UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL

PROGRAMA DE PÓS-GRADUAÇÃO EM CIÊNCIAS MÉDICAS:

ENDOCRINOLOGIA

HIPERPARATIREOIDISMO SECUNDÁRIO À HIPOVITAMINOSE D DEPENDE DOS NÍVEIS SÉRICOS DE MAGNÉSIO

TESE DE MESTRADO

TIAGO SCHUCH

Porto Alegre, janeiro de 2010

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Tese de Mestrado apresentada ao Programa de Pós-Graduação em Ciências Médicas: Endocrinologia da Universidade Federal do Rio Grande do Sul (UFRGS) como requisito parcial para obtenção do título de Mestre em Endocrinologia.

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SUMÁRIO

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LISTA DE ABREVIATURAS

eGFR	*Estimated glomerular filtration rate*
Mg	*Magnesium*
PTH	*Parathyroid hormone*
25-OHD	*25-hydroxivitamin D*

Resumo

Contexto. A deficiência de vitamina D em adultos pode precipitar ou agravar osteopenia e osteoporose, causar fraqueza muscular e osteomalácia, e aumentar o risco de fraturas ósseas. Alguns destes efeitos podem ser mediados pelo hiperparatireoidismo secundário a níveis diminuídos de 25-hidroxivitamina D (25-OHD). Não está claro porque alguns indivíduos não desenvolvem elevação dos níveis de hormônio da paratireóide (PTH) em conseqüência à deficiência de vitamina D.

Objetivos. Estimar a prevalência de hipovitaminose D e hiperparatireoidismo secundário em uma amostra de pacientes adultos ambulatoriais, e analisar possíveis causas de ausência de correlação entre os níveis de 25-OHD e PTH.

Delineamento e cenário. Estudo transversal de 91 pacientes ambulatoriais de um centro de atenção terciária no sul do Brasil (latitude 30^0 sul).

Pacientes. Adultos a partir de 40 anos de idade.

Desfechos principais. Níveis séricos de 25-OHD medidos por quimioluminescência e níveis de PTH medidos por eletroquimioluminescência.

Resultados. Idade média foi 60,3 ± 12 anos, 56 (61,5%) eram mulheres, e 70 (76,9%) eram brancos. Hipovitaminose D foi encontrada em 69 (75,9%), 11 (12,1%) tinham hiperparatireoidismo secundário e nenhum tinha hipomagnesemia (Mg <1,5 mg/dl). Não houve correlação significativa entre os níveis de 25-OHD e PTH, porém esta correlação tornou-se significativa quando apenas indivíduos com níveis de magnésio acima de 2,1 mg/dl foram considerados na análise ($r = 0,37$, $p = 0,02$). Houve correlação positiva entre os níveis de PTH e magnésio na faixa normal ($r = 0,29$, $p < 0,01$).

Conclusões. A associação entre hipovitaminose D e hiperparatireoidismo secundário é dependente dos níveis séricos de magnésio.

INTRODUÇÃO

A vitamina D desempenha um papel importante na saúde humana, com funções que estendem-se além dos seus bem conhecidos efeitos sobre o metabolismo mineral e ósseo, como função muscular, diferenciação celular, e imunidade (1). Níveis inadequados deste hormônio parecem ser achado comum na população adulta de todo o mundo, apesar de diferenças na prevalência de hipovitaminose D em relação à idade, grupo étnico, latitude, estação do ano, quantidade de exposição solar, fortificação alimentar ou uso de suplementos de vitamina D (2,3). A hipovitaminose D pode causar hiperparatireoidismo secundário, precipitar ou agravar osteopenia e osteoporose, causar osteomalácia e fraqueza muscular, aumentar o risco de quedas e fraturas ósseas (4), e tem sido associada ao desenvolvimento de câncer (5), diabetes (6), e doenças autoimunes (7). Uma vez que a deficiência de vitamina D pode ser corrigida facilmente e por meios seguros e baratos, tem sido dada atenção aumentada para identificar e corrigir este problema de saúde (8).

O método padrão para avaliação do status de vitamina D é a medida dos níveis séricos de seu principal metabólito, 25-hidroxivitamina D (25-OHD) (9), devido à sua meia-vida longa, correlação com a absorção de cálcio, e porque a etapa de 25-hidroxilação não é regulada. Entretanto, há considerável variação e falta de padronização entre os diferentes ensaios utilizados para sua dosagem (10-11).

A hipovitaminose D é associada ao desenvolvimento de hiperparatireoidismo secundário, quando os níveis de PTH estão relativamente elevados para a concentração de cálcio associada, apesar destes ainda poderem estar no intervalo de referência (1). Baseado na correlação inversa entre os níveis séricos de 25-OHD e PTH, alguns experts sugerem que os níveis adequados de vitamina D para supressão do PTH deveriam ser de pelo menos 30ng/ml, apesar de

ainda não haver consenso (12-14). Não obstante, alguns pacientes com hipovitaminose D não apresentam níveis elevados de PTH, uma condição descrita como hipoparatireoidismo funcional (15), a qual não é rara (1,16). Estes pacientes parecem ter menos conseqüências sobre a saúde do que aqueles com hiperparatireoidismo secundário, como níveis elevados de marcadores de remodelamento ósseo e aumento do risco de mortalidade (15,17,18). As causas desta condição ainda não estão claras. Um estudo relatou depleção de magnésio em todos pacientes diagnosticados com hipoparatireoidismo functional (19), e em outros esta condição tem sido também associada à hipoalbuminemia (20), uso de diuréticos tiazídicos (21), e a um índice de massa corporal aumentado (22).

O objetivo deste estudo foi avaliar a prevalência de hipovitaminose D e hiperparatireoidismo secundário em pacientes ambulatoriais adultos do sul do Brasil (latitude 30^0), e identificar fatores associados envolvidos na resposta do PTH à hipovitaminose D.

Referências

1. Lips, P., *Vitamin D deficiency and secondary hyperparathyroidism in the elderly: consequences for bone loss and fractures and therapeutic implications*. End Rev, 201. **22**: p. 477-501.

2. Lips P., et al., *A global study of vitamin D status and parathyroid function in postmenopausal women with osteoporosis: baseline data from the multiple outcomes of raloxifene evaluation clinical trial*. J Clin Endocrinol Metab, **86**: p. 1212-1221.

3. Mithal, A., et al., *Global vitamin D status and determinants of hypovitaminosis D. Osteoporos Int,* 2009. **20**: p. 1807-1820.

4. Holick, M.F., *Vitamin D deficiency*. N Eng J Med, 2007. **357**: p. 266-281.

5. Lappe, J.M., et al., *Vitamin D and calcium supplementation and the risk of colon cancer. Am J Clin Nutr*, 2007. **85**: p. 1586-1591.

6. Pittas, A.G., et al., *The role of vitamin D and calcium in type 2 diabetes: A systematic review and meta-analysis*. J Clin Endocrinol Metab, 2007. **92**: p. 2017-2019.

7. Ponsonby, A.L., et al., *Ultraviolet radiation and autoimmune disease: insights from epidemiological research*. Toxicology, 2002. **181-182**; p. 71-78.

8. Orwoll, E., et al., *Vitamin D deficiency in older men*. J Clin Endocrinol Metab, 2009. **94**: p. 1214-1222.

9. Binkley, N., et al., *Assay variation confounds the diagnosis of hypovitaminosis D: a call for standardization*. J Clin Endocrinol Metab, 2004. **89**: p. 3152-3157.

10. Holick, M.F., et al., *The use and interpretation of assays for vitamin D and its metabolites*. J Nutr, 1990. **120**: p. 1464-1469.

11. Heaney, R.P., et al., *Calcium absorptive effects of vitamin D and its major metabolites*. J Clin Endocrinol Metab, 1997. **82**: p. 4111-4116.

12. Dawson-Hughes, B., et al., *Estimates of optimal vitamin D status*. Osteoporos Int, 2005. **16**: p. 713-716.

13. Chapuy, M.C., et al., *Prevalence of vitamin D insufficiency in an adult normal population*. Osteoporos Int, 1997. **7**: p. 439-443.

14. Thomas, M.K., et al., *Hypovitaminosis D in medical inpatients*. N Eng J Med, 1998. **338**: p. 777-783.

15. Sahota, O., et al., *The relationship between vitamin D and parathyroid hormone: calcium homeostasis, bone turnover, and bone mineral density in postmenopausal women with established osteoporosis.* Bone, 2004. **35**: p. 312-319.

16. Binkley, N., et al., *Low vitamin D status despite abundant sun exposure*. J Clin Endocrinol Metab, 2007. **92**: p. 2130-2135.

17. Chen, J.S., et al., *Hypovitaminosis D and parathyroid hormone response in the elderly: effects on bone turnover and mortality*. Clin Endocrinol, 2008. **68**: p.290-298.

18. Sambrook, P.N., et al., *Serum parathyroid hormone is associated with increased mortality independent of 25-hydroxy vitamin D status, bone mass, and renal function in the frail and very old: a cohort study*. J Clin Endocrinol Metab, 2004. **89**: p.5477-5481.

19. Sahota, O., et al., *Vitamin D insufficiency and the blunted PTH response in established osteoporosis: the role of magnesium deficiency*. Osteoporos Int, 2006. **17**: p.1013-1021.

20. Premaor, M.O., et al., *Hyperparathyroidism secondary to hypovitaminosis D in hypoalbuminemic is less intense than in normoalbuminemic patients: a prevalence study in medical inpatients in southern Brazil.* Endocrine, 2004. **24**: p.47-53.

21. Rejnmark, L., et al., *Effects of thiazide- and loop-diuretics, alone or in combination, on calciotropic hormones and biochemical bone markers: a randomized controlled study*. J Intern Med, 2001. **250**: p. 144-153.

22. Kamycheva, E., et al., *Serum parathyroid hormone level is associated with body mass index: The 5th Tromso Study*. Eur J Endocrinol, 2004. **151**: p. 167-172.

ARTIGO

Hyperparathyroidism secondary to hypovitaminosis D depends on serum levels of magnesium

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Abstract

Context. Vitamin D deficiency in adults may precipitate or worsen osteopenia and osteoporosis, cause muscular weakness and osteomalacia, and increase the risk of bone fractures. Some of these effects may be mediated by secondary hyperparathyroidism induced by low 25-hydroxyvitamin D (25-OHD) levels. It is not clear why some individuals do not develop elevation in parathyroid hormone (PTH) levels following vitamin D deficiency.

Objective. To estimate the prevalence of hypovitaminosis D and secondary hyperparathyroidism in a sample of adult ambulatory patients, and analyze possible causes of absence of correlation between 25-OHD and PTH levels.

Design and setting. Cross-sectional study of 91 outpatients of a tertiary care center in Southern Brazil (latitude 30^0S).

Patients. Adults aged 40 years or older.

Main Outcome Measures. Serum levels 25-OHD measured by chemiluminescence and serum levels of PTH measured by electrochemiluminescence.

Results. Mean age was 60.3 ± 12 years, 56 (61.5%) women, and 70 (76.9%) white. Hypovitaminosis D was found in 69 (75.9%), 11 (12.1%) had secondary hyperparathyroidism and none had hypomagnesemia (Mg <1.5 mEq/L). There was no significant correlation between serum levels of 25-OHD and PTH, but this correlation became significant when individuals with magnesium serum level > 2.1 mg/dl were considered in the analysis ($r = 0.37$, $p = 0.02$). There was a positive correlation between PTH and serum magnesium levels in the normal range ($r = 0.29$, $p < 0.01$).

Conclusions. The association between hypovitaminosis D and secondary hyperparathyroidism is dependent on serum levels of magnesium.

Introduction

Vitamin D has a major role in human health, with functions that extend beyond its well known effects over mineral and bone metabolism, such as muscle function, cellular differentiation, and immunity (1). Inadequate levels of this hormone seems to be a common finding in the adult population throughout the world, despite differences in prevalence regarding to age, ethnicity, latitude, season, amount of sun exposure, vitamin D supplementation or food fortification (2,3). Hypovitaminosis D may cause secondary hyperparathyroidism, precipitate or worsen osteopenia and osteoporosis, cause osteomalacia and muscle weakness, increase the risk of falls and bone fracture (4), and it is been associated with development of cancer (5), diabetes (6), and autoimmune diseases (7). Since vitamin D deficiency can be corrected by easy, safe, and inexpensive means, increased attention has been given to identify and correct this health issue (8).

The standard method for evaluation of vitamin D status is the measurement of serum levels of its main metabolite, 25-hydroxyvitamin D (25-OHD) (9), because of its long serum half life, correlation with calcium absorption, and the 25-hydroxilation step is unregulated, even though there is considerable variation and lack of standardization between different assays (10-11).

Hypovitaminosis D is associated to development of secondary Hyperparathyroidism, when PTH levels are relatively elevated for the associated serum calcium concentration, although it may be still in the reference range (1). Based on the inverse correlation between serum levels of 25-OHD and parathyroid hormone (PTH), some experts suggest that this should be at least 30 ng/ml, although there is still no consensus (12-14). However, some patients with hypovitaminosis D do not show elevated PTH levels, a condition described as functional hypoparathyroidism (15). Functional hypoparathyroidism is not uncommon (1,16),

and these patients seem to have less health consequences than those with secondary hyperparathyroidism, such as elevated bone remodeling markers and increased mortality risk (15,17,18). Causes of this condition are still unclear. One study reported magnesium depletion in all patients diagnosed with functional hypoparathyroidism (19), and in others PTH concentrations have also been associated with hypoalbuminemia (20), thiazide diuretic use (21), and body mass index (22).

The aim of this study was to evaluate the prevalence of hypovitaminosis D and secondary hyperparathyroidism in adult ambulatory patients in Southern Brazil (latitude 30^0) and to identify associated factors implied in parathyroid hormone response to hypovitaminosis D.

Patients and methods

Study participants: consecutive ambulatory patients sent between April and May/2008 (early autumn) for blood collection by their assistant physician to the laboratory area of Hospital de Clinicas de Porto Alegre were enrolled in the study. Inclusion criterion was age $\geq$40 years old. Exclusion criteria were: inability to walk, vegetarian or lactovegetarian feeding habit, alcohol or illicit drugs abuse, renal or hepatic failure, chronic diarrhea, history of previous gastrointestinal surgery, and hypercalcemia. Renal failure was defined as a serum creatinine above 1.5 mg/dl. The study protocol was approved by the Institucional Ethics in Research Committee and individuals gave written informed consent. Eligible patients were instructed to fill a standardized questionnaire about lifestyle and medical history, containing data about age, smoking status, alcohol use or illicit drug abuse, ethnicity, physical activity levels (graded according to ref. 23), use of sunscreen blockers or drugs known to affect mineral metabolism (calcium and vitamin D supplements, thiazide diuretics, bisphosphonates, glucocorticoids, anticonvulsivants and rifampicine). Two additional blood samples for the

study were collected, at the same time of the blood collection ordered by their attending physicians.

Biochemical analysis

25-OHD was measured by chemiluminescence (LIAISON® kit, DiaSorin Inc., Stillwater, MN-USA) – intra-assay CV 8-13% and interassay CV 8-15%. PTH was measured by electrochemiluminescence (Elecsys-Modular E-170, Roche Diagnostics, Indianapolis-USA) – intra-assay CV 0.6-1.8% and interassay CV 1.6-3.4%. Serum calcium, albumin, magnesium and creatinine were measured by standard routine methods (Modular-P, Roche Diagnostics, Indianapolis-USA). All blood samples were collected in the morning. Samples for 25-OHD were kept frozen at -70^0C for a single time testing. The other tests were performed from a separate sample processed within the first hour after specimen collection. The equation of MDRD (Modification of Diet in Renal Disease) was used for calculation of the estimated glomerular filtration rate (eGFR) (24). Hypovitaminosis D was defined as serum 25-OHD levels below 30 ng/ml. Secondary hyperparathyroidism was defined as PTH levels above 65 pg/ml (the upper limit of the reference range).

Statistical methods

Results are expressed in mean ± standard deviation. Comparisons between variables were made by t-student test and one-way ANOVA for continuous variables with normal distribution, and by chi-squared test for categorical variables. Correlations between two continuous variables were determined by Pearson's correlation coefficient. Multivariate analyses were done by multiple linear regression analysis (stepwise) with endpoints considered as dependent variables. Statistical analysis were made using the 13^{th} version of the Statistical Package for Social Sciences (SPSS). Analysis with an α error $\leq$ 5% were considered as statistically significant.

Results

A total of 97 patients were screened, and 6 patients were excluded due to creatinine levels above 1.5 mg/dl. Therefore, 91 patients were analyzed. The mean age was 60.3 ± 12 years, 56 (61.5%) were women, and 70 (76.9%) were white.

Vitamin D status

Hypovitaminosis D was observed in 69 (75.9%) patients. Clinical and laboratory features of patients with and without hypovitaminosis D are shown in table 1.

Patients with hypovitaminosis D were older (P = 0.04), and had a lower level of physical activity (P = 0.01) than those with adequate levels of this hormone. There were no significant differences between groups regarding to gender, ethnicity, sunscreen use, calcium or vitamin D supplement use, thiazide diuretic, bisphosphonate or glucocorticoid use. Also, no significant differences were found regarding to mean serum levels of PTH, calcium, albumin, magnesium and creatinine, and eGFR.

There were no significant correlations between serum levels of 25-OHD and calcium (r = -0.16; P = 0.12), albumin (r = 0.04; P = 0.69), magnesium (r = -0.04; P = 0.74), creatinine (r = 0.09; P = 0.42), and eGFR (r = -0.04; P = 0.68).

Secondary hyperparathyroidism

PTH levels above 65 pg/ml were found in 11 (12.1%) patients. Of those, 8 (72.7%) had hypovitaminosis D. Clinical and laboratory features of patients with and without secondary hyperparathyroidism are shown in table 2.

Patients with secondary hyperparathyroidism were older (P = 0.04), did not use sunscreen (P = 0.03), and as expected had higher serum levels of creatinine (P < 0.01), with consequently lower eGFR (P < 0.01) than patients without secondary hyperparathyroidism. There were no significant differences between groups regarding to gender, ethnicity, physical

activity levels, calcium or vitamin D supplement use, thiazide diuretic, bisphosphonate, or glucocorticoid use. Also, no significant differences were found regarding to mean serum levels of 25-OHD, calcium, albumin or magnesium.

There was no correlation between serum levels of 25-OHD and PTH ($r = 0.10$; $P = 0.35$). However, that correlation reached significance when only patients in the upper quartile of magnesium levels (above 2.1 mg/dl) were considered in the analysis ($r = 0.37$; $P = 0.02$; $n = 40$) (Figure 1.). Also, serum levels of PTH were correlated with age ($r = 0.32$; $P = 0.02$), creatinine ($r = 0.382$; $P <0.01$), eGFR ($r = -0.379$; $P <0.01$), and magnesium levels ($r = 0.29$; $P = 0.01$). No correlation was found between PTH and calcium ($r = 0.02$; $P = 0.85$) or albumin ($r = 0.19$; $P = 0.08$).

In multivariate linear regression analysis of all patients, with serum levels of PTH as the dependent variable and age, eGFR, serum levels of 25-OHD and magnesium as independent variables, only eGFR (adjusted R^2: 0.15; β coefficient: -0.39; $P <0.01$) and magnesium (adjusted R^2: 0.22; β coefficient: 0.28; $P <0.01$) remained significantly associated with PTH. Considering only patients with serum levels of magnesium >2.1 mg/dl (n=40), the variation of PTH was significantly associated with magnesium (adjusted R^2: 0.14; β coefficient: 0.36; $P = 0.01$), eGFR (adjusted R^2: 0.25; β coefficient: -0.33; $P = 0.02$), and 25-OHD (adjusted R^2: 0.31; β coefficient: -0.28; $P = 0.04$).

Discussion

In this sample of adult outpatients from Southern region from Brazil, hypovitaminosis D was observed in approximately 76%, especially in older and sedentary patients. Notwithstanding, we found a low prevalence (12%) of secondary hyperparathyroidism, which was not expected. Also, we didn't find correlation between serum 25-OHD and PTH levels, unless we considered only patients in the upper quartile of magnesium concentrations.

Global estimates of vitamin D have found large differences in the prevalence of vitamin D inadequacy around the world, depending on different cutoff points and laboratory methods used for dosing 25-OHD and defining vitamin D status (3). As an example, in a review study by Holick M., 40 to 100% of community living elderly from U.S. and Europe where vitamin D deficient (4). Previous reports from Brazil found prevalence rates of vitamin D inadequacy in postmenopausal women ranging from 42.4 to 66.7% using the serum 25-OHD level cutoff point of 30 ng/ml (25,26), and in 57.3% of community living elderly, using the cutoff point of 20 ng/ml (27). The higher latitude of Porto Alegre in relation to the other cities in Brazil were previous studies were conducted could have accounted for the higher prevalence rate of hypovitaminosis D observed.

Another factor that could be attributed to the differences in the hypovitaminosis D rates is that different methods are used for dosing 25-OHD. In fact, one study (26) mentioned above used the Nichols ADVANTAGE assay, which showed a poor correlation with the gold-standard method of chromatography-tandem mass spectrometry (LC-MS/MS) (28). However, the method used in this study was previously shown to have acceptable correlation with the DiaSorin RIA method (25), and also with the LC-MS/MS method (28,29). In fact, a study using LC-MS/MS as the method of reference for dosing serum levels of 25-OHD reported a hypovitaminosis D prevalence of 71.1% in elderly men living in U.S. communities (mean age 73.8 years), similarly to our findings (8).

We observed a low rate of secondary hyperparathyroidism in spite of a high rate of vitamin D inadequacy. Very few studies have specifically addressed this issue, and the prevalence of this condition is still undefined, being described to be up to 75% (17). It is clinically relevant to identify patients with functional hyperparathyroidism, since they seem to have more favorable outcomes when compared to patients that develop secondary

hyperparathyroidism (15,17-19,30). One report, on a cohort of 1280 elderly men and women living in residential care facilities, found elevation in bone remodeling markers (PINP and CTX-I) and increased mortality risk only in patients with hypovitaminosis D and elevated PTH levels (17). Another authors, evaluating postmenopausal women with vertebral fractures, found increased bone turnover markers only in those with hypovitaminosis D and secondary hyperparathyroidism (15). Moreover, the Fracture Risk Epidemiology in the Frail Elderly (FREE) Study reported increased mortality in frail elderly patients with elevated PTH and high bone turnover independent of vitamin D status (18,30). We identified a magnesium dependency over the elevation of serum PTH following hypovitaminosis D, as the correlation between serum 25-OHD and PTH became significant only when patients in the upper quartile of magnesium levels were included in statistical analysis. To our knowledge, only one study had described similar findings. Sahota et al. reported, in a small group of 10 patients with functional hypoparathyroidism, that all of them had magnesium deficiency when evaluated by a magnesium loading test, and still, those showed a significant elevation in PTH and bone turnover markers after oral magnesium supplementation (19).

Possible limitations of this study include small sample size, which could have blunted the correlation between 25-OHD and variables such as gender, sunscreen use and ethnicity, as reported in previous studies. Also, we are aware that magnesium status may be better stated through a magnesium load/retention test, but the finding that serum magnesium levels in the normal range influence the serum PTH response to hypovitaminosis D is a new interesting aspect that should be properly addressed in future studies.

In conclusion, hypovitaminosis D is highly prevalent, and in a significant proportion of patients this is not coupled to secondary hyperparathyroidism. To our knowledge, the

correlation between serum magnesium levels in the normal range and PTH in a population of vitamin D inadequacy has not been previously reported.

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References:

1. Lips P 2001 Vitamin D deficiency and secondary hyperparathyroidism in the elderly: consequences for bone loss and fractures and therapeutic implications. End Rev 22:477-501

2. Lips P, Duong T, Oleksik A, Black D 2001 A global study of vitamin D status and parathyroid function in postmenopausal women with osteoporosis: baseline data from the multiple outcomes of raloxifene evaluation clinical trial. J Clin Endocrinol Metab 86:1212-1221

3. Mithal A, Wahl DA, Bonjour JP, Burckhardt P, Dawson-Hughes B, Eisman JA, El-Hajj Fulerhan G, Josse RG, Lips P, Morales-Torres J for the IOF Commitee of Scientific Advisors (CSA) Nutrition Working Group 2009 Global vitamin D status and determinants of hypovitaminosis D. Osteoporos Int 20:1807-1820

4. Holick MF 2007 Vitamin D deficiency. N Eng J Med 357:266-281

5. Lappe JM, Travers-Gustafson D, Davies KM, Recker RR, Heaney RP 2007 Vitamin D and calcium supplementation and the risk of colon cancer. Am J Clin Nutr 85:1586-1591

6. Pittas AG, Lau J, Hu FB, Dawson-Hughes B 2007 The role of vitamin D and calcium in type 2 diabetes: A systematic review and meta-analysis. J Clin Endocrinol Metab 92:2017-2019

7. Ponsonby AL, McMichael A, van der Mei I 2002 Ultraviolet radiation and autoimmune disease: insights from epidemiological research. Toxicology 181-182;71-78

8. Orwoll E, Nielson CM, Marshall LM, Lambert L, Holton KF, Hoffman AR, Barrett-Connor E, Shikany JM, Dam T, Cauley JA for the Osteoporotic Fractures in Men (MrOS) Study Group 2009 Vitamin D deficiency in older men. J Clin Endocrinol Metab 94:1214-1222

9. Binkley N, Krueger D, Cowgill CS, Plum L, Lake E, Hansen KE, DeLuca HF, Drezner MK 2004 Assay variation confounds the diagnosis of hypovitaminosis D: a call for standardization. J Clin Endocrinol Metab 89:3152-3157

10. Holick MF 1990. The use and interpretation of assays for vitamin D and its metabolites. J Nutr 120:1464-1469

11. Heaney RP, Barger-Lux MJ, Dowell MS, Chen TC, Holick MF 1997 Calcium absorptive effects of vitamin D and its major metabolites. J Clin Endocrinol Metab 82:4111-4116

12. Dawson-Hughes B, Heaney RP, Holick MF, Lips P, Meunier PJ, Vieth R 2005 Estimates of optimal vitamin D status. Osteoporos Int 16:713-716

13. Chapuy MC, Preziosi P, Maamer M, Arnaud S, Galan P, Hercberg S, Meunier PJ 1997 Prevalence of vitamin D insufficiency in an adult normal population. Osteoporos Int 7:439-443

14. Thomas MK, Lloyd-Jones DM, Thadhani RI, Shaw AC, Deraska DJ, Kitch BT, Vamvakas EC, Dick IM, Prince RL, Finkelstein JS 1998 Hypovitaminosis D in medical inpatients. N Eng J Med 338:777-783

15. Sahota O, Mundey MK, San P, Godber IM, Lawson N, Hoskin DJ 2004 The relationship between vitamin D and parathyroid hormone: calcium homeostasis, bone turnover, and bone mineral density in postmenopausal women with established osteoporosis. Bone 35:312-319

16. Binkley N, Novotny D, Krueger D, Kawahara T, Daida YG, Lensmeyer G, Hollis BW, Drezner MK 2007 Low vitamin D status despite abundant sun exposure. J Clin Endocrinol Metab 92:2130-2135

17. Chen JS, Sambrook PN, March L, Cameron ID, Cumming RG, Simpson JM, Seibel MJ 2008 Hypovitaminosis D and parathyroid hormone response in the elderly: effects on bone turnover and mortality. Clin Endocrinol 68:290-298

18. Sambrook PN, Chen JS, March LM, Cameron ID, Cumming RG, Lord SR, Schwartz J, Seibel MJ 2004 Serum parathyroid hormone is associated with increased mortality independent of 25-hydroxy vitamin D status, bone mass, and renal function in the frail and very old: a cohort study. J Clin Endocrinol Metab 89:5477-5481

19. Sahota O, Mundey MK, San P, Godber IM, Hosking DJ 2006 Vitamin D insufficiency and the blunted PTH response in established osteoporosis: the role of magnesium deficiency. Osteoporos Int 17:1013-1021

20. Premaor MO, Alves GV, Crossetti LB, Furlanetto TW 2004 Hyperparathyroidism secondary to hypovitaminosis D in hypoalbuminemic is less intense than in normoalbuminemic patients: a prevalence study in medical inpatients in southern Brazil. Endocrine 24:47-53

21. Rejnmark L, Vestergaard P, Heinckendorff L, Andreasen F, Moselkilde L 2001 Effects of thiazide- and loop-diuretics, alone or in combination, on calciotropic hormones and biochemical bone markers: a randomized controlled study J Intern Med 250:144-153

22. Kamycheva E, Sundsfjord J, Jorde R 2004 Serum parathyroid hormone level is associated with body mass index: The 5th Tromso Study. Eur J Endocrinol 151:167-172

23. Tuomilehto J, Lindström J, Eriksson JG, Valle TT, Hämäläinen H, Illane-Parikka P, Keinanen-Kiukaanniemi S, Laakso M, Louheranta MS, Rastas M, Salminen V, Aunola S, Cepaitis Z, Moltchanov V, Harumaki M, Mannelin M, Martikkala V, Sundvall J, Uusitupa M, for the Finnish Diabetes Prevention Study Group 2001 Prevention of type 2 diabetes

by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med 344:1343-1350

24. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D; and for the Modification of Diet in Renal Disease Group 1999 A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. Ann Int Med 130:461-470

25. Russo LAT, de Gregorio LH, Lacativa PGS, Marinheiro LPF 2009 Concentração plasmática de 25 hidroxivitamina D em mulheres na pos-menopausa com baixa densidade mineral ossea. Arq Bras Endocrinol Metab 53:1079-1087

26. Lips P, Hosking D, Lippuner K, Norquist JM, Wehren L, Maalouf G, Ragi-Eis S, Chandler J 2006 The prevalence of vitamin D inadequacy amongst women with osteoporosis: an international epidemiological investigation. J Int Med 260:245-254

27. Saraiva GL, Cendoroglo MS, Ramos LR, Araújo LM, Vieira JG, Kunii I, Hayashi LF, Correa MP, Lazaretti-Castro M 2005 Influence of ultraviolet radiation on the production of 25-hydroxivitamin D in the elderly population in the city of São Paulo (23 degrees 34´S), Brazil. Osteoporos Int 16:1649-1654

28. Terry AH, Sandrock T, Meikle AW 2005 Measurement of 25-hydroxyvitamin D by the Nichols ADVANTAGE, DiaSorin LIAISON, DiaSorin RIA, and Liquid Chromatography-Tandem Mass Spectrometry. Clin Chem 51:1565-1566

29. Ersfeld DL, Rao DS, Body JJ, Sackrison Jr. JL, Miller AB, Parikh N, Eskridge TL, Polinske A, Olson GT, MacFarlane GD 2004 Analytical and clinical validation of the 25 OH vitamin D assay for the LIAISON automated analyzer. Clin Biochem 37:867-874

30. Sambrook PN, Chen CJ, March L, Cameron ID, Cumming RG, Lord SR, Simpson JM, Seibel MJ 2006 High bone turnover is an independent predictor of mortality in the frail elderly. J Bone Min Res 21:549-555

Table 1. Clinical and laboratory features of patients according to vitamin D status

	Vitamin D status		
	Hypovitaminosis D	Adequate	P
	69 (75.8)	22 (24.2)	
Age (years)	60.6 ± 12.3	59.6 ± 11.5	0.04
Women	46 (66.6)	10 (45.5)	0.07
White	53 (76.8)	17 (77.3)	0.96
Physical activity			
None / mild	62 (92.5)	16 (72.7)	0.01
Moderate / intense	5 (7.5)	6 (27.2)	
Sunscreeen use	21 (30.4)	4 (18.2)	0.26
Vit. D supplement	7 (10.1)	4 (18.2)	0.31
Calcium supplement	10 (14.5)	5 (22.7)	0.37
Thiazide diuretic	23 (33.3)	11 (50)	0.16
Bisphosphonate	5 (7.2)	1 (4.5)	0.66
Glucocorticoid	1 (1.4)	1 (4.5)	0.39
PTH (pg/ml)	44.2 ± 17.2	44.2 ± 15.7	0.99
Total calcium (mg/dl)	9.1 ± 0.5	9 ± 0.4	0.21
Albumin (g/L)	4.4 ± 0.3	4.4 ± 0.3	0.7
Magnesium (mg/dl)	2.1 ± 0.2	2.1 ± 0.2	0.97
Creatinine (mg/dl)	0.8± 0.2	0.9 ± 0.2	0.16
eGFR	89.5 ± 22.1	85.3 ± 21.1	0.44
25-OHD (ng/ml)	18.6 ± 5.8	38.4 ± 7.9	---

Table 2. Clinical and biochemical features of patients with or without secondary hyperparathyroidism

	Secondary hyperparathyroidism		
	Present	Absent	P
	11 (12.1)	80 (87.9)	
Age (years)	67.3 ± 9.1	59.4 ± 12.1	0.04
Women	5 (45.5)	51 (63.8)	0.24
Whites	6 (54.5)	64 (80)	0.06
Physical activity			
None / mild	8 (72.7)	44 (56.4)	0.30
Moderate / intense	3 (27.3)	34 (43.6)	
Sunscreen use	0	25 (31.3)	0.03
Vit. D supplement	1 (9.1)	10 (12.5)	0.74
Calcium supplement	1 (9.1)	14 (17.5)	0.48
Thiazide diuretic	4 (36.4)	30 (37.5)	0.94
Bisphosphonate	1 (9.1)	5 (6.3)	0.72
Glucocorticoids	1 (9.1)	1 (1.3)	0.09
25-OHD (ng/ml)	22.0 ± 9.8	23.5 ± 10.7	0.67
Total calcium (mg/dl)	9.1 ± 0.4	9.1 ± 0.4	0.51
Albumin (g/L)	4.4 ± 0.3	4.3 ± 0.2	0.31
Magnesium (mg/dl)	2.2 ± 0.3	2.1 ± 0.2	0.12
Creatinine (mg/dl)	1.1 ± 0.2	0.8 ± 0.2	< 0.01
eGFR	65.3 ± 19.1	91.6 ± 20.3	< 0.01
PTH (pg/ml)	77.7 ± 9.1	39.6 ± 11.5	---

Figure 1. PTH concentrations according to 25-OHD levels. Panel A: all patients (n=91); Panel B: patients with serum magnesium > 2.1mg/dl (n = 40)

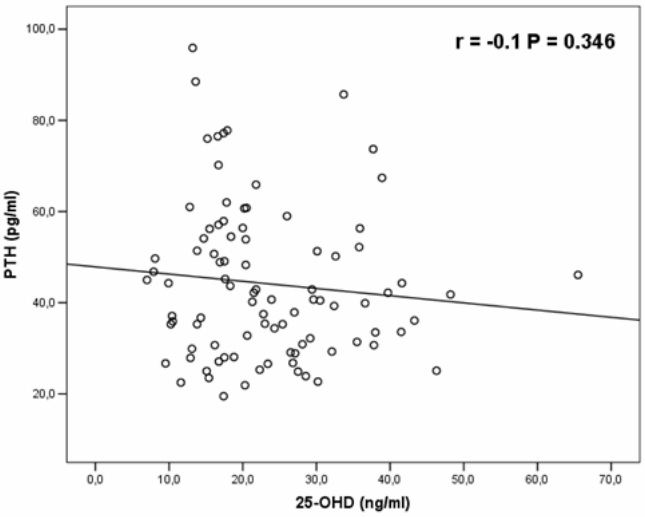

Figure 1a. PTH concentrations according to 25-OHD levels in all patients (n=91)

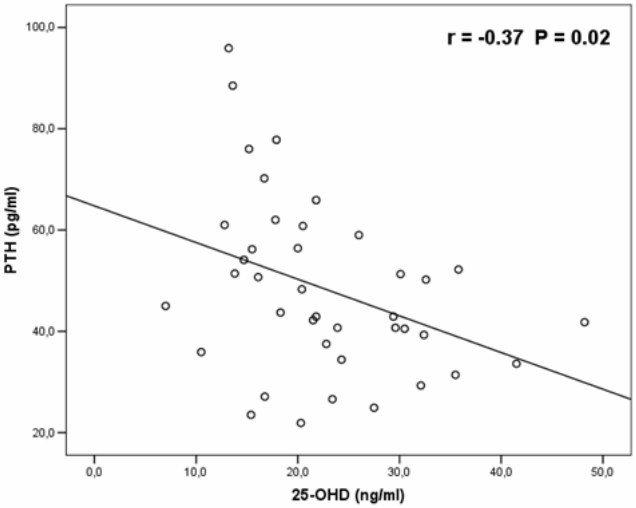

Figure 1b. PTH concentrations according to 25-OHD levels in patients with serum magnesium > 2.1 mg/dl (n=40)

PERSPECTIVAS FUTURAS

Como seguimento da linha de pesquisa em vitamina D e hiperparatireoidismo secundário, pretendemos estudar o efeito da sazonalidade sobre os níveis de vitamina D e PTH, bem como avaliar as relações entre magnésio, PTH e vitamina D através do teste de sobrecarga/retenção de magnésio e através da reposição oral deste eletrólito.

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