J. Endocrinol. Invest. 31: 991-995, 2008

Hypovitaminosis D and secondary hyperparathyroidism in resident physicians of a general hospital in southern Brazil

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ABSTRACT. ***Objectives:*** **To evaluate the prevalence of hypovitaminosis D and secondary hyperparathyroidism in resident physicians of a general hospital in southern Brazil and identify associated factors.** ***Design:*** **Cross-sectional study.** ***Population:*** **Resident physicians of Hospital de Clinicas de Porto Alegre, Porto Alegre, southern Brazil.** ***Participants:*** **Seventy-three subjects age 26.4±1.9.** ***Measurements:*** **Serum PTH, 25-hydroxyvitamin D [25(OH)D], total calcium, phosphorus, magnesium, creatinine, and alkaline phosphatase were measured. In addition calcium, creatinine, and magnesium were measured in urine. Fractional excretion of calcium and magnesium were calculated. Calcium intake was estimated by a food intake questionnaire.** ***Results:*** **Mean serum levels of 25(OH)D were 17.9±8.0 ng/ml and 57.4% presented 25(OH)D below 20 ng/ml. Secondary hyperparathyroidism, defined as serum PTH ≥48 pg/ml and normal or low serum calcium, was identified in 39.7% of the individuals. Mean serum levels of magnesium were higher (*p*=0.02) and the fractional excretion of calcium was lower (*p*<0.001) in individuals with secondary hyperparathyroidism. Serum PTH levels were positively correlated with body mass index (r=0.33 and *p*=0.006) and serum magnesium levels (r=0.33 and *p*=0.02) and negatively correlated with serum 25(OH)D levels (r=–0.33 and *p*=0.008), estimated calcium intake (r=–0.25 and *p*=0.04), and fractional excretion of calcium (r=–0.34 and *p*=0.009).** ***Conclusion:*** **Vitamin D deficiency and secondary hyperparathyroidism was very common in resident physicians. Therefore, measures to prevent this situation should be recommended.**
(J. Endocrinol. Invest. 31: 991-995, 2008)

INTRODUCTION

Vitamin D deficiency is common in locations where the exposure to solar radiation, more precisely ultraviolet B, is low (1) and this has been described as a cause of secondary hyperparathyroidism (SHP). Low intake of calcium (2), renal failure (3, 4) and hyperphosphatemia may also provoke SHP (5). Hypovitaminosis D is also common in some populations, such as the elderly, Arabian and Chinese immigrants in the United Kingdom (6). In addition, it has already been identified in young adults (1), young physicians, and medical students (7).

Resident physicians work in closed environments, with little sunlight exposure (8). They are overwhelmed by long work shifts, they do not have a predictable meal time and many times they fail to take care of their own health (9, 10). These factors may increase the risk of hypovitaminosis D and SHP in these individuals. For this reason, our objectives were to estimate the prevalence of hypovitaminosis D and SHP in resident physicians of a general hospital in southern Brazil, and to identify possible associated factors.

MATERIALS AND METHODS

Study design and population

A cross-sectional study was conducted at Hospital de Clínicas de Porto Alegre (HCPA), in the City of Porto Alegre, parallel 30°, South Brazil. The calculated number of subjects to detect a 30% prevalence, with a precision of 10, for a significance level of 0.1, was 56. No one was excluded and a simple random sample of the resident physicians was obtained through randomization tables.

The study was approved by the Ethics Committee of HCPA. All individuals provided an informed consent term. Data were collected in October and November 2003 and 2004.

Measurements

The following data were obtained during recruitment using a standardized questionnaire: age, sunlight exposure (number of hours per week), tobacco, and alcohol use. Weight, height, and skin phototype were determined the same day by the authors. The skin phototype was classified from I to VI as proposed by Fitzpatrick (11) (sunburn and tanning history defines the phototype: I) the skin burns easily and never tans; II) the skin burns easily and tans minimally with difficulty; III) the skin burns moderately and tans moderately and uniformly; IV) the skin burns minimally and tans moderately and easily; V) the skin rarely burns and tans profusely; and VI) the skin never burns and tans profusely). The body mass index (BMI) was calculated by the formula: weight (kg)/height^2 (cm^2). Calcium intake was estimated through a questionnaire of food intake previously validated in our environment.

Blood samples were collected between 09:00 and 11:00 h, after a fasting of at least 4 h, and a urine sample was collected in the second morning voiding. All samples were frozen at –70 C and analyzed at the same time. Serum 25-hydroxyvitamin D [25(OH)D] and serum PTH levels were measured, respectively, by chemiluminescence (LIAISON – DiaSorin Inc, Stillwater/MN, CV 6% intra-assay) and electrochemiluminescence (Elecsys – Roche Diagnostics, Indianapolis/USA, CV 2% intra-assay). Serum phosphorus, magnesium, total calcium, creatinine, and alkaline phosphatase levels, and urinary crea-

Key-words: Parathyroid hormone, resident physicians, secondary hyperparathyroidism, vitamin D, vitamin D deficiency.

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Accepted February 8, 2008.

Table 1 - *Baseline characteristics of the resident physicians.*

	All	With SHP	Without SHP	*p*
Clinical data				
Age (yr)	26.4±1.9 (72)	26.9±2.5 (29)	26.1±1.5 (43)	0.12
Phototype I and II[a]	40/70 (57.1)	14/27 (51.85)	26/43 (60.5)	0.51
Female	36/73 (49.3)	12/29 (41.3)	24/44 (54.5)	0.34
Exposure to sun[b]	23/72 (32)	12/29 (41.37)	11/43 (25.6)	0.20
Smokers	3/72 (4.2)	2/29 (6.9)	1/43 (2.3)	0.56
Alcohol use	19/71 (26.8)	6/28 (21.4)	13/43 (30.2)	0.58
Weight (kg)	68.3±12.4 (71)	71.4±12.6 (28)	66.3±12.0 (43)	0.10
BMI (kg/m^2)	23±2.7 (71)	23.7±2.5 (28)	22.4±2.7 (43)	0.06
Calcium intake (mg/day)	495±420 (69)	410.6±388 (28)	553.0±435 (41)	0.09
Biochemical parameters				
PTH (pg/ml)	45.8±22.7(73)	30.8±10.7 (29)	68.7±15.8 (44)	<0.000
25(OH)D (ng/ml)	17.9±8.0 (53)	15.4±7.4 (18)	19.3±8.1 (25)	0.09
Total calcium (mg/dl)	9.2±0.4 (53)	9.1±0.4 (17)	9.2±0.4 (36)	0.33
Phosphorus (mg/dl)	4.0±0.5 (65)	4.0±0.5 (21)	4.0±0.5 (44)	0.57
Magnesium (mg/dl)	2.0±0.2 (53)	2.2±0.1 (18)	2.0±0.2 (35)	0.02
Alkaline phosphatase (U/l)	91.4±66 (65)	99.7±73 (21)	74.3±44 (44)	0.09
Creatinine (mg/dl)	1.0±0.2 (65)	1.0±0.2 (21)	1.0±0.2 (44)	0.45
FE_{Ca} (%)	0.8±0.5 (58)	0.5±0.3 (20)	0.9±0.5 (38)	0.001
FE_{Mg} (%)	1.8±1.0 (27)	1.6±0.9 (14)	1.9±1.0 (13)	0.46

Data are shown as mean±SD (no.) and no./no. total (%).[a]Sunburn and tanning history defines the skin phototype: I) the skin burns easily and never tans, II) the skin burns easily and tans minimally with difficulty, III) the skin burns moderately and tans moderately and uniformly, IV) the skin burns minimally and tans moderately and easily, V) the skin rarely burns and tans profusely, and VI) the skin never burns and tans profusely (11). [b]Exposure to sun >3 h/week. SHP: secondary hyperparathyroidism, defined as serum PTH levels >48 pg/ml and normal or low serum total calcium levels; BMI: body mass index; 25(OH)D: 25-hydroxyvitamin D; FE_{Ca}: fractional excretion of calcium; FE_{Mg}: fractional excretion of magnesium.

tinine, magnesium, and calcium were measured by routine methods at HCPA.

Hypovitaminosis D was defined as 25(OH)D <20 ng/ml. Normal range for serum PTH levels were calculated in a prior study, by

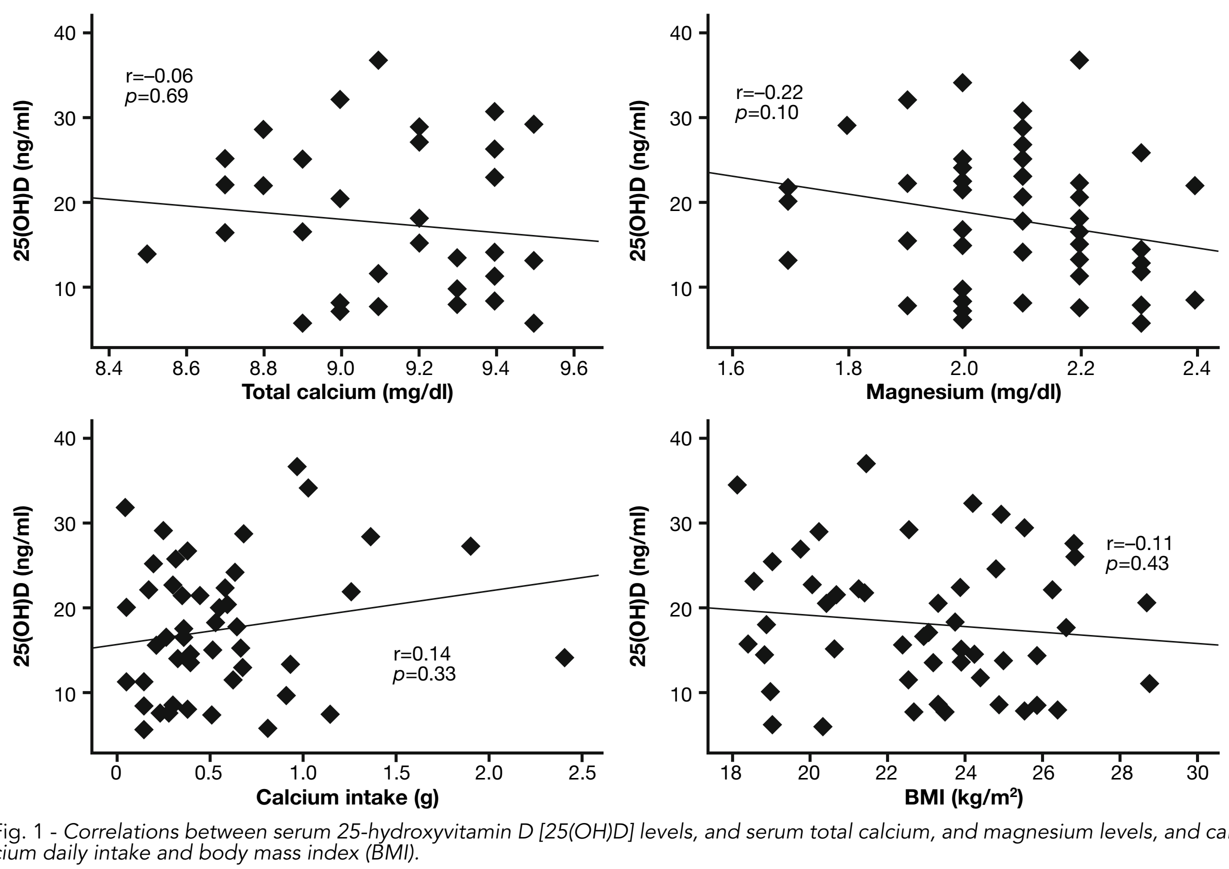

Fig. 1 - *Correlations between serum 25-hydroxyvitamin D [25(OH)D] levels, and serum total calcium, and magnesium levels, and calcium daily intake and body mass index (BMI).*

the mean±2 SD, in patients with serum 25(OH)D levels ≥20 ng/ml (12, 13). SHP was defined as serum PTH levels >48 pg/ml, with normal or low serum total calcium levels. The fractional excretion of calcium and magnesium (FE_{Ca} and FE_{Mg}) were calculated through the formulas: FE_{Ca} =(urinary calcium/serum calcium)/(urinary creatinine/serum creatinine)×100% and FE_{Mg}= (urinary magnesium/serum magnesium)/(urinary creatinine/serum creatinine)×100%.

Statistical analysis

The prevalence of hypovitaminosis D and secondary hyperparathyroidism were calculated. Associated factors were evaluated through Student's t test, Mann-Whitney's test, Fisher's Exact test, χ^2 and Pearson's, and Spearman's correlation coefficients, when indicated. As the following variables: serum PTH, 25(OH)D, alkaline phosphatase, and calcium intake presented an asymmetrical distribution, they were transformed into their natural logarithm. A multiple linear regression was used to evaluate factors associated with serum PTH.

RESULTS

In total, 89 individuals were invited to participate in the study. Seven refused and 9 did not conclude it.
The baseline characteristics for this population are described in Table 1. The mean serum 25(OH)D levels were 17.9±8.0 ng/ml and 57.4% presented serum 25(OH)D levels below 20 ng/ml. SHP was identified in 39.7% of the subjects and 60.9% had an estimated calcium intake below 500 mg/day. There was no correlation between serum 25(OH)D, total calcium (r=–0.10 and *p*=0.53), phosphorus (r=0.06; *p*=0.66), alkaline phosphatase l (r=0.21; *p*=0.13), and magnesium levels. FE_{Mg} (r=0.09; *p*=0.66), FE_{Ca} (r=0.05; *p*=0.70), calcium intake, and BMI were also not correlated with it. Such data are partially shown in Figure 1.
Serum PTH levels were negatively correlated with serum 25(OH)D levels, calcium intake and FE_{Ca} (r=–0.34 *p*=0.009), and were positively correlated with the serum magnesium levels and BMI. There was no correlation between serum creatinine (r=0.16; *p*=0.21), total calcium (r=–0.07; *p*=0.60), phosphorus (r=0.07; *p*=0.58), alkaline phosphatase (r=–0.074; *p*=0.56), and PTH levels. FEMg (r=–0.35; *p*=0.07) was also not correlated with it. Such data are partially shown in Figure 2.
Individuals with SHP had significantly higher mean serum magnesium levels and significantly lower FE_{Ca} than individuals without SHP (Table 1). In addition, there were no clinical data associated with SHP (Table 1). We also found no clinical (Table 2) or biochemical (data not shown) data associated with vitamin D deficiency.
The factors associated with the serum PTH variation were also studied in a linear regression model. BMI and serum 25(OH)D levels were associated independently with serum PTH levels, as shown in Table 3.

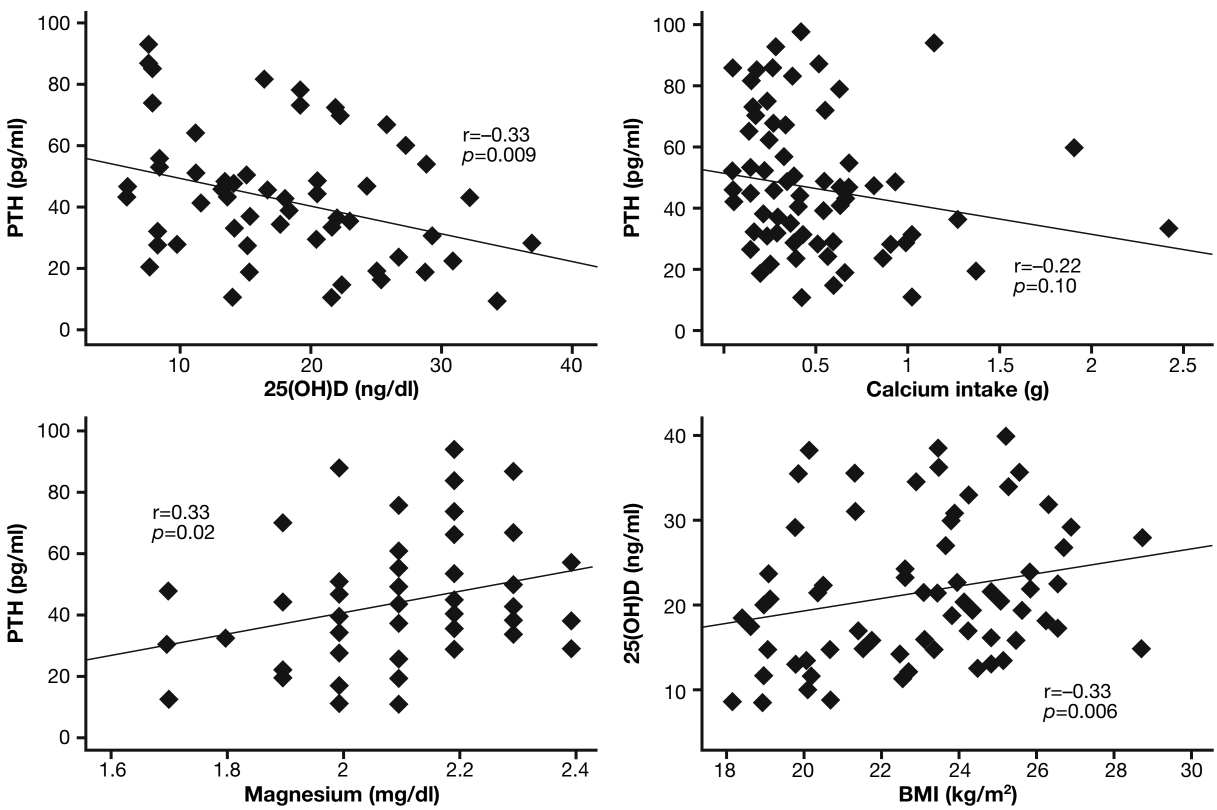

Fig. 2 - *Correlations between serum PTH levels and serum magnesium levels, calcium daily intake, body mass index (BMI), and serum 25-hydroxyvitamin D [25(OH)D] levels.*

Table 2 - *Characteristics of resident physicians with vitamin D deficiency or not (no.=52).*

	25(OH)D<20 ng/ml	25(OH)D≥20 ng/ml	*p*
Age (yr)	23.3±1.6 (n)	26.4±2.7(n)	0.85
Phototype I and II[a]	19/30 (63.3)	12/21 (57.1)	0.77
Female	14/30 (46.6)	15/23 (65.2)	0.26
Exposure to sun[b]	8/30 (26.7)	8/22 (36.4)	0.54
Smokers	3/30 (10)	0/22	0.25
Alcohol use	6/29 (20.6)	8/22 (36.4)	0.34
Weight (kg)	68.2±12.3 (29)	66.8±13.6 (22)	0.70
BMI (kg/m^2)	23.1±2.6 (29)	22.6±3.0 (22)	0.57
Calcium intake (mg/day)	503±446 (30)	582±482 (21)	0.83

Data are shown as mean±SD (no.) and no./no. total (%). 25(OH)D: 25-hydroxyvitamin D; BMI: body mass index. [a]Sunburn and tanning history defines the skin phototype: I) the skin burns easily and never tans, II) the skin burns easily and tans minimally with difficulty, III) the skin burns moderately and tans moderately and uniformly, IV) the skin burns minimally and tans moderately and easily, V) the skin rarely burns and tans profusely, and VI) the skin never burns and tans profusely (11). [b]Exposure to sun >3 h/week.

DISCUSSION

The health of resident physicians has been the object of great concern by the scientific community (10). They present a higher incidence of depressive symptoms related to stress (9, 14). Little is known about the prevalence of other health problems in this population. Additionally, their life habits are usually unhealthy: they remain in closed places for long periods with little sunlight exposure (9), they sleep few hours (9), have unscheduled meal times (9), and possibly eat calorie-rich foods with poor nutritional value. Furthermore, as long hours with no sunlight are an important risk factor for vitamin D deficiency, the hypovitaminosis D prevalence of 57.4% in these resident physicians was not surprising.

To our knowledge, there are very few studies on the prevalence of hypovitaminosis D and secondary hyperparathyroidism in this population. Studies on the prevalence of hypovitaminosis D in other populations of young adults found 2 to 30% of the adults with vitamin D deficiency (6, 7). In selected populations, such as women wearing clothes that cover the whole body (15), descendents of Arabian or Indian immigrants in European countries (6, 16) and in regions with little solar radiation, such as the city of Boston (7, 17), in the United States, in the winter, the prevalence of hypovitaminosis D is more than 50%.

In a cohort study conducted with elderly people in the city of Sao Paulo (18), parallel 23° south, Brazil, the mean serum 25(OH)D levels decreased more than 20 ng/dl from summer to winter. Similar data were observed in post-menopause women in Buenos Aires, Argentina, 34°S (19, 20). The city of Porto Alegre is located at parallel 30° south, and our data were collected in October and November 2003, which correspond to the first and second spring months, respectively, in our country. This factor might have contributed to the high prevalence of hypovitaminosis D, in the present study, and it is possible that the serum 25(OH)D levels would be higher in summer.

Table 3 - *Model of multiple linear regression for possible factors associated with serum PTH in resident physicians (no.=53).*

	B	SE	β	*p*
BMI (kg/m^2)	2.96	0.92	0.32	0.002
LN 25(OH)D (ng/ml)	–12.03	5.36	–2.25	0.030

Variables that were included in the model: age, body mass index (BMI), serum total calcium, serum phosphorus, serum magnesium, serum creatinine, natural logarithm of serum 25-hydroxyvitamin D [LN 25(OH)D], and natural logarithm of calcium daily intake. Variables that remained in the model: BMI and LN 25(OH)D. Dependent variable: serum PTH.

Vitamin D supplementation in the diet is not usual in our country, which probably contributed to the high prevalence of vitamin D deficiency. The low calcium intake, observed in most individuals who participated in our study, may also have influenced this prevalence. A low calcium diet increases the 25(OH)D consumption due to a compensatory increased production of 1,25(OH)2D, which is required to maximize calcium absorption as much as possible (21, 22). Interestingly, many studies have shown that only part of the individuals with vitamin D deficiency have SHP (23). In the present study, only 60% of the subjects with serum 25(OH)D levels lower than 20 ng/dl had SHP. The cause of this phenomenon is unknown; nevertheless, one possible mechanism could be magnesium deficiency, since it inhibits the appropriate PTH increase in response to the reduced serum calcium levels (24, 25). Subjects who had SHP in our study had also higher mean serum magnesium levels. Moreover, these levels were positively correlated with serum PTH levels which suggest the above assumption is correct.

The prevalence of SHP in resident physicians in our study was 39.7% and, as expected, the mean serum PTH levels were inversely correlated with the calcium intake and the serum 25(OH)D levels. Such data agree with those found in the 5th Tromsø study which shows vitamin D deficiency and low calcium intake as the main causes for SHP (2). Low calcium intake was not associated with SHP in the multivariate analysis, probably because the calcium intake was very low in most individuals (in 82.6% it was <700 mg/day).

A positive correlation between serum PTH levels and BMI was also observed in the 5th Tromsø study (26). In this study, BMI was associated with serum PTH levels, even after correction for age, tobacco use, coffee consumption, and serum 25(OH)D levels. Another study conducted in Iceland (27), in adults between 30 and 85 yr of age, also found an association between serum PTH levels and BMI. The mechanism of this association is unknown; however, it is believed that sodium-rich hypercaloric diets which increase body weight, may also lead to an increase in natriuresis. The consequent higher calcium excretion in urine could cause a compensatory increase in serum PTH levels (28). In our study, this association remained independent after the correction for serum 25(OH)D and magnesium levels, and calcium intake. Unfortunately, we did not measure the sodium intake and the urinary sodium excretion.

Vitamin D deficiency and SHP could be considered a major problem in these resident physicians. Since the concern about the health of these physicians is a medical community obligation, we should implement measures to improve their health habits and to reduce the risks to which they are exposed. A healthier diet, vitamin D supplementation, and exposure to sunlight should be encouraged in all residency programs.

ACKNOWLEDGMENTS

Financial support

The study was supported by the Research Incentive Fund of HCPA.

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