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Severe vitamin D deficiency in the institutionalized elderly

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ABSTRACT. Severe vitamin D deficiency has been found to be prevalent in institutionalized elderly persons in several countries. The aim of the present work was to assess the vitamin D status of institutionalized elderly and compare it to that of community-living independent elderly in southern Greece during summer. Serum 25-hydroxyvitamin D [25(OH)D] and plasma PTH were measured in 58 (aged 68-103 yr, median 83.5) elderly inmates of a nursing home (IE) in the town of Kalamata (latitude N 37°) and in 48 (aged 60-89 yr, median 72) community-dwelling elderly (CDE) in Athens (latitude N 38°). The CDE had mean serum 25(OH)D 67.6 nmol/l [95% confidence interval (CI) 57.4 to 79.5], not far from the value of 80 nmol/l which is generally considered to be the lower limit of vitamin D sufficiency. The IE had significantly lower mean 25(OH)D 19.0 nmol/l (17.1 to 21.1); values of 25(OH)D below 20 nmol/l characterize severe vitamin D deficiency and may cause osteomalacia. The group of CDE had significantly lower mean plasma PTH 1.5 pmol/l (1.0 to 1.8) compared to 4.5 (3.9 to 5.3) of IE. Ninety percent of CDE had normal plasma PTH whereas 60% of IE had secondary hyperparathyroidism (PTH values >4.0 pmol/l). In conclusion, the majority of institutionalized elderly in southern Greece had severe vitamin D deficiency and secondary hyperparathyroidism in contrast to the fairly good vitamin D status and lack of hyperparathyroidism in the community-living elderly during summer. These findings indicate the need for vitamin D and calcium supplementation of the institutionalized elderly throughout the year.
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INTRODUCTION

The serum concentration of the vitamin D metabolite 25-hydroxyvitamin D [25(OH)D] is considered to be the best index of the vitamin D status (1, 2). Values of serum 25(OH)D below 20-25 nmo/l are characteristic of severe vitamin D deficiency which may cause osteomalacia. Serum 25(OH)D concentrations above 80 nmol/l throughout the year are considered to be sufficient to prevent the bone disease and myopathy associated with vitamin deficiency, whereas values between 20 and 80 nmol/l may cause secondary hyperparathyroidism, osteoporosis, and increased risk of hip fracture (1-3). Vitamin D deficiency has been found to be prevalent among independent community-dwelling elderly persons worldwide (4, 5). In some reports, institutionalized, housebound, and sunlight-deprived elderly had lower serum 25(OH)D concentrations compared to community-living elderly (6-12). We have previously reported that vitamin D deficiency is not uncommon in the community-living elderly in Athens especially during the winter, whereas during summer their vitamin D status improved significantly (13). The aim of the present work was to investigate the vitamin D status in institutionalized elderly in the southern town of Kalamata in Greece and compare it to the vitamin D status of independent community dwelling elderly in Athens. This comparison was carried out during the summer when vitamin D status is best for the community living people (13).

Key-words: Vitamin D, elderly, institutionalized, secondary hyperparathyroidism.
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MATERIALS AND METHODS

For the study, a group of institutionalized elderly (IE) and a group of independent community dwelling elderly (CDE) were enrolled. The IE group comprised 58 (42 women and 16 men, aged 68-103 yr, median age 83.5, geometric mean age 83.8 with 95% CI 81.7 to 86.0) inmates of a municipal nursing home in the town of Kalamata, Greece (Latitude N 37°). Of these people, 14% had difficulty in walking without some assistance, 22% were walking using a cane or frame, and the rest, although generally frail, could visit places outside the institution occasionally. The CDE group comprised 48 residents of Athens (Latitude N 38°) (44 women and 4 men, aged 60-89 yr, median age 72, geometric mean age 71.6 with 95% CI 69.6 to 73.7). These subjects were examined in the municipal recreation centers for the elderly of Athens during their regular day time visits. Only persons of Greek ethnicity with similar social and dietary habits and not very different skin pigmentation were included in the study. Fasting blood specimens were withdrawn at about 09:00 h. All the participants in the study were examined between August 15 and September 15 in 2003. Exclusion criteria for both groups were serum creatinine higher than 1.5 mg/dl, evidence of primary hyperparathyroidism, any medication known to affect calcium metabolism such as thiazide diuretics and treatment for osteoporosis (current or during the last 5 yr). No person was receiving calcium or vitamin D supplements. The subjects who were finally enrolled in the study were selected after initially screening 70 IE and 62 CDE persons. The calcium intake was estimated to vary between 400-700 mg daily for the IE and 500-850 mg daily for the CDE group; this estimation was based on their consumption of diary products. The CDE of this study were exposed to the sun every day during their regular outdoor activities, and some of them swam in the sea about noontime several times weekly. Taking into account the common summer apparel in Greece which allows exposure to the sun of the arms and part of the upper chest, and the rate of vitamin D biosynthesis after exposure of the skin to the UV light (14) we estimated that all the CDE persons were gaining at least 400 IU vitamin D per day from the sun. For the IE persons direct exposure to the sun was variable from nil to minimal compared to the CDE. The IE who participated in the study had been inmates of the nursing home for at least 1 yr. Both CDE and IE persons were examined after their informed consent. The study was approved by the Scientific Committee of the Hospital.

PTH was determined using the Nichols Advantage® Bio-Intact PTH (1-84) two-site immunochemiluminometric assay. This assay detects only the bioactive PTH (1-84) molecule, excluding PTH fragments (7-84) or smaller, with a sensitivity 0.16 pmol/l. 25(OH)D was measured with a liquid phase radioimmunoassay (25-Hydroxyvitamin D RIA®,Nichols Institute Diagnostics, USA). The sensitivity of this method was 3.0 nmol/l. The cross-reactivity in the assay of 25(OH)D_2 was 75%, of 24,25-dihydroxyvitamin D_3 100% and of cholecalciferol and ergocalciferol less than 0.3%. The normal values we have reported previously (13) obtained from a group of healthy blood donors in summer were for PTH 2.04±0.66 pmol/l (mean±SD) and for 25(OH)D 85.7±44.6 nmol/l. Serum calcium, phosphorus, proteins, and creatinine were measured by an autoanalyzer by routine methods.

The geometric mean and its 95% confidence interval (CI) for the 25(OH)D and PTH values of each group are presented because these parameters did not have normal distribution. Comparisons between 2 groups were performed using the Mann-Whitney test. Comparisons between 2 proportions were made using Fisher's exact test. For the other parameters mean and SD are given and t test was used for comparisons. The statistical analysis was performed using GraphPad Prism Software, SanDiego, CA, USA.

RESULTS

25 hydroxyvitamin D

Community-living elderly had significantly higher mean serum 25(OH)D concentration compared to the institutionalized subjects [67.6 nmol/l (57.4 to 79.5) *vs* 19.0 (17.1 to 21.1), geometric mean (95% CI)], $p<0.0001$ (Fig. 1). The subjects of each group were classified according to the serum 25(OH)D concentration in 4 categories: with 25(OH)D <20 nmol/l, 20-50, 50.1-80 and >80. This categorization was based on the critical values of serum 25(OH)D <20 nmol/l and >80 nmol/l accepted by the majority of investigators as defining severe vitamin D deficiency and vitamin D sufficiency respectively, as discussed by Heaney (1). Levels of 25(OH)D between these two critical values are considered characteristic of mild vitamin D deficiency (also known as vitamin D insufficiency) (1). However, by provocative testing with vitamin D_2 in healthy adults a different value of 50 nmol/l was defined as the lower limit of vitamin D sufficient status as mentioned by Holick (2), and therefore we included a subcategory of 20-50 nmol/l as an alternative vitamin D insufficiency range in our classification. About 69% of the IE had 25(OH)D concentrations below 20 nmol/l, while no person in the CDE group had such a low value. Only about 4% of the IE had 25(OH)D values above 50 nmol/l, and no person in this group had values above 80 nmol/l. The frequency distribution of the subjects of each group according to their 25(OH)D levels (with 95% CI) is shown in Figure 2. The proportions of CDE and IE subjects were significantly different in all the categories of 25(OH)D, except in the 20.1-50 nmol/l 25(OH)D category ($p<0.0001$, Fisher's test).

Parathyroid hormone

Mean plasma PTH concentration was significantly lower in CDE compared to the IE [1.5 pmol/l (1.2 to 1.8) *vs* 4.5 (3.8 to 5.2)], $p<0.0001$ (Fig. 1). Sixty-one percent of the institutionalized subjects had PTH concentrations above 4.0 pmol/l (the upper reference limit in young blood donors), whereas 10.6% of the CDE had such high PTH values ($p<0.0001$).

Mean serum calcium corrected for albumin was slightly but not significantly lower in the IE compared to the CDE group. There were no significant differences in the other biochemical parameters between the 2 groups (Table 1). The 2 groups presented above had significantly different age ($p<0.001$, Mann-Whitney test). These original groups resulted after applying the exclusion criteria to a greater number of persons studied initially. When individuals younger than 68 yr and older than 89 yr were also excluded, the IE group comprised 30 individuals with a geometric mean age 77.7 yr (95% CI 76.0 to 79.5) and

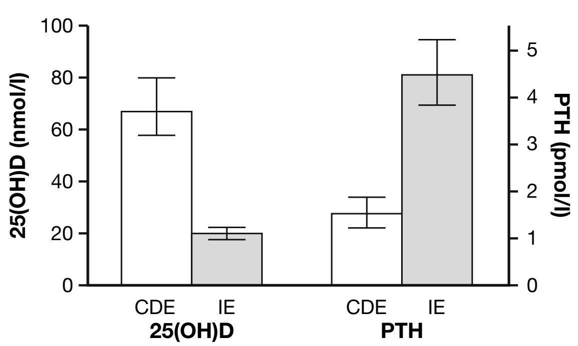

Fig. 1 - *Serum 25-hydroxyvitamin D [25(OH)D] and plasma parathyroid hormone (PTH) in community-dwelling (CDE) and institutionalized (IE) elderly during summer. Geometric mean and 95% confidence interval of the mean values are illustrated. The IE had significantly lower 25(OH)D (p<0.0001) and significantly higher PTH (p<0.0001) compared to the CDE, Mann-Whitney test.*

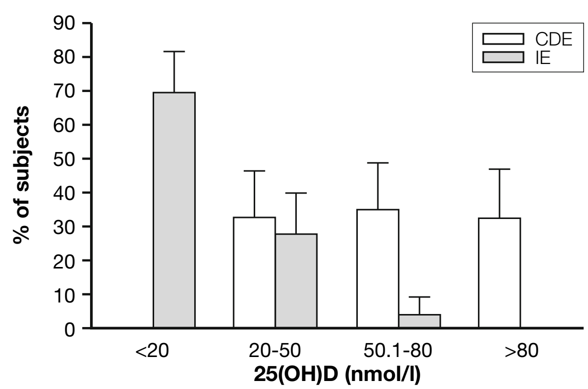

Fig. 2 - *Frequency distribution of the community-dwelling (CDE) and institutionalized (IE) elderly subjects in categories of various serum 25-hydroxyvitamin D [25(OH)D] concentrations. The error bars signify 95% confidence intervals. The differences between the proportions of IE and CDE in each category were significant (p<0.001, Fisher test), except in the 20-50 25(OH)D category.*

Table 1 - *Comparison of various parameters between community dwelling elderly and institutionalized elderly persons.*

Original groups	Group CDE (no.=48)	Group IE (no.=58)	*p*
Age, g. mean (95%CI)[a]	71.6 (69.6 to 73.7)	83.8 (81.7 to 86.0)	<0.0001
25(OH)D, nmol/l[a]	67.6 (57.4 to 79.5)	19.0 (17.1 to 21.1)	<0.0001
PTH, pmol/l[a]	1.5 (1.2 to 1.8)	4.5 (3.8 to 5.2)	<0.0001
Serum calcium, mg/dl[b]	9.4±0.6	9.2±0.7	ns
Serum phosphorus, mg/dl[b]	3.2±0.6	3.3±0.7	ns
Serum total proteins, g/dl[b]	7.1±0.6	7.2±0.5	ns
Serum albumin, g/dl[b]	4.2±0.3	4.0±0.2	ns
Serum creatinine, mg/dl[b]	0.9±0.1	1.0±0.2	ns
Age-range matched groups	Group CDE (no.=32)	Group ID (no.=30)	
Age, g. mean (95%CI)[a]	75.5 (73.6 to 77.4)	77.7 (76 to 79.5)	ns
25(OH)D, nmol/l[a]	60.2 (50.5 to 71.8)	20.7 (17.2 to 24.9)	<0.0001
PTH, pmol/l[a]	1.4 (1.0 to 1.8)	4.6 (3.9 to 5.3)	<0.0001
Serum calcium, mg/dl[b]	9.5±0.5	9.3±0.5	ns
Serum phosphorus, mg/dl[b]	3.3±0.60	3.2±0.7	ns
Serum total proteins, g/dl[b]	7.0±0.6	7.1±0.60	ns
Serum albumin, g/dl[b]	4.1±0.3	4.2±0.3	ns
Serum creatinine, mg/dl[b]	1.0±0.2	0.9±0.1	ns

CDE: community dwelling elderly; IE: institutionalized elderly. Age is expressed in years. [a]g. mean: geometric mean; 95%CI: 95% confidence interval of g. mean. [b]Mean±SD. Serum calcium corrected for albumin. Significant is two-tailed $p \leq 0.05$.

the CDE group comprised 32 persons with geometric mean age of 75.5 yr (95% CI 73.6 to 77.4). The mean age of these 2 age range-matched groups was not statistically different (Mann Whitney test, $p=0.08$). In these age-matched groups serum 25(OH)D was 60.2 nmol/l (50.5 to 71.8) for the CDE *vs* 20.7 (17.2 to 24.9) for IE ($p<0.0001$); serum PTH was 1.4 pmol/l (1.0 to 1.8) for the CDE *vs* 4.6 (3.9 to 5.3) ($p<0.001$). The values of 25(OH)D and PTH were not significantly different between the age-matched and the respective original larger groups (CDE or IE). These data are summarized in Table 1.

DISCUSSION

The cause of the vitamin D deficiency frequently found among the elderly in many regions (1, 2, 13) is considered to be their limited exposure to the sun in association with the reduced capacity of the aged skin for biosynthesis of vitamin D_3 (15). The main source of vitamin D_3 in humans is the skin where it is biosynthesized under the influence of UV light; non-fortified foods contain very little vitamin D, with the exemption of oily fish (2). Fish consumption seems to be important in mitigating vitamin D deficiency in some elderly Japanese populations (16). We have previously reported a marked seasonal variation of the vitamin D status and of the prevalence of secondary hyperparathyroidism in community-living independent elderly persons in Athens; these people had normal mean plasma PTH and serum 25(OH)D similar to young blood donors during summer, significantly improved compared to their abnormal levels during the winter (13). The seasonal variation of serum 25(OH)D and plasma PTH in the CDE in Athens was ascribed to better exposure to the sun during summer. In the present work we showed that vitamin D deficiency associated with frequent secondary hyperparathyroidism affected institutionalized elderly in the southern Greek town of Kalamata (latitude N 37°) even during summer, in contrast with the control group of independent community-living elderly in Athens (latitude N 38°). In the group of institutionalized elderly of our study immobile patients confined to bed were not included, in order to eliminate possible suppressive effects of the immobilization on plasma PTH, as was demonstrated in institutionalized and immobile elderly persons by Theiler et al. (17). The difference in vitamin D status between independent community-living elderly in Athens and of institutionalized elderly in the town of Kalamata during summer should be ascribed to the minimal exposure to the sun of the persons of the latter group since dietary habits, including fish consumption (16), were estimated to be similar between the 2 groups. Serum calcium was only slightly lower in the IE compared to the CDE. The lack of hypocalcemia in our IE subjects can probably be explained by the fact that their average vitamin status was not extremely low, their mean 25(OH)D level being near the critical value of 20 nmol/l. None of the IE of this study had undetectable 25(OH)D or symptoms and signs of clinical osteomalacia.

The vitamin D status of the elderly community-dwelling populations varies considerably among different countries (10, 18, 19). The best situation seems to be in the United States, and the worst in central Europe, with the Scandinavian countries in between (20). The reason for this diversity seems to be the fortification with vitamin D of milk and margarine in the USA and Scandinavia respectively and no such food fortification in other European countries, including Greece. A seasonal variation of serum 25(OH)D values in the community-dwelling elderly was found in various regions of the world (21-23). This seasonal variation was not found in institutionalized elderly (6, 8). The possibility of seasonal variation in the vitamin status of the IE of the present study was not investigated. A limitation of this study is that comparison of the bone turnover using bone markers and of the fracture risk between the 2 groups was not feasible because the pertinent data were not available. Extremely low vitamin status, high bone turnover, and increased fracture risk in home bound centenarians was reported recently from Italy by Passeri et al. (12). Thus, low vitamin status seems to be prevalent in home-bound or institutionalized elderly people in both these Mediterranean countries.

The conclusions from the present study is that, in southern Greece, institutionalized elderly persons often have severe vitamin D deficiency with secondary hyperparathyroidism even during summer and therefore need vitamin D and calcium supplementation throughout the year. This is in contrast to the community-living elderly persons who, during summer, seem to have a better although not entirely sufficient vitamin status (13).

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