Effectiveness and Safety of a High-Dose Weekly Vitamin D (20,000 IU) Protocol in Older Adults Living in Residential Care

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OBJECTIVES: To report 25 hydroxyvitamin D (25OHD) concentrations, an indicator of vitamin D status, in older adults living in residential care 1 year after a protocol of weekly 20,000 IU of vitamin D was started.

DESIGN: Cross-sectional.

SETTING: Five residential care facilities in British Columbia, Canada.

PARTICIPANTS: Residents aged 65 and older from five facilities (N = 236).

MEASUREMENTS: Participants provided a blood sample. Demographic and health information was obtained from the medical record.

RESULTS: Mean 25OHD was 102 nmol/L (95% confidence interval (CI) = 98–106 nmol/L). Three percent of residents had a 25OHD concentration of less than 40 nmol/L, 6% <50 nmol/L, and 19% <75 nmol/L. In those who received 20,000 IU/wk or more for 6 months or longer (n = 147), mean 25OHD was 112 nmol/L (95% CI = 108–117 nmol/L), and none had a 25OHD level of less than 50 nmol/L. Hypercalcemia (>2.6 mmol/L), a potential consequence of too much vitamin D, was present in 14%, although 25OHD levels did not differ in those with and without hypercalcemia (108 vs 101 nmol/L; $P = .17$).

CONCLUSION: Twelve months after implementation of a 20,000-IU/wk vitamin D protocol for older adults in residential care, mean 25OHD concentrations were high, and there was no evidence of poor vitamin D status. Given the absence of demonstrated benefit of high 25OHD concentrations to the residential care population, dosages less than 20,000 IU/wk of vitamin D are recommended. **J Am Geriatr Soc 62:1546–1550, 2014.**

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Older adults in residential care facilities (providing 24-hour personal and nursing care) are at high risk of low vitamin D levels because of their comorbidities, limited ultraviolet light exposure, diminished cutaneous vitamin D production, and limited intake of vitamin D from food sources.[1–5] Vitamin D supplementation with or without calcium has been shown to reduce the rates of fracture and fall in elderly adults in many but not all studies.[6–8] In addition, adequate vitamin D levels as measured by serum 25 hydroxyvitamin D (25OHD) has been associated with lower risk of cardiovascular disease, some forms of cancer, viral infection, and certain autoimmune conditions.[9]

A recent report[10] from the Institute of Medicine indicated that a serum 25OHD level of 50 nmol/L (1 nmol/L = 0.4006 ng/mL) achieved through dietary intake or sunlight exposure would meet the needs of almost everyone in the population. For older adults (≥70), it was estimated that 800 IU day of vitamin D from dietary sources was needed to achieve this concentration, and this amount was set as the recommended dietary allowance (RDA). The serum 25OHD cutoff that the Institute of Medicine set was based solely on bone health outcomes because the evidence was insufficient to establish requirements based on other endpoints.[10] Nevertheless, others have suggested that 75 nmol/L or greater is optimal for all health outcomes.[11] Based on achieving this 75 nmol/L, the American Geriatrics Society Workgroup on Vitamin D Supplementation for Older Adults recently recommended that all older adults achieve an average vitamin D intake of 4,000 IU/d from all sources (diet and supplements).

Vitamin D supplementation in residential care is needed, but daily supplementation is problematic for reasons of polypharmacy, cost, and workload. To address these concerns, in 2011, Fraser Health (British Columbia, Canada) (a health authority that operates 14 residential care facilities (1,876 beds) and funds another 86 facilities (approximately 5,600 beds)) created and implemented a

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high-dose 20,000 IU week vitamin D protocol for all older adults (≥65) in residential care facilities. The protocol was developed based on a number of assumptions based on a review of vitamin D literature at the time and vitamin D expert consensus opinion.

- The majority of older adults in residential care facilities are vitamin D insufficient (25OH vitamin D levels <50 nmol/L).[12]
- The desired 25OH vitamin D level is between 75 and 100 nmol/L to address all potential benefits of vitamin D.[13]
- Vitamin D toxicity is rare even at high doses of vitamin D.[14–16]
- Weekly rather than daily vitamin D dosing would be more efficient and cost-effective within the residential care setting. The efficacy of higher-dose, less-frequent therapy has been demonstrated in controlled trials showing that it is safe and improves 25OHD concentration.[11]

Residents with known hypercalcemia or severe renal failure (glomerular filtration rate <20 mL/min) were excluded from the protocol. This dose exceeds the RDA (5,600 IU, expressed on a weekly basis) but is below the tolerable upper intake level (28,000 IU, expressed on a weekly basis).[5]

The effectiveness of this protocol in raising 25OHD concentration to values above 75 nmol/L in a residential care setting is unclear. Herein the 25OHD concentrations of a group of older adults living in residential care facilities 1 year after the commencement of the vitamin D protocol are reported. The determinants of 25OHD concentrations in this population such as age, sex, weight, and dose and duration of supplementation (which, despite the protocol, varied to some degree among participants) are also examined. Serum calcium becomes high in vitamin D toxicity, and this is a safety concern.[10] Accordingly, a secondary aim was to examine safety by determining whether the presence of hypercalcemia was associated with 25OHD concentration.

METHODS

Participants

Between November 2012 and February 2013, a convenience sample from five of the 14 residential care facilities that Fraser Health operates was recruited to participate. These five facilities house approximately half of the residents living in Fraser Health–operated residential care facilities. To be included, residents needed to be aged 65 and older and to have resided in the facility for longer than 3 months. Informed written consent was obtained from residents or their alternate decision-makers. Ethics approval was obtained from the Fraser Health and University of British Columbia clinical research ethics boards.

Data Collection Procedures

A research assistant (CM) obtained demographic and health information from the medical record on age; weight and height (used to calculate body mass index (BMI; kg/m^2)); ethnicity; smoking status; and supplement use, dose, route, and duration. A nonfasting blood sample was collected from each resident into an evacuated tube containing no anticoagulant. Serum was separated from whole blood, and samples were stored at −80°C. Serum 25OHD was determined at the School of Dietetics and Human Nutrition laboratory, McGill University (Montreal, Canada) using a chemiluminescence immunoassay (LIAISON 25-OH Vitamin D TOTAL Assay; DiaSorin, Stillwater, MN). This chemiluminescence immunoassay detects 25-hydroxyvitamin D2 and 25-hydroxyvitamin D3 metabolites.[17] The laboratory participates in the Vitamin D External Quality Assessment Scheme, an external quality control program for 25OHD measurement.[18] Accuracy for Level 1 (SRM 972 Lot 968e 17.7 ± 0.4 nmol/L) Standard Reference Material (National Institute of Standards and Technology, U.S. Department of Commerce, Washington, DC) was 97.0 ± 5.4% across seven assays with an interkit coefficient of variation (CV) of 5.8%. The interkit CV for the high (78.3–167 nmol/L) and low (20.0–53.0 nmol/L) kit controls were 7.2% and 6.9%, respectively. Interkit CV for two samples measured across four kits was 1.1% and 3.2%. Serum calcium and albumin were measured using a clinical chemistry analyzer (Ortho-Clinical Diagnostics VITROS 5600 System; Johnson & Johnson, New Brunswick, NJ) at British Columbia Children's Hospital.

Data Analyses

Statistical analyses were performed using SPSS Statistics 18.0 for Macintosh (SPSS Inc., Chicago, IL). The data were checked for normality using histograms. Mean 25OHD concentrations were calculated, and results were compared with three commonly used cutoffs for 25OHD (40,[10] 50,[10] and 75 nmol/L[11]). Forty nmol/L is analogous to the estimated average requirement and can be used to assess the prevalence of inadequacy in a population,[10,19] whereas 50 nmol/L is analogous to the RDA and is appropriate for clinicians monitoring vitamin D levels of individual residents. Serum calcium was corrected for serum albumin. Hypercalcemia was defined as more than 2.6 mmol/L and severe hypercalcemia as more than 3.0 mmol/L. Multiple regression analysis was used to examine the independent relationship between serum 25OHD concentration and potential determinants of vitamin D. An unpaired *t*-test was used to compare the mean 25OHD concentration of residents with and without hypercalcemia.

RESULTS

Of the 739 residents, 236 participated in the study. Of the 503 residents who did not participate, 329 were unable to consent, and their alternative decision-maker could not be contacted; 100 residents or their alternate decision-maker refused; 38 were younger than 65; 20 had been in the residential care facility for less than 3 months; and 16 were in palliative care.

Participant characteristics are given in Table 1. The mean ± SD age of the residents was 85 ± 8 (range 65–103) and the median length of stay was 20 months (interquartile range 10–38 months). Participants typically had a

Table 1. Characteristics of Residents in Fraser Health (British Columbia, Canada) Long-Term Care Facilities (LTCFs)

Characteristic	Participants, n = 236	Nonparticipant Residents from Same Five LTCFs, n = 503	Nonparticipant Residents from Other Nine LTCFs, n = 785[a]
Age, mean ± standard deviation	85.0 ± 7.7	84.9 ± 8.3	83.6 ± 8.4
Female, %	74.7	72.5	68.3
Diagnosis, %			
Dementia	44.3	56.8	50.9
Diabetes mellitus	20.9	19.8	21.1
Hypertension	47.7	47.4	42.9
Stroke	28.5	28.5	23.7
Chronic obstructive pulmonary disease	14.0	10.0	11.9

[a] LTCFs operated by Fraser Health Authority, British Columbia, Canada.

number of chronic diseases. There were few major differences between the study participants and other residents from the same facilities or other Fraser Health facilities. One notable exception was that the study included fewer participants with dementia than nonparticipating residents in the same facilities ($P = .002$).

The majority of the participants followed the protocol; 64% (n = 150) received 20,000 IU/wk, and an additional 17% (n = 39) received 20,000 IU/wk plus 400 IU of vitamin D per day from a multivitamin supplement for a total supplemental intake of 22,800 IU/wk. A small proportion received smaller doses for various reasons; 5% (n = 11) received 10,000 IU/wk, 8% (n = 18) received some other dose (8,400–16,800 IU/wk), and 8% (n = 18) did not receive a vitamin D supplement.

Mean overall 25OHD was 102 nmol/L (95% confidence interval (CI) = 98–106 nmol/L) (Table 2). Seven participants had a 25OHD level of less than 40 nmol/L, a concentration analogous to the estimated average requirement, indicating that the prevalence of inadequacy was less than 3% in this population. (None of these seven participants were taking a vitamin D supplement.) Six percent had a 25OHD concentration of less than 50 nmol/L, a concentration above which is suitable for 97.5% of individual requirements. Fewer than 20% had a 25OHD concentration of less than 75 nmol/L, a concentration that some recommend for optimal health. For those who had received at least 20,000 IU/wk for 6 months or longer, the mean concentration was 112 nmol/L (95% CI = 108–117 nmol/L), the lowest was 57 nmol/L, and the highest was 187 nmol/L. Fourteen percent of the participants (n = 32) had hypercalcemia, and fewer than 1% of these (n = 2) had severe hypercalcemia. Hypercalcemia was not associated with higher 25OHD concentrations (108 vs 101 nmol/L; $P = .17$).

In adjusted analysis (Table 3), smoking, being underweight (BMI <18.5 kg/m^2), taking any vitamin D supplement, and taking a supplement for longer than 6 months were associated with significantly higher 25OHD concentrations. For example, those who were underweight had a 25OHD approximately 20 nmol/L higher than those in other BMI categories.

Table 2. Serum 25 Hydroxyvitamin D, Albumin, and Calcium (Mean and by Cutoff) 1 Year After Commencement of a Protocol of 20,000 IU of Vitamin D per Week (N = 236)

Biochemical Indicator	Value
Serum 25 hydroxyvitamin D, nmol/L	
Mean (95% CI)	102 (98–106)
<40, n (%)	7 (3)
<50, n (%)	15 (6)
<75, n (%)	45 (19)
<100, n (%)	114 (48)
≥100, n (%)	122 (52)
Serum albumin, g/L, mean (95% CI)	36 (35–36)
Hypoalbuminemia (serum albumin <35 g/L), n (%)	96 (41)
Corrected serum calcium, mmol/L, mean (95% CI)[a]	2.47 (2.45–2.49)
Hypercalcemia (corrected serum calcium >2.6 mmol/L), n (%)	32 (14)
Severe hypercalcemia (corrected serum calcium >3.0 mmol/L), n (%)	2 (1)

[a] Calculated as [serum calcium + ((40–serum albumin) × 0.02)].
CI = confidence interval.

DISCUSSION

One year after commencement of a 20,000-IU of vitamin D per week protocol, vitamin D insufficiency was virtually nonexistent. The prevalence of inadequacy was very low in this population (<3%). None of those who had received at least the 20,000 IU/wk protocol for 6 months or more had a 25OHD below 50 nmol/L, an amount analogous to the RDA and thought to meet the needs of almost everyone in the population.[10] Eighty-one percent achieved 75 nmol/L, the lower end of the protocol target, but 52% exceeded the upper end of 100 nmol/L. Although hypercalcemia was present in some residents, it was not associated with serum 25OHD concentration, suggesting that the dose given was safe.

The mean 25OHD concentration in this study for residents who followed the protocol for 6 months was 112 nmol/L. This is similar to that reported previously[20] in residents in an Edmonton nursing home who had a mean 25OHD concentration of 120 nmol/L despite taking a lower dose of 2,000 IU/d (14,000 IU/wk). The mean

Table 3. Serum 25 Hydroxyvitamin D According to Selected Participant Characteristics in Unadjusted (Mean) and Adjusted (β) Models 1 Year After Starting a Protocol of 20,000 IU of Vitamin D per Week (N = 236)

		25 Hydroxyvitamin D Concentration, nmol/L			
Characteristic	n (%)[a]	Mean (95% CI)	*P*-Value	β (95% CI)	*P*-Value
Age (per 1-year increase)				0.2 (−0.5–0.7)	.67
Sex					
Female	176 (75)	103 (98–108)	.24	Reference	.49
Male	60 (25)	98 (90–106)		−1 (−9–7)	
Ethnicity					
Nonwhite	20 (9)	90 (76–103)	.09	Reference	.12
White	216 (91)	103 (99–107)		10 (−3–22)	
Smoker					
No	225 (95)	101 (97–105)	.12	Reference	.04
Yes	11 (5)	116 (97–135)		18 (−1–34)	
Body mass index, kg/m^2					
<18.5 (underweight)	23 (10)	121 (106–135)		Reference	
18.5–24.9 (normal)	110 (47)	102 (96–107)	.009	−3 (−13–7)	.56
25.0–29.9 (overweight)	63 (27)	100 (92–108)	.008	−2 (−12–9)	.75
≥30.0 (obese)	40 (17)	93 (83–103)	.001	−21 (−35 to −6)	.01
Vitamin D supplement					
No	18 (8)	43 (35–51)	<.001	Reference	<.001
Yes	218 (92)	107 (103–110)		61 (48–74)	
Supplement duration >6 months[b]					
No	49 (22)	97 (90–104)	.005	Reference	.01
Yes	169 (78)	109 (105–114)		11 (2–20)	

[a] May not sum to 100% because of rounding.

[b] Eighteen nonsupplement users were excluded, n = 218.

CI = confidence interval.

25OHD concentration in the current study is consistent, albeit on the high side, with that predicted from controlled trials of vitamin D supplements and 25OHD.[21] Other than supplement use and duration, only BMI and smoking were independent significant predictors of 25OHD. Surprisingly, smokers had higher 25OHD concentrations than nonsmokers; most studies have shown the opposite.[22] Smoking is not permitted inside public places in British Columbia, so the higher 25OHD may be related to sunlight exposure while smoking outdoors. A number of studies have shown lower 25OHD concentrations in obese individuals than in those in other BMI categories.[23] In the current study, being underweight was associated with higher 25OHD concentrations than in all other categories. The amount of vitamin D would have been greater on a per-kg basis in underweight individuals, but this did not appear to extend to the other BMI categories.

A question arising from the findings is whether high 25OHD concentrations (52% >100 nmol/L) are desirable or potentially harmful, even in absence of hypercalcemia. Many prospective studies show evidence of reductions in mortality as serum 25OHD concentrations increase above the deficiency state. For example, a meta-analysis[24] of prospective cohort studies of serum 25OHD and all-cause and disease-specific mortality found that, compared with serum values of approximately 27.5 nmol/L, the summary relative risk of mortality was 0.86 (95% CI = 0.82–0.91) for those with 25OHD levels of approximately 40 nmol/L, 0.77 (95% CI = 0.70–0.84) for those with levels of 50 nmol/L, and 0.69 (95% CI = 0.50–0.78) for those with levels of 75 nmol/L. There was no evidence of further reductions in mortality at higher serum values, and although few studies included large numbers of subjects with very high values, mortality tended to increase as serum 25OHD increased above approximately 80 nmol/L. Observational studies have subsequently reported evidence of greater mortality at serum 25OHD levels of greater than 50 to 60 nmol/L[25] or greater than 50 to 90 nmol/L.[26] Although randomized trials are needed to demonstrate causality, collectively, these studies suggest that high 25OHD concentrations are not beneficial and could have adverse effects. The relevance of this in residential care residents needs to be established.

LIMITATIONS

This study had a number of limitations. Because of its cross-sectional nature, what residents' 25OHD concentrations were before supplementation is unknown. Information about supplementation before admission was not available. Older people may be entering residential care with higher 25OHD concentrations than expected. Health Canada recommends that people aged 50 and older take a vitamin D supplement, and a recent survey shows that 60% of older British Columbians take a vitamin D–containing supplement.[27] Ideally, all residents would be screened for 25OHD vitamin D within the first few months of entering residential care and possibly every 6 months until stable, with supplementation prescribed only if their 25OHD was low, but British Columbia's publicly funded healthcare system does not pay for routine 25OHD primarily because of cost. In addition, the American Geriatrics

Society Workgroup on Vitamin D stated that routine measurement of 25OHD is not necessary before starting supplementation.

A second limitation of the study is that only whether the participant was prescribed and given vitamin D, not whether it was taken, was recorded. Third, subjects were not fasting, which may explain some of the hypercalcemia seen in the study. Fourth, 25OHD was measured at one time of the year, and there is known to be seasonal variation in 25OHD concentrations, although this effect would be expected to be minimal in a residential care setting. Finally, it cannot be assumed that the sample was representative of the older adults living in residential care facilities in Canada, although the mean age of the participants was 85, and 75% were female, consistent with older adults living in residential care in Fraser Health and Canada.[28]

In conclusion, the Fraser Health Protocol of giving 20,000 IU of vitamin D weekly to older adults living in residential care facilities is feasible and safe and appears to have virtually eliminated vitamin D insufficiency. Serum 25OHD concentrations were higher than expected, with more than half the residents surveyed having a 25OHD concentration greater than 100 nmol/L. With no proven benefit of high 25OHD concentrations in the residential care population, lower dosages of weekly vitamin D or enhanced vitamin D intakes through fortified or bioenriched foods would be recommended. A study is needed to determine the 25OHD concentration of older adults entering residential care to better inform the need for supplementation.

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