Hypovitaminosis D and elevated serum alkaline phosphatase in elderly Irish people

Malachi J McKenna, MB, MRCPI, Rosemarie Freaney, MSc, PhD, Aiden Meade, MB, and Francis P Muldowney MD, FRCP

ABSTRACT The vitamin D status of 181 elderly Irish community-dwelling and institutionalized subjects was studied during Winter-Spring. The mean serum 25-hydroxyvitamin D level was 10 nmol/L (95% range < 5.0–59 nmol/L); values were below 25 nmol/L in 79 percent of subjects. A significant seasonal variation of serum 25-hydroxyvitamin D levels was noted in elderly community-dwelling subjects. The previously documented age-related increase in serum alkaline phosphatase activity was significantly less in vitamin D replete subjects than in vitamin D deplete subjects in this study (P < 0.005). The higher serum alkaline phosphatase values found in the vitamin D deplete subjects may represent mild secondary hyperparathyroidism or osteomalacia. The relationship of vitamin D status to both dietary intake and effective sunlight (latitude) is examined. Am J Clin Nutr 1985;101:101-109.

KEY WORDS Elderly, hypovitaminosis D, vitamin D-related alkaline phosphatase activity, diet, solar irradiation

Introduction

Vitamin D is derived from an endogenous source (skin) and an exogenous source (diet). Production of the vitamin by the action of sunlight on skin is now considered to be the most important source in young adults (1). Diet as a source of the vitamin is more important in the elderly population, because they are more likely to be housebound and have less sunlight exposure (2).

The advent of assays for vitamin D metabolites in serum, made possible the study of vitamin D status in elderly populations. Initial reports from the United Kingdom by Preece et al (3) and Corless et al (4), showed that low serum 25-hydroxyvitamin D (25-OHD) levels commonly occurred in elderly people. Subsequent studies from other countries with a temperate climate showed a similar pattern of hypovitaminosis D (5–15). However, this privational state was less frequently observed in countries where solar irradiation is intense and/or vitamin D intake is substantial (16–23). Parfitt et al (24) reviewing vitamin D and bone health in elderly people, suggested that more studies are required to evaluate the extent of vitamin D deficiency in aged populations.

A preliminary study of sick elderly Irish people demonstrated a high prevalence of hypovitaminosis D (25). This paper expands studies documenting the presence of vitamin D deficiency across a broad cross-section of the elderly Irish population. Comparison of results from this and other series are made, and the correlation of vitamin D intake and effective sunshine exposure (latitude of coun-

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try) with serum 25(OH)D levels is demonstrated.

Materials and methods

One hundred and eighty-one elderly people were studied during Winter/Spring over a two year period (Table 1). The following groups were studied:

1. Healthy elderly people. This group consisted of 30 subjects with ages ranging from 61 to 78 years. Fourteen subjects were chosen at random from a practitioner’s list, and 16 subjects were healthy pensioners attending a health scan program.

2. Elderly people attending a day-center. This group consisted of 49 subjects with ages ranging from 58 to 85 years. All subjects, who volunteered to be studied, attended a day-center for elderly people. They lived either at home or in sheltered housing, and interview confirmed that they were outdoors frequently.

3. Nursing home residents. Fifty-one residents of a private nursing home consented to participate in the study. Ages ranged from 64 to 93 years. They consisted of a heterogenous group as regards sunlight exposure and mobility, ranging from infirm to freely ambulant.

4. Long-stay hospital patients. Fourteen patients, with ages ranging from 71 to 85 years, in a long-stay hospital were randomly selected for study. All were infirm and confined indoors.

5. Consecutive acute-hospital admissions. This group consisted of 37 consecutive admissions to an acute geriatric unit in a general hospital; 29 were admitted directly from their homes and eight were transferred from other wards. Their ages ranged from 66 to 94 years. None had disorders that would predispose to low 25(OH)D levels (25).

Groups 1 and 5 were reported, in part, previously (25). Subjects taking preparations, that contained vitamin D, were identified. Forty-one subjects attending the day-center (Group 2) were studied both in wintertime and at the end of summer (August), to assess the capacity of elderly subjects to respond to available sunlight.

A dietitian assessed vitamin D intake in 10 healthy elderly subjects (Group 1) and 6 nursing home residents (Group 3).

All bloods were taken with venistasis. Subjects in groups 2 and 3 were fasting. Serum total calcium, phosphate, and 25(OH)D were measured in all subjects and serum total alkaline phosphatase in 165 subjects.

Serum total calcium was measured by atomic absorption spectroscopy and phosphorus by centrifugal analyzer using a phosphomolydate method (Spin Chem Kit No 89440). Serum alkaline phosphatase was measured on a centrifichem analyzer at 30°C using an adaption of technique of Wilkinson et al (26). Serum 25(OH)D was estimated by a competitive protein binding assay, according to Haddad and Chyu (27). This measures vitamin D derived from D3 and D2. Serum 5’-nucleotidase was estimated by the Persin method in patients in whom serum alkaline phosphatase values were elevated above the 95 percentile range for young adults. Values for serum 25(OH)D and alkaline phosphatase values in the above groups were compared with values obtained in young adults. Comparison of vitamin D levels was made with reference to the season of estimation (28).

Log-transformation of serum 25(OH)D and alkaline phosphatase was performed prior to statistical analysis. Difference between means was determined by the paired or unpaired Student’s t test, where appropriate. Linear regression analysis was performed by the least squares method. The protocol was approved by the human subjects committee of Our Lady’s Manor Dalkey.

Results

The mean serum 25(OH)D in 181 elderly subjects was 10.0 nmol/L (95% range: <5.0 to 59 nmol/L). This is significantly lower (t = 7.02, P < 0.001) than values obtained in 28 young adults (mean = 33.5 nmol/L, 95% range 11.5 to 98 nmol/L). Mean vitamin D levels were significantly lower in both the day-center group and the institutionalized groups than in the healthy elderly group (Fig 1); the latter group had lower vitamin D levels than the young adults (t = 2.56, P < 0.02).

A significant gender difference was not observed for serum 25(OH)D and alkaline phosphatase in elderly groups.

Fifty-six percent of the elderly subjects had a serum 25(OH)D level below 5 nmol/L which is the limit of detectability of the assay (Table 2), and 79 percent had a value below 25 nmol/L—a level that is reported to indicate vitamin D depletion (24, 29). Eighteen of 181 subjects, who were taking vitamin D

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Groups studied</th>
<th>N</th>
<th>M/F</th>
<th>Age</th>
<th>Period of study</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Healthy elderly people</td>
<td>30</td>
<td>23:7</td>
<td>69 ± 5</td>
<td>Jan–Apr</td>
<td></td>
</tr>
<tr>
<td>2. Elderly people attending day-center</td>
<td>49</td>
<td>7:42</td>
<td>74 ± 7</td>
<td>March</td>
<td></td>
</tr>
<tr>
<td>3. Nursing home residents</td>
<td>51</td>
<td>5:46</td>
<td>79 ± 8</td>
<td>Feb–Mar</td>
<td></td>
</tr>
<tr>
<td>4. Long-stay hospital patients</td>
<td>14</td>
<td>8:6</td>
<td>78 ± 6</td>
<td>Jan</td>
<td></td>
</tr>
<tr>
<td>5. Consecutive acute hospital admissions</td>
<td>37</td>
<td>7:30</td>
<td>79 ± 7</td>
<td>Jan–Mar</td>
<td></td>
</tr>
</tbody>
</table>

M = male, F = female. Values for age are expressed as mean ± SD.
containing preparations prescribed by their family doctors, had the highest vitamin D levels (mean = 30 nmol/L, 95% range: <5 to 165 nmol/L); 7 of the subjects had values below 25 nmol/L. The mean daily vitamin D intake was 52 IU (1.29 μg) in 6 nursing home residents and 65 IU (1.63 μg) in 10 healthy elderly subjects. This is markedly below the recommended daily intake of 400 IU (10 μg) for elderly people (30).

Forty-one community-dwelling subjects (Group 2) were studied at the end of winter and at the end of summer; 10 of the 41 were taking vitamin D supplements. Serum 25(OH)D levels did not change significantly with season in the 10 subjects who were taking vitamin D supplements. In those subjects not taking vitamin D supplements, a significant seasonal rise in serum 25(OH)D levels was noted (t = 10.6, P < 0.001, Fig 2). However levels were still undetectable in 4 subjects, and less than 25 nmol/L in 8 subjects. The mean seasonal increment in serum 25(OH)D levels was 24 nmol/L. A small group of young adults (N = 8), residing in the area, were also studied during the period, the mean increment in serum 25(OH)D levels was 44 nmol/L (Fig 2). This approximates the mean seasonal increment (ie 49 nmol/L) previously observed in young Irish adults (28).

Serum alkaline phosphatase values in the 41 community-dwelling subjects (Group 2) fell slightly, but not significantly, during the Summer period (t = 1.85, P < 0.1).

Serum total calcium, phosphate and alkaline phosphatase values for all groups are shown in Table 2. Significant statistical difference between groups was obtained for the calcium values (t = 3.1, P < 0.01) and alkaline phosphatase (t = 2.4, P < 0.05) between the consecutive hospital admission group and the healthy elderly subjects. There were significant but weak correlations between the

**TABLE 2**

Serum chemistry results in elderly groups (1–5)

<table>
<thead>
<tr>
<th>Group</th>
<th>Calcium mmol/L</th>
<th>Phosphate mmol/L</th>
<th>Alkaline phosphatase IU/L</th>
<th>25(OH)D nmol/L</th>
<th>Prevalence of hypovitaminosis D Serum 25(OH)D</th>
<th>&lt;5 nmol/L</th>
<th>&lt;25 nmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>2.33 ± 0.08</td>
<td>1.05 ± 0.15</td>
<td>58 (44–77)</td>
<td>21 (&lt;5–105)</td>
<td>17%</td>
<td>50%</td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>2.31 ± 0.10</td>
<td>1.12 ± 0.14</td>
<td>60 (46–78)</td>
<td>10 (&lt;5–58)</td>
<td>59%</td>
<td>80%</td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>2.33 ± 0.14</td>
<td>1.14 ± 0.12</td>
<td>65 (46–93)</td>
<td>9 (&lt;5–46)</td>
<td>63%</td>
<td>84%</td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>2.28 ± 0.15</td>
<td>0.96 ± 0.21</td>
<td>56 (36–87)</td>
<td>8 (&lt;5–27)</td>
<td>64%</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td>2.20 ± 0.20</td>
<td>0.98 ± 0.19</td>
<td>85 (51–142)</td>
<td>8 (&lt;5–33)</td>
<td>73%</td>
<td>86%</td>
<td></td>
</tr>
</tbody>
</table>

Serum calcium and phosphate values are expressed as: mean ± SD.
Alkaline phosphatase values and 25(OH)D values are expressed as: mean (95% range).
following biochemical parameters: 25(OH)D and alkaline phosphatase \( r = -0.224, P < 0.01 \); 25(OH)D and total calcium \( r = 0.173, P < 0.005 \); alkaline phosphatase and total calcium \( r = -0.245; P < 0.01 \).

The data were also considered in an additional way. Serum calcium, phosphate and alkaline phosphatase values were compared in vitamin D deplete and vitamin D replete groups. Elderly subjects were divided into three groups according to their serum 25(OH)D levels: \(<5 \text{ nmol/L (vitamin D deplete); } \geq 25 \text{ nmol/L (vitamin D replete); } >5 \text{ to } <25 \text{ nmol/L (borderline vitamin D depletion).} \)

Having excluded 8 subjects with liver dysfunction (ie elevated serum 5'-nucleotidase levels), it was noted that serum alkaline phosphatase values were significantly lower in the vitamin D replete group, than either the deplete group \( t = 3.00, P < 0.005 \) or the group with borderline depletion \( t = 2.72, P < 0.01 \). The documented rise in serum alkaline phosphatase with age was moderated in the vitamin D replete (Serum 25-OHD \( > 25 \text{ nmol/L} \)) group (Fig 3). The vitamin D replete (serum 25-OHD \( > 25 \text{ nmol/L} \)) subjects as a group still showed a significant increase over values obtained for young adults. However, 89 percent of alkaline phosphatase values in elderly D replete (serum 25-OHD \( > 25 \text{ nmol/L} \)) subjects now were within the young adult range (Fig 3). Fasting serum calcium-phosphate product was not significantly different in the vitamin D deplete and replete subjects.

Dietary vitamin D intake was closely correlated with serum 25(OH)D levels in this and other studies \( r = 0.93, \text{ Fig 4} \). In contrast, serum 25(OH)D levels from the same studies correlated less significantly \( r = -0.50 \) with latitude of country (an index of solar irradiation). The above studies consisted of heterogeneous elderly groups—institutionalized and free-living—studied in different seasons (Table 3). When healthy elderly groups studied in Winter–Spring (Table 3) are compared, a similar degree of correlation \( r = -0.44 \) between serum 25(OH)D and latitude of country is seen. The relationship improves significantly \( r = -0.85 \) if the results from Denmark are excluded (Fig 5). The reason for this apparent discordance between Danish and other results is not clear (31). Only studies that employed a vitamin D assay...
FIG 3. Serum alkaline phosphatase values in young adults and elderly subjects with varying serum 25(OH)D concentrations: <5 nmol/L (deplete); >5 to <25 nmol/L (borderline); >25 nmol/L (replete). The shaded area represents the young adult reference range.

Discussion

This paper reports a high prevalence of hypovitaminosis D in a cross section of the elderly Irish population. Low serum 25(OH)D levels were noted more frequently in institutionalized subjects than in free-living individuals, which agrees with previous reports (7, 12). A seasonal rise in serum 25(OH)D levels was observed, reflecting the capacity of elderly subjects to respond to available sunlight, in accordance with cyclical variations noted in other elderly populations (5, 10, 17, 22, 32).

A low vitamin D level in serum identifies subjects at high risk of developing bone disease. Hypovitaminosis D osteopathy probably evolves according to a definite pattern, whereby secondary hyperparathyroidism precedes the development of osteomalacia (24, 33). Serum alkaline phosphatase is a useful indicant of both disorders, if liver dysfunction has been excluded (34). In the present study, the finding of higher alkaline phosphatase values in the vitamin D deplete groups than in the replete group suggests sub-clinical bone disease. In addition, the concomitant decrease in serum alkaline phosphatase values with seasonal rise in serum 25(OH)D levels might
signify healing of mild bone disease. Omdahl et al (22) in a cross-sectional study showed a similar pattern of seasonal change in alkaline phosphatase activity.

An increase in alkaline phosphatase values with age has been reported both in studies in females (35) and in studies in both sexes (36–38). In the present study, the effect of vitamin D status on alkaline phosphatase is clearly demonstrated for the first time. The age-related elevation of alkaline phosphatase is tempered by vitamin D repletion.

Since parent vitamin D is derived from two independent sources, it is necessary to
evaluate the relative contribution of each source to vitamin D nutritional status. Reported studies (8, 9, 32) with one exception (2) suggest that vitamin D stores in the elderly are mainly derived from skin sources. However comparison of reports from various countries discloses a close relationship between serum 25(OH)D and vitamin D consumption; countries with the highest intakes have the highest levels of vitamin D. The pervasive effect of vitamin D intake on vitamin D status is further demonstrated by the fact that hypovitaminosis D can occur in climates with a plentiful supply of sunlight, such as America (22) and Saudi Arabia (23), whereas infrequent sunshine in Denmark (16) does not necessarily predispose to vitamin D depletion. Indeed, for elderly populations, the primacy of exogenous vitamin D in the maintenance of adequate vitamin D stores is strongly suggested by reported studies.

Interpretation of such studies must be performed with caution, since results were obtained in different laboratories. However, a collaborative study, whereby duplicate samples from young adults were analyzed in two different laboratories in Denmark and England, showed a good correlation ($r = 0.88$, $p < 0.001$) between laboratory results (31). Also, observed was a higher level of vitamin D in the young Danish adults, mainly as a consequence of regular supplementary intake of vitamin D tablets. Obviously, this finding could account for the clear difference in vitamin D status of the young adults in the two countries.

In conclusion, hypovitaminosis D is common in elderly Irish people, and predisposes to the development of bone disease. The importance of sunlight exposure for elderly Irish people in the provision of vitamin D is emphasized by the seasonal variation of vitamin D levels in community-dwelling subjects and the finding of lower vitamin D levels in institutionalized people compared with free-living individuals. In our sun-deprived climate, elderly people—particularly housebound—are primarily dependent on dietary sources, which are nevertheless unable to supply the total daily requirement. The value of increased vitamin D intake, either by direct supplementation or augmented fortification of foodstuffs with vitamin D, is manifest.

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References

32. Hodkinson HM, Bryson E, Klierman L, Clarke
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