A system for improving vitamin D nutrition in residential care

Alison ER Wigg, Caroline Prest, Peter Slobodian, Allan G Need and Leslie G Cleland

ABSTRACT

Objective: To assess the feasibility of administering an inexpensive preparation of vitamin D_3 100 000 IU orally 3 monthly to aged-care residents.

Design: Prospective, controlled open-label implementation trial.

Setting: Residential aged care, November 2003 to May 2004 (primary study).

Participants: 137 ambulant residents: 107 treated (mean age, 85 years; 79 were women), 30 untreated controls (mean age, 87 years; 22 were women).

Interventions: Lactose microencapsulated vitamin D_3 100 000 IU orally at baseline, then 3 monthly (three or more doses); untreated subjects were observed contemporaneously.

Main outcome measures: Serum levels of 25-hydroxyvitamin D [25(OH)D] at 6 months compared with baseline; acceptability of the program to residents and staff.

Results: At baseline, 95% of residents assessed ($n = 137$) had serum 25(OH)D levels below the desirable range of 60–160 nmol/L. At 6 months, all treated residents ($n = 98$) achieved desired levels, with the mean (± SD) 25(OH)D level increasing from 36.4 ± 12.6 nmol/L (range, 12–75 nmol/L) at baseline to 124.0 ± 27.9 nmol/L (range, 68–244 nmol/L). In no resident did 25(OH)D approach toxic levels. The mean serum 25(OH)D level remained low in the control group ($n = 27$): 42.8 ± 18.3 nmol/L (range, 18–98 nmol/L). The difference between the mean 25(OH)D levels of treatment and control groups at 6 months was 81.2 nmol/L (95% CI, 69.7–92.0 nmol/L). The cost of the supplement was $4 per resident per annum. Substudies showed mean trough serum 25(OH)D levels in the desired range at 3 months ($n = 31$), but below the desired range at 6 months ($n = 50$). Subjects given 3-monthly doses for up to 2 years maintained serum 25(OH)D levels within the desired range, with no trend toward undesirable accumulation ($n = 11$).

Conclusions: Vitamin D_3 100 000 IU given orally 3 monthly is a practical, safe, effective and inexpensive way to meet the vitamin D_3 requirements of aged-care residents.

MJA 2006; 185: 195–198

The high prevalence of vitamin D insufficiency among aged-care residents is well documented.[1-3] Contributing factors include lack of exposure to sunlight,[3] poor conversion in aged skin of pre-vitamin D_3 to vitamin D_3,[4] and a paucity of vitamin D-rich dietary items. The undesirable effects of vitamin D deficiency include reduced bone mineral density,[5] high bone turnover,[6,7] and an increased risk of falls and fracture.[3,8,9] Supplementation with vitamin D, its derivatives, or a combination of vitamin D and calcium increases bone mineral density,[10,11] reduces the risk of hip and other fragility fractures,[12-15] improves muscle function, and reduces falls among aged-care residents.[3,16,17]

Despite a clear definition of unmet needs and the availability of solutions, little has been achieved with regard to systematic, broad-scale approaches to vitamin D nutrition in aged care. A policy-based approach within aged-care facilities, subject to medical consent to exclude those with contraindications, should eliminate the vagaries of reliance on individual prescriptions. Such an approach requires an intervention that is inexpensive in terms of both materials and staff inputs.

Our study was designed to determine the feasibility of a program of administering an inexpensive preparation of high-dose vitamin D_3 quarterly within a residential care setting. We used a similar regimen to that of Trivedi and coworkers[14] who found that 4-monthly oral supplementation with 100 000 IU vitamin D_3 given over 5 years reduced fractures in community-dwelling men and women aged over 65 years.

METHODS

Subjects

With approval from the Research Ethics Committee of the Royal Adelaide Hospital, residents were recruited at multiple facilities of three aged-care organisations in South Australia, designated A, B, and C. Managers at all participating facilities were provided with a 1-hour information session, and vitamin D fact sheets and protocols. Written informed consent was obtained from residents (or their next of kin) and their general practitioner. Residents were excluded if they suffered from severe dementia or a progressive illness limiting life expectancy, if they were already taking vitamin D supplements, or if there was a contraindication as assessed by their GP (eg, known hypercalcaemia, renal calculi, sarcoidosis, disseminated malignancy). Consenting residents were allocated to the treatment or control group at each facility sequentially on a 3 to 1 (treatment to control) basis by a research nurse. Facilities were visited in order of geographical convenience. The untreated control group allowed monitoring of possible seasonal variations in dietary intake or sunlight exposure. Treated subjects received vitamin D_3 100 000 IU 3 monthly.

Vitamin D_3 preparation

The vitamin D_3 preparation used was Duphasol D3-100 dry stable CWD PhEur (Solvay Pharmaceuticals, The Netherlands). It was purchased in bulk from Fernz Specialty Chemicals, Villawood, NSW. The product is essentially tasteless, has an acacia gum matrix, a lactose coating, and is water soluble. Individual doses of 1 g containing 100 000 IU vitamin D_3 were prepared and packaged in small glass bottles in the Royal Adelaide Hospital pharmacy. At the aged-care facilities, the dose was mixed with water, juice or milk, depending on the resident's preference, and administered orally under nursing supervision during routine drug rounds.

Primary study

All participants had blood taken for measurement of serum 25-hydroxyvitamin D [25(OH)D] level at baseline (November 2003) and at 6 months (May 2004). The latter were taken 1 week after the third dose, and in the same week for the controls.

Substudies

Additional samples were taken from treated subjects for several substudies.

Substudy 1 (3-month trough level): Blood from a convenience sample of about 10 residents from each of the three organisations was taken 1 week before the third

(6-month) dose to determine whether 25(OH)D levels were maintained during a 3-month dosing interval.

Substudy 2 (supplementation for 6 months, no supplementation for 6 months): Subjects from residential care organisations B and C who had discontinued vitamin D_3 after the third (6-month) dose were tested at 12 months to determine the extent to which serum 25(OH)D level declined during a 6-month dosing interval.

Substudy 3a (continuous supplementation for 12 months) and **Substudy 3b** (continuous supplementation for 24 months): One residential care organisation (A) continued vitamin D_3 supplementation after the 6-month primary study was completed. Residents received 100 000 IU vitamin D_3 every 3 months for up to 2 years, with testing at 12 and 24 months. This substudy determined whether ongoing 3-monthly dosing achieved stable serum 25(OH)D values without undesirable accumulation.

Primary outcome measure: 25(OH)D assay

25(OH)D level was measured by radioimmunoassay (IDS Ltd, Bolden, Tyne and Wear, UK) at the Institute of Medical and Veterinary Science (IMVS) Clinical Chemistry Laboratory by assessors who were blinded to the subjects' group allocation. The assay is standardised against 25(OH)D_3 but has 75% cross-reactivity with 25(OH)D_2. The coefficient of variance at 30 nmol/L is 8.6% and at 120 nmol/L is 9.7%

Secondary outcome measure: consumer surveys

The acceptability of the program to residents and staff was evaluated at 6 months by surveys that were completed by all treated residents (or a nurse on their behalf) and by a staff representative from each facility.

Statistical analyses

Variables were assessed using paired and unpaired *t* tests. Data are presented as mean ± SD (range) with lower and upper 95% confidence intervals for means and differences between means.

RESULTS

Primary study

A total of 137 residents (107 treated, 30 control) from 11 facilities participated in the study (three facilities from Organisation A, and four each from B and C). Participants' demographic characteristics are summarised in Box 1. At 6 months, 10 residents had died (seven treatment, three control), one subject from the treatment group was not in residence due to hospitalisation, and difficulties with venous access precluded blood testing in another.

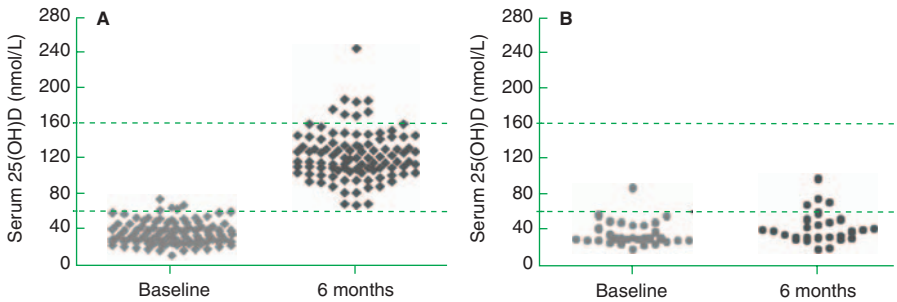
Baseline and 6-month serum 25(OH)D levels are shown in Box 1 and Box 2. The desirable range for serum 25(OH)D level, as defined by the IMVS laboratory, is 60–160 nmol/L. At baseline, the means of the control and treatment groups were similar. Combined, these groups yielded a baseline mean ± SD of 36.4 ± 12.7 nmol/L (range, 12–87 nmol/L; 95% CI of the mean, 34.2–38.5 nmol/L, with 130/137 (95%) residents being below the desirable range (< 60 nmol/L). According to Vieth's classification,[18] vitamin D deficiency was mild (25–49 nmol/L) in 98 (72%) subjects, moderate (12.5–24 nmol/L) in 17 (12%), and severe (< 12.5 nmol/L) in one subject (0.7%).

At 6 months, after the third dose of vitamin D_3, mean serum 25(OH)D level for the treatment group had risen significantly ($P < 0.0001$; paired *t* test) with a change of mean from baseline of 87.6 nmol/L (95% CI, 81.5–92.1 nmol/L). At the same time, there was a small but statistically significant rise in serum 25(OH)D level in the control group ($P < 0.02$, paired *t* test), with a change of mean from baseline of 6.4 nmol/L (95% CI, 1.23–10.6 nmol/L). The difference between the means of the treatment and control groups at 6 months (81.2 nmol/L; 95% CI, 69.7–92.0 nmol/L) was highly significant ($P < 0.001$, unpaired *t* test). In the treatment group, the number of residents with serum 25(OH)D levels within the desirable range increased from 6 (6%) to 98 (100%). No resident was classified as deficient, and none had any adverse effects associated with dosing. The serum 25(OH)D level for one resident was 244 nmol/L — higher than the upper boundary of the desirable range, but

1 Characteristics of the aged-care residents in the primary study, and serum 25-hydroxyvitamin D [25(OH)D] levels at baseline and at 6 months

	Treatment group	Control group
Baseline		
Number of residents	107	30
Mean age ± SD (range), years	85 ± 6.1 (68–99)	87 ± 5.4 (74–97)
Number (%) of women	79 (74%)	22 (73%)
Number (%) of low-care residents	90 (84%)	26 (87%)
Mean 25(OH)D ± SD (range) nmol/L	36.4 ± 12.6 (12–75)	36.4 ± 13.6 (19–87)
95% CI of mean	34.0–38.8	31.3–41.5
Six months (three doses)		
Number of residents	98	27
Mean 25(OH)D ± SD (range) nmol/L	124.0 ± 27.9 (68–244)	42.8 ± 18.3 (18–98)
95% CI of mean	118.1–129.2	35.6–50.0
Percentage change in 25(OH)D levels	+ 241%	+ 17%

2 Serum 25-hydroxyvitamin D [25(OH)D] level at baseline and at 6 months — A: treatment group; B: control group



Dotted lines define the desired range for 25(OH)D.

3 Substudy 1: 3-month trough level of 25-hydroxyvitamin D [25(OH)D] ($n = 31$)

	25(OH)D level (nmol/L)		
	At baseline	At 6 months before 3rd dose*	At 6 months after 3rd dose†
Mean ± SD	36.4 ± 10.4	86.4 ± 16.9	114.1 ± 25.4
Range	24–68	60–137	69–175
95% CI of mean	32.6–40.2	80.2–92.7	105–123

* Blood for this "trough" level was taken 3 months after the preceding (2nd) dose. † Blood taken 1 week after 3rd dose. ◆

4 Substudy 2: 25-hydroxyvitamin D [25(OH)D] level — supplementation for 6 months, no supplementation for 6 months ($n = 50$)

	25(OH)D level (nmol/L)		
	At baseline	At 6 months (3 doses)	At 12 months (3 doses)
Mean ± SD	35.7 ± 11.0	115 ± 22.9	54.2 ± 11.7
Range	12–61	68–183	27–80
95% CI of mean	32.5–38.8	108–121	50.9–57.6

well below toxic levels (> 690 nmol/L).[19] In the control group, the number of residents with serum 25(OH)D levels within the desired range increased from one (3%) to four (15%). According to Vieth's criteria,[18] mild vitamin D deficiency persisted in 18 (67%) and moderate deficiency in two (7%) of these untreated residents.

Substudies

The results of the substudies are summarised in Box 3, Box 4, and Box 5.

Substudy 1: All of the 31 residents who had 3-month trough levels of 25(OH)D analysed had values in the desired range (Box 3).

Substudy 2: Of 28 subjects treated at Organisation B, 25 survived to 6 months when vitamin D supplementation was discontinued. Of these, 18 had blood samples taken at 12 months (three had died, three refused further blood testing and another was too ill). Of the 44 subjects treated at Organisation C, 40 survived to 6 months when vitamin D supplementation was discontinued. Of these, 32 had blood samples taken at 12 months (three had died, three refused further testing and two were no longer in residence). In these 50 subjects, the mean serum 25(OH)D level at 12 months was below the desirable range (Box 4).

Substudy 3a and 3b: Of 35 subjects starting treatment at Organisation A (which continued the 3-monthly vitamin D supplementation beyond 6 months), 33 survived to 6 months and 31 survived to 12 months. Of these, eight who had been in substudy 1 chose not to submit to further blood testing and another eight had ceased the regular supplement, leaving 15 available for testing at 12 months (Box 5). At 2 years, of these 15 subjects, two had died, one had been discharged and another was too agitated to provide a blood sample. This left 11 treated subjects. The mean serum 25(OH)D level was within the desired range, with no trend towards undesirable accumulation at both 12 and 24 months (Box 5).

Consumer surveys

There was a 100% response rate to the surveys. Ninety-nine residents and 13 staff members (at least one from each facility) completed the surveys. All but one resident found the taste of the vitamin D_3 solution acceptable. All stated the vitamin D_3 solution was easy to drink and indicated a willingness to continue the regimen. All staff were satisfied with the information provided and displayed an accurate understanding of why residents were receiving the vitamin D_3 supplement. All stated dosing administration could easily be incorporated into routine drug rounds on a facility-wide basis. Staff members were unanimous in their perception that residents, other facility staff and GPs would accept the program and support its continuation.

DISCUSSION

Our study confirms that vitamin D insufficiency is highly prevalent among aged-care residents in southern Australia, and vitamin D_3 100 000 IU, given 3 monthly, safely increases levels of serum 25(OH)D to the desired range. The substudies suggest that with ongoing supplementation, this effect can be maintained over a 2-year period and that a 3-monthly, but not 6-monthly, dose interval is sufficiently frequent. Observations in the untreated group indicate that, without vitamin D supplementation, serum 25(OH)D level remains undesirably low.

The case of the single resident who had an increase in 25(OH)D at 6 months to above the target range (244 nmol/L) is informative. This woman was 87 years old and had a body mass index of only 16.9 kg/m^2. Unknown to the investigators, she had been given a high-energy alimentary preparation after the study was underway, which contained vitamin D_3 equivalent to an additional 400 IU per day. Although a second blood test 1 month later showed 25(OH)D levels had fallen to an acceptable level (168 nmol/L), this experience shows the potential for vitamin D supplements given concurrently to increase serum 25(OH)D level to beyond the target range. Individuals with low adipose mass may be especially prone to this effect.

5 Substudy 3a and 3b: 25-hydroxyvitamin D [25(OH)D] level (nmol/L) after 12 and 24 months of continuous supplementation

	25(OH)D level (nmol/L)						
	3a: Supplementation for 12 months ($n = 15$)			3b: Supplementation for 24 months ($n = 11$)			
	At baseline	At 6 months (3 doses)	At 12 months (5 doses)	At baseline	At 6 months (3 doses)	At 12 months (5 doses)	At 24 months (9 doses)
Mean ± SD	39.5 ± 11.9	138 ± 22.2	110 ± 16.9	41.6 ± 12.4	141 ± 24.7	110 ± 19.7	114 ± 15.3
Range	22–63	98–186	84–150	24–63	98–186	84–150	81–131
95% CI of mean	35.1–44.0	129–146	103–116	33.2–50	125–158	97.0–123	104–125

Our study assessed the feasibility of implementing a low-cost, institutionally based approach to vitamin D nutrition in aged-care residents, with avoidance of inappropriate administration. Nursing staff were able to accommodate the quarterly dosing readily into work flows. With the exception of the resident described above, no problems with vitamin D_3 supplementation were encountered.

An advantage of the approach described is its low cost, $1 per dose or $4 per resident per year. The cost of a retail product containing an equivalent dose of vitamin D_3 (capsules of 1000 IU vitamin D_3 for daily ingestion) is about $50 per annum. With the latter, there would be additional staff costs for daily administration of tablets or capsules. The Royal Adelaide Hospital supplement is inexpensive enough for the aged-care facilities to be willing to meet the cost, making the program potentially cost neutral for health service authorities, and could be a requirement of nursing home accreditation. A wider scale implementation program in up to 2000 residents has commenced at the participating organisations. While falls and fracture endpoints were not measured in our study, retrospective and prospective falls and fracture data will be collected in this larger study to evaluate the effect of a broader scale intervention on these endpoints.

A potential criticism of our study is lack of randomisation and concealment of subject allocation in the primary study and substudy 1. However, in studying the effectiveness of a policy-based approach, it is hard to envisage how resulting biases could have confounded, in an important way, the objective primary outcome measure — serum 25(OH)D level — as the laboratory technicians were blinded to treatment allocation. Furthermore, the subjects were not themselves responsible for the vitamin D_3 administration.

Another potential criticism is the lack of co-supplementation with calcium. Based on the article by Chapuy et al[12] and the interdependence of vitamin D and calcium metabolism, it can be argued that vitamin D_3 should only be given with calcium, preferably in the same preparation. In support of combination formulations, it has been suggested that the serum 25(OH)D assay can be used as a surrogate for compliance with co-administered calcium. However, several factors need to be considered — the very different periodicity of dosing for vitamin D and calcium, differences in tolerance, and direct and indirect costs. Dosing frequency can be quarterly or less for vitamin D_3, but calcium needs to be given daily, implying greater nursing demands.

We have shown that 3-monthly vitamin D_3 is well tolerated. In contrast, inability to swallow large capsules and constipation are frequent, treatment-limiting effects of calcium supplementation. Indeed, lack of tolerance for the calcium component of combined vitamin D and calcium regimens has been invoked to explain the failure of recent community-based studies to show benefits from long-term supplementation with vitamin D with calcium.[20] These studies contrast with the positive effect on fracture risk in the long-term community-based study of Trivedi et al,[14] in which vitamin D_3 was given without calcium. Our study shows that this inexpensive approach is also appropriate in residential aged-care.

In conclusion, vitamin D_3 100 000 IU given orally 3 monthly is a practical, safe, effective and inexpensive way to meet vitamin D_3 requirements of aged-care residents.

ACKNOWLEDGEMENTS

The study was supported by funding from the Australian Government Department of Health and Ageing through a National Arthritis and Musculoskeletal Conditions Improvements Grant. We would also like to acknowledge the generous support of staff and residents of Helping Hand Aged Care, Resthaven Incorporated and the Aged Care and Housing Group in South Australia.

COMPETING INTERESTS

None identified.

AUTHOR DETAILS

Alison E R Wigg, BAppScPhysio, MAppScPhysio, MBA, Preventive Program Manager, Rheumatology Unit[1]
Caroline Prest, RN, Research Nurse, Rheumatology Unit[1]
Peter Slobodian, BPharm, MClinPharm, Specialist Pharmacist, Pharmacy Department[1]
Allan G Need, MD, FRACP, FRCPA, Head, Clinical Biochemistry,[2] Clinical Associate Professor[3]
Leslie G Cleland, MD, FRACP, Director, Rheumatology Unit,[1] Clinical Professor[3]
1 Royal Adelaide Hospital, Adelaide, SA.
2 Institute of Medical and Veterinary Science, Adelaide, SA.
3 Department of Medicine, University of Adelaide, Adelaide, SA.
Correspondence: Lcleland@mail.rah.sa.gov.au

REFERENCES

1 Morris HA, Morrison GW, Burr M, et al. Vitamin D and femoral neck fractures in elderly South Australian women. *Med J Aust* 1984; 140: 519-521.
2 Sambrook PN, Cameron ID, Cumming RG, et al. Vitamin D deficiency is common in frail institutionalised older people in northern Sydney [letter]. *Med J Aust* 2002; 176: 560.
3 Flicker L, Mead K, MacInnis RJ, et al. Serum vitamin D and falls in older women in residential care in Australia. *J Am Geriatr Soc* 2003; 51: 1533-1538.
4 MacLaughlin J, Holick MF. Aging decreases the capacity of human skin to produce vitamin D3. *J Clin Invest* 1985; 76: 1536-1538.
5 Outila TA, Karkkainen MU, Lamberg-Allardt CJ. Vitamin D status affects serum parathyroid hormone concentrations during winter in female adolescents: associations with forearm bone mineral density. *Am J Clin Nutr* 2001; 74: 206-210.
6 Kipen E, Helme RD, Wark JD, et al. Bone density, vitamin D nutrition, and parathyroid hormone levels in women with dementia. *J Am Geriatr Soc* 1995; 43: 1088-1091.
7 Jesudason D, Need AG, Horowitz M, Flicker L. Relationship between serum 25-hydroxyvitamin D and bone resorption markers in vitamin D insufficiency. *Bone* 2002; 31: 626-630.
8 Diamond T, Smerdely P, Kormas N, et al. Hip fracture in elderly men: the importance of subclinical vitamin D deficiency and hypogonadism. *Med J Aust* 1998; 169: 138-141.
9 Weatherall M. A meta-analysis of 25 hydroxyvitamin D in older people with fracture of the proximal femur. *N Z Med J* 2000; 113: 137-140.
10 Parfitt A. Osteomalacia and related disorders. In: Avioli LV, Krane SM, editors. Metabolic bone disease and clinically related disorders. Philadelphia: WB Saunders Company, 1990: 329-396.
11 Mithal A, Sen I, Naik V, et al. Spectacular recovery of bone mineral density following treatment of osteomalacia [abstract]. *J Bone Miner Res* 2000; 15: S577.
12 Chapuy M, Arlot M, Duboeuf F, et al. Vitamin D_3 and calcium to prevent hip fractures in elderly women. *N Engl J Med* 1992; 327: 1637-1642.
13 Heikinheimo RJ, Inkovaara JA, Harju EJ, et al. Annual injection of vitamin D and fractures of aged bones. *Calcif Tissue Int* 1992; 51: 105-110.
14 Trivedi DP, Doll R, Khaw KT. Effect of four monthly oral vitamin D_3 (cholecalciferol) supplementation on fractures and mortality in men and women living in the community: randomised double blind controlled trial. *BMJ* 2003; 326: 469-472.
15 Bischoff-Ferrari HA, Willett WC, Wong JB, et al. Fracture prevention with vitamin D supplementation: a meta-analysis of randomized controlled trials. *JAMA* 2005; 293: 2257-2264.
16 Bischoff HA, Stahelin HB, Dick W, et al. Effects of vitamin D and calcium supplementation on falls: a randomized controlled trial. *J Bone Miner Res* 2003; 18: 343-351.
17 Bischoff-Ferrari HA, Dawson-Hughes B, Willett WC, et al. Effect of vitamin D on falls: a meta-analysis. *JAMA* 2004; 291: 1999-2006.
18 Vieth R. Vitamin D supplementation, 25-hydroxyvitamin D concentrations, and safety. *Am J Clin Nutr* 1999; 69: 842-856.
19 Mason RS, Posen S. The relevance of 25-hydroxycalciferol measurements in the treatment of hypoparathyroidism. *Clin Endocrinol (Oxf)* 1979; 10: 265-269.
20 Grant AM, Avenell A, Campbell MK, et al. Oral vitamin D_3 and calcium for secondary prevention of low-trauma fractures in elderly people (Randomised Evaluation of Calcium OR vitamin D, RECORD): a randomised placebo-controlled trial. *Lancet* 2005; 365: 1621-1628.

(Received 11 Jan 2006, accepted 28 Jun 2006) ❑