A system for improving vitamin D nutrition in residential care

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

Objective: To assess the feasibility of administering an inexpensive preparation of vitamin D3 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 D3 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 D3 100 000 IU given orally 3 monthly is a practical, safe, effective and inexpensive way to meet the vitamin D3 requirements of aged-care residents.

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 D3 100 000 IU 3 monthly.

Vitamin D3 preparation

The vitamin D3 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 D3 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 who 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
vitamin D3 supplementation after the 6-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 D3 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 D3 supplementation after the 6-month primary study was completed. Residents received 100 000 IU vitamin D3 every month primary study was completed. Residents received 100 000 IU vitamin D3 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)D3, but has 75% cross-reactivity with 25(OH)D2. 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.

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 of 34.2–38.5 nmol/L, with 130/137 (95%) residents being below the desirable range (< 60 nmol/L).

According to VIETH's classification, 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 D3, 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, 69.7–92.1 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
well below toxic levels (>690 nmol/L).

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 contributed 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 (106 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.

### DISCUSSION

---

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

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

* 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)**

<table>
<thead>
<tr>
<th>25(OH)D level (nmol/L)</th>
<th>At baseline</th>
<th>At 6 months (3 doses)</th>
<th>At 12 months (9 doses)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean±SD</td>
<td>35.7±11.0</td>
<td>115±22.9</td>
<td>54.2±11.7</td>
</tr>
<tr>
<td>Range</td>
<td>12–61</td>
<td>68–183</td>
<td>27–80</td>
</tr>
<tr>
<td>95% CI of mean</td>
<td>32.5–38.8</td>
<td>108–121</td>
<td>50.9–57.6</td>
</tr>
</tbody>
</table>

---

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

**3a: Supplementation for 12 months (n = 15)**

<table>
<thead>
<tr>
<th>25(OH)D level (nmol/L)</th>
<th>At baseline</th>
<th>At 6 months (3 doses)</th>
<th>At 12 months (5 doses)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean±SD</td>
<td>39.5±11.9</td>
<td>138±22.2</td>
<td>110±16.9</td>
</tr>
<tr>
<td>Range</td>
<td>22–63</td>
<td>98–186</td>
<td>84–150</td>
</tr>
<tr>
<td>95% CI of mean</td>
<td>35.1–44.0</td>
<td>129–146</td>
<td>103–116</td>
</tr>
</tbody>
</table>

**3b: Supplementation for 24 months (n = 11)**

<table>
<thead>
<tr>
<th>25(OH)D level (nmol/L)</th>
<th>At baseline</th>
<th>At 6 months (3 doses)</th>
<th>At 12 months (5 doses)</th>
<th>At 24 months (9 doses)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean±SD</td>
<td>41.6±12.4</td>
<td>141±24.7</td>
<td>110±19.7</td>
<td>114±15.3</td>
</tr>
<tr>
<td>Range</td>
<td>24–63</td>
<td>98–186</td>
<td>84–150</td>
<td>81–131</td>
</tr>
<tr>
<td>95% CI of mean</td>
<td>33.2–50</td>
<td>125–158</td>
<td>97.0–123</td>
<td>104–125</td>
</tr>
</tbody>
</table>

---

**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 were satisfied with the information provided towards undesirable accumulation at both 12 and 24 months (Box 5).

---

**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 (three had died, three refused further testing 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).

**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).

---

**MJA • Volume 185 Number 4 • 21 August 2006**
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 D₃ 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 D₃ (capsules of 1000 IU vitamin D₃ 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 sub-study 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 D₃ 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 D₃ 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 D₃, but calcium needs to be given daily, implying greater nursing demands.

We have shown that 3-monthly vitamin D₃ 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.¹⁰ These studies contrast with the positive effect on fracture risk in the long-term community-based study of Trivedi et al.¹¹ in which vitamin D₃ was given without calcium. Our study shows that this inexpensive approach is also appropriate in residential aged-care.

In conclusion, vitamin D₃ 100 000 IU given orally 3 monthly is a practical, safe, effective and inexpensive way to meet vitamin D₃ 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, MAAppScPhysio, MBA, Preventive Program Manager, Rheumatology Unit¹
Caroline Prest, RN, Research Nurse, Rheumatology Unit¹
Peter Slobodian, BPharm, MCLinPharm, Specialist Pharmacist, Pharmacy Department¹
Allan G Need, MD, FRACP, FRCPA, Head, Clinical Biochemistry,² Clinical Associate Professor¹
Leslie G Cleland, MD, FRACP, Director, Rheumatology Unit¹, Clinical Professor¹
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

(Received 11 Jan 2006, accepted 28 Jun 2006)