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Letter

Parathyroid hormone plasma concentrations in response to low 25-OH vitamin D circulating levels increases with age in elderly women

SIR—Several reports have concluded that low 25-OH vitamin D (25-OH D) circulating levels are a common feature in elderly women who are either community-dwelling or living in nursing homes [1–3]. Impaired vitamin D metabolism and subsequent increase in parathyroid hormone (PTH) secretion are considered significant determinants of age-related osteoporosis [1,4]. High PTH levels in the elderly are associated with low vertebral bone density [5], decrease cortical thickness [6], increase in bone turnover rate [1,7] and increased risk of hip fracture [8]. Supplementation of elderly subjects with vitamin D and calcium was shown to significantly reduce non-vertebral fractures [9] but only if serum PTH is concomitantly decreased [10]. We previously reported that 25-OH D levels were reduced to a similar extent, after adjustment for age, in elderly women who were community-dwellers or nursing home residents [11]. However, we also showed that in very old women (over 80 years old), non-significant differences in vitamin D levels between nursing home residents and community-dwellers could translate into a significant difference in PTH. In the present paper, we investigate whether or not the response of PTH secretion to a decrease in circulating levels of vitamin D is influenced by the age of the subjects. For the present trial, we used the values of 25-OH D and PTH circulating levels obtained from a previously described epidemiological survey [11,12]. Briefly, general practitioners trained for participating in osteoporosis clinical trials recruited from their practice women aged 70 years and over, either community-dwelling or living in nursing homes. In this survey, 1483 women consented to participate and we obtained serum samples from 748 (50.4%) subjects. Serum 25-OH D and PTH were assessed by commercially marketed radioimmunoassay kits (Incstar, Stillwater, MN). In our experience, the intra- and inter-assay coefficients of variation are respectively 8% and less than 12% for 25-OH D and 6% and less than 10% for PTH. Daily calcium intake was evaluated, on the day on which blood was drawn, by a previously validated and published self-administered questionnaire [13].

Results were expressed as mean $\pm$ SEM. To compare the daily calcium intake in the community-dwellers and nursing home groups, a Student's *t*-test was applied. Log transforms were used for vitamin D and PTH to normalize their distribution. To assess the (linear) relation between two continuous variables, the Pearson correlation coefficient was calculated. A multiple regression was applied to study PTH secretion. The effects of group, age and vitamin D were tested. All results were considered to be significant at the 5% level ($p < 0.05$). Statistical calculations were carried out using the SAS software package (SAS Institute Cary, NC).

Daily calcium intake was not significantly different in community-dwellers (612 $\pm$ 34 mg/day) (mean $\pm$ SEM) and nursing home residents (606 mg/day). No significant relation was shown between age and daily calcium intake in the whole population ($p = 0.88$), in community-dwellers ($p = 0.74$) or in nursing home residents ($p = 0.82$). The mean values (SEM) of 25-OH D and PTH were respectively 12.2 (0.1) ng/ml and 34.1 (1.0) pg/ml in our population of elderly women. Age was correlated negatively with 25-OH D ($r = -0.22$, $p < 0.001$) and positively with PTH ($r = 0.16$, $p < 0.001$). PTH was inversely correlated with 25-OH D ($r = -0.26$; $p < 0.001$). After adjustment for type of living (community-dwelling or nursing home residence), it appeared that age remained a significant determinant ($p < 0.001$) of the relation between 25-OH D and PTH (Fig. 1). Applied to our population of elderly women, this age-dependent effect corresponds to a difference of more than 20% in PTH levels for similar 25-OH D values, between the age of 70 and 95 years (Table 1).

The levels of 25-OH D measured in the present study are slightly lower than those reported recently in a population of elderly European women (born between 1913 and 1918), even for those living at the same latitude (50–55° N) as our city [3]. However, they are compatible with those found in French

Table 1. Mean PTH values, for 25-OH D levels at 12, 18, 25, 30 and 45 ng/ml, in women between 70 and 95 years old

Vitamin D (ng/ml)	PTH (pg/ml)					
	70 years	75 years	80 years	85 years	90 years	95 years
12	24.5	25.6	26.8	28.0	29.3	30.7
18	22.3	23.4	24.4	25.6	26.8	28.0
25	20.7	21.7	22.7	23.7	24.8	26.0
30	19.9	20.8	21.8	22.8	23.8	24.9
45	18.1	19.0	19.9	20.8	21.7	22.7

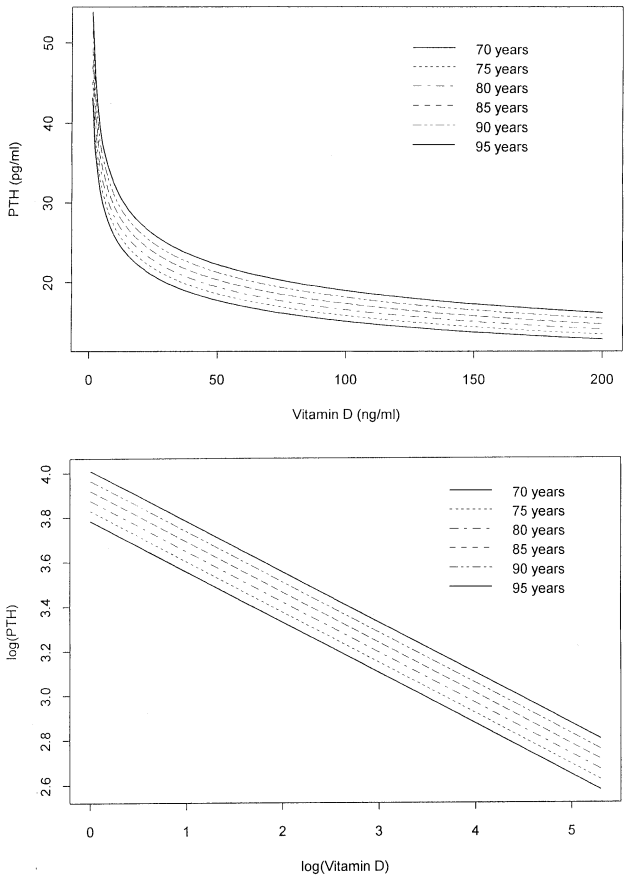

Fig. 1. Relation between mean 25-OH D and mean PTH circulating levels of subjects between 70 and 95 years old: **a** before logarithmic transformation, **b** after logarithmic transformation.

women, both at home or institutionalized [1,14]. A progressive decrease in 25-OH D and an increase in PTH with age was previously documented [15,16]. The interesting feature of our results is the increased levels in PTH with aging, for similar values of 25-OH D. Serum calcium was not measured in the survey. One cannot thus completely exclude the possibility of increased PTH secretion as a consequence of a decrease in serum calcium with age. Daily calcium intake was not age-related in our population and thus cannot account for our results. Alteration in 1,25-$(OH)_2$ vitamin D production is known to be a feature of the process of aging. Secondary hyperparathyroidism in the elderly was also related to progressive renal insufficiency [18], even though some authors consider that a decrease in renal function is not the major factor accounting for the rise in serum PTH with age [16]. In our study, severe renal insufficiency was an exclusion criterion. Intestinal resistance to the action of 1,25-$(OH)_2$ D would be another potential explanation. Decreasing growth hormone and insulin-like growth factor I concentrations were also suggested to play a possible role in the mineral homeostasis of the elderly [15]. We did not measure these parameters in our study. Whatever the mechanism underlying this increase in PTH levels in response to low 25-OH D in the elderly, the major consequence is that the level of 25-OH D deficiency leading in relevant hyperparathyroidism in the elderly is likely to be much lower than currently defined. 25-OH D levels of 30 ng/ml in a 90-year-old woman are associated with mean PTH levels higher than those observed with 25-OH D at 12 ng/ml at the age of 75 years. We [11] and others [1,3] have already mentioned the underestimation of the high prevalence of vitamin D deficiency in elderly European women. Our present results stress the importance of adequate vitamin D repletion, particularly in elderly women, to avoid secondary hyperparathyroidism.

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