vitamin D status, agreement is close to universal that <40 nmol/L is insufficient.

Vitamin D supplementation did not affect 1,25-dihydroxyvitamin D or calcium status (as expected); however, both 1,25-dihydroxyvitamin D and serum calcium increased in sessions 2 and 3 in all subjects. As in other studies conducted in Antarctica, bone-specific alkaline phosphatase increased over time, which indicated that bone formation may have increased (23, 24). It is possible that 1,25-dihydroxyvitamin D and calcium increased in

response to a feedback mechanism to maintain available calcium when bone remodeling increased, as evidenced by the increase in bone-specific alkaline phosphatase.

Clearly, PTH concentrations decrease as serum 25-hydroxyvitamin D concentrations increase (10, 29, 30), but there is some disagreement as to whether they reach a plateau or keep decreasing (8, 31, 32). In the present study, it was not possible to determine whether PTH reached a plateau as serum 25-hydroxyvitamin D concentrations increased, because only very few subjects had a high 25-hydroxyvitamin D concentration (Figure 1).

Many factors besides ultraviolet light exposure and dietary intake can affect vitamin D status (33). One example is body weight. In many studies, obesity has been associated with lower serum 25-hydroxyvitamin D concentrations (34–36). Mechanisms that have been proposed to explain this include sequestration of vitamin D in fat, increased clearance of 25-hydroxyvitamin D, and negative feedback from higher 1,25-dihydroxyvitamin D concentrations in serum or from decreased ultraviolet light exposure (35, 37–39). In the present study, serum 25-hydroxyvitamin D was negatively correlated with body weight in session 1, before vitamin D supplementation and in session 3 after 5 mo of supplementation (Figure 2). This relation was also true for body mass index and serum 25-hydroxyvitamin D (data not shown). These results agree with data from Wortsman et al (35), who found that peak serum vitamin D status was negatively correlated with body weight after whole-body irradiation and also after a 50,000-IU dose of vitamin D_2. Their data and ours suggest that increased body weight is related to a decrease in circulating vitamin D. The effect of this on physiologic effects of vitamin D is unknown.

Another factor that should be considered is initial serum 25-hydroxyvitamin D status, because this can affect how individuals respond to different doses of vitamin D_3. For the 2000-, 1000-, and 400-IU/d groups, serum 25-hydroxyvitamin D was <50 nmol/L in 72%, 79%, and 58% of the subjects, respectively. When we analyzed the change in 25-hydroxyvitamin D to determine whether initial status or dose had an effect, we found that initial status did not significantly affect the change in vitamin D status, but the dose did have an effect as expected.

This study was limited because a placebo group was not included. Although the inclusion of a placebo control would have been ideal, others have made the case that vitamin D supplementation studies do not require placebo controls because it is highly unlikely that a placebo effect could occur (40). In any event, the inclusion of the group of subjects who did not take
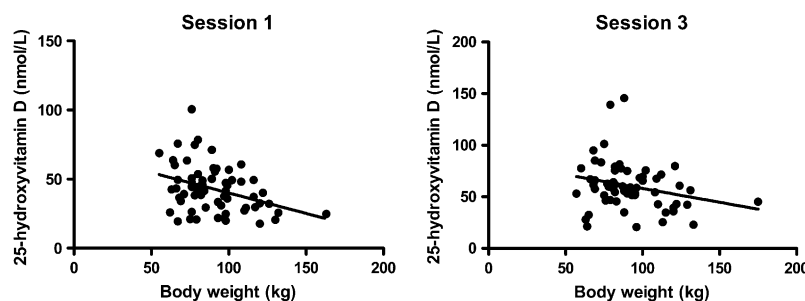
FIGURE 2. Correlation between body weight and serum 25-hydroxyvitamin D at the baseline blood draw before supplements were administered (session 1; $n = 63$) and after 5 mo of vitamin D supplementation (session 3; $n = 63$). Serum 25-hydroxyvitamin D was negatively correlated with body weight in sessions 1 ($r = -0.36$, $P < 0.01$) and 3 ($r = -0.26$, $P < 0.05$). When the outlier (greatest body weight) was removed, this relation remained true in session 1 ($r = -0.34$, $P < 0.01$) but there was only a trend in session 3 ($r = -0.25$, $P = 0.053$).

study pills most likely provides a view of the unsupplemented condition. The lack of any change in serum 25-hydroxyvitamin D in these subjects over the course of the winter (when it increased in supplemented subjects, even in the subjects who took the lowest dose we provided—400 IU/d), and their dietary intake (which included any nonstudy supplements and was not different from the dietary intake of the supplemented subjects), strongly suggests that these subjects can serve as viable controls for our efforts.

Another limitation of this study was the lack of breadth in the endpoints. Although we accomplished our goal of evaluating the effect of supplementation on vitamin D status, we could not implement a broader study in this environment at this time. The Antarctic and other isolated environments are known to affect many systems, including the immune and endocrine systems, along with cognitive and behavioral function in the central nervous system (41–46). The lack of understanding of the interrelations between vitamin D and these other systems remains a problem.

Subject compliance was another limiting issue in this study. Some subjects did not return their pill bottles at the end of the study, but the subjects who did return the bottles had 84 ± 17% compliance in the number of pills taken (77 ± 16%, 90 ± 17%, and 83 ± 17% in the 400-, 1000-, and 2000-IU/d groups, respectively). The general issue of compliance with vitamin D supplementation has led to efforts to reduce the frequency of dosing by increasing the dose (40). At extreme levels of dosing, and before broad-based supplementation efforts are considered, the safety and efficacy of supplementation need to be clearly documented. We based our highest supplement level (2000 IU) on the No Observed Adverse Events Level of 2000 IU/d defined by the Institute of Medicine. Whereas many have argued that this intake is too low and too conservative, a rational approach needs to be taken when applying vitamin D supplementation to a healthy population.

As we have learned more about the critical role that vitamin D plays in health, it has become increasingly important to identify the optimal amount of vitamin D supplementation for groups that have difficulties obtaining satisfactory vitamin D concentrations from UVB exposure. Many difficulties are encountered in vitamin D research, ranging from problems with measuring or controlling dietary intakes and input from sun exposure, to metabolism and sequestration in the body, to analytic problems in the laboratory. We report here the results of a small but reasonably well-controlled study in a specific population of individuals who received no ultraviolet light exposure. We hope that our findings are useful in setting recommendations for travelers to space and polar regions and for those who have limited sun exposure for other reasons.

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