Nutrition 29 (2013) 1147–1151

Contents lists available at ScienceDirect

Nutrition

journal homepage: www.nutritionjrnl.com

Applied nutritional investigation

Parathyroid hormone has an important role in blood pressure regulation in vitamin D–insufficient individuals

Vivian Cristina Garcia M.Sc., Natielen Jacques Schuch Ph.D., Antonela Siqueira Catania M.D., Ph.D., Sandra Roberta Gouvea Ferreira M.D., Ph.D., Lígia Araújo Martini Ph.D. *

Nutrition Department, School of Public Health, University of Sao Paulo, Brazil

ARTICLE INFO

Article history:
Received 22 August 2012
Accepted 20 March 2013

Keywords:
Vitamin D
Parathyroid hormone
Blood pressure
Hypertension
Cardiovascular disease

ABSTRACT

Objective: The aim of the present study was to evaluate whether vitamin D status is related to blood pressure (BP) in adults.
Methods: We evaluated the relationship between vitamin D status, intact parathyroid hormone (iPTH) and BP in 332 adults. Anthropometric measurements, BP, and a fasting blood sample was obtained. Participants were stratified into the following BP categories: 1) normal BP; 2) high BP; 3) normal BP through medication. Vitamin D insufficiency was defined as 25-hydroxvitamin D $\leq$ 75 nmol/L; high iPTH as $>$ 65 pg/mL. The relationships between vitamin D status, iPTH and BP were adjusted for body mass index, waist circumference, blood lipids, physical activity, and sunscreen use.
Results: No differences in prevalences of vitamin D insufficiency and high iPTH were observed among BP groups. No significant association was observed between BP and vitamin D status. Positive correlations were observed between iPTH and systolic BP ($r = 0.168$; $P = 0.002$) and between iPTH and diastolic BP ($r = 0.168$; $P = 0.002$). iPTH remained correlated with BP even with adjustments.
Conclusions: The present study contributes to the understanding of calcemic hormones and BP regulation.

Introduction

Hypertension remains a major risk factor for cardiovascular disease (CVD). About 1 billion people worldwide suffer from hypertension, and this may be responsible for approximately 7.1 million deaths per year [1]. Recently, the Brazilian Society of Hypertension [2] published data showing that in 2007, approximately 309,000 deaths were caused by CVD and that the estimated prevalence of hypertension was greater than 30%. According to the World Health Organization (WHO) [3], CVDs are the leading cause of death globally and by 2030, 23.6 million people will die from this illness.

There is much evidence to show that vitamin D is involved in several mechanisms in addition to bone metabolism [4]. Vitamin D insufficiency/deficiency has been associated with hypertension worldwide [5–7] and with the cardiovascular complications of hypertension [8–10]. As depicted in a recent review [11], vitamin D may be involved in regulation of gene expression through the presence of vitamin D receptors in various cells. Regarding the regulation of blood pressure (BP), there is evidence that 25-hydroxyvitamin D (25[OH]D) acts through the renin–angiotensin system, as well as through modulation of cell growth and proliferation, including vascular smooth muscle cells and cardiomyocytes.

Moreover, several studies have observed vitamin D insufficiency/deficiency even in sunny countries, especially in adults and the elderly [12,13]. Factors that reduce its synthesis, such as high levels of air pollution and low levels of outdoor activities, may be the cause of this situation. Nevertheless, the effects of vitamin D insufficiency/deficiency on BP have not been evaluated in Brazilian populations.

Thus, the aim of the present study was to evaluate whether vitamin D status is related to BP in adults.

Participants and methods

Study design

This cross-sectional study was conducted among non-institutionalized adults attending a public primary care unit linked to the School of Public

* Corresponding author. Tel.: +55 11 30617859; fax: +55 11 30617731.
E-mail address: lmartini@usp.br (L. A. Araújo Martini).

0899-9007/$ - see front matter © 2013 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.nut.2013.03.022

Health, University of Sao Paulo. The local ethics committees approved the study protocol, and all participants signed an informed consent statement.

The exclusion criteria were that the participants could not be younger than age 18 y; could not be pregnant or lactating; and could not have had previous cardiovascular events or diseases that might modify their vitamin D metabolism (chronic kidney disease, neoplasia, diabetes, or osteoporosis). Black individuals; individuals with abnormal concentrations of creatinine, calcium, or phosphorus; and those who reported using vitamin D and/or calcium or multivitamin supplements were also excluded.

A sample of 460 individuals was screened between August 2007 and January 2010; 128 were excluded due to diabetes mellitus (n = 57) or abnormal creatinine, calcium, or phosphorus (n = 19). Six individuals presented outlying serum concentrations of parathyroid hormone (PTH); 1 had outlying serum concentrations of 25(OH)D and another 45 fulfilled other exclusion criteria. Thus, 332 individuals who agreed to participate were included in this analysis.

Measurements

Height was measured using a fixed stadiometer with a vertical backboard and movable headboard, with participants standing on the floor. Weight was taken by asking each individual to stand at the center of the platform of a Tanita™ digital scale (Tanita Corporation of America Inc., Illinois, USA). Body mass index (BMI = weight [kg]/height [m]^2) was calculated. Waist circumference (WC) was measured while participants were standing up, with a tape placed at the midpoint level between the lower intercostal border and the anterior superior iliac supine as the participants were gently exhaling. Percent body fat mass (%FM) and percent body fat-free mass (%FFM) were assessed by means of tetrapolar bioelectrical impedance analysis (Quantum BIA 101Q, RJL, Detroit, USA).

BP was obtained using an automatic BP monitor (Omron model HEM-712C, Omron Health Care, Inc., USA). Three measures were taken at rest in a sitting position, with intervals of 5 min between the measurements. The average from the last two measurements was taken for analysis. The participants were stratified into categories: 1) normal BP (NBP): those with systolic/diastolic BP (SBD/DBP) $\leq$ 140/90 mm Hg; 2) high blood pressure (HBP): taken to be individuals with BP $\geq$ 140/90 mm Hg; and 3) normal BP through medication (NBPM): when individuals had normal BP achieved through pharmacological treatment.

After 12 h of fasting, a blood sample was collected from each individual, and was frozen and stored at −80°C until analysis. Serum triacylglycerol, total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and glucose were determined by enzymatic colorimetric assay (Celm™, Barueri, SP, Brazil), and creatinine was determined using a colorimetric assay (Celm™, Barueri, SP, Brazil). Calcium and phosphorus were determined using another colorimetric assay (Bioclin™, Belo Horizonte, MG, Brazil). Serum concentrations of 25(OH)D were measured by high-performance liquid chromatography (Immundiagnostik AG, Bensheim, Germany) with intra-assay coefficients of variation (CVs) of 5.2% and inter-assay CVs of 8.4%. The serum concentrations of intact PTH (iPTH) were measured using an electrochemiluminescence assay (Roche Diagnostics™, São Paulo, SP, Brazil), the intra-assay and inter-assay were both 6% with a reference range of 15 to 65 pg/mL. High PTH was defined as serum concentrations of PTH > 65 pg/mL. Serum 25(OH)D concentrations < 75 nmol/L were defined as cases of insufficiency [14].

The individuals also were asked about the regular physical exercise and use of sunscreen.

Statistical analysis

The results were expressed as means and SDs. Statistical analyses were performed using the Statistical Package for the Social Sciences, version 17.0 (SPSS Inc., Chicago, USA). The significance level taken was 5%. Some skewed variables were log-transformed to obtain normal distribution (PTH, BMI, triacylglycerol, and HDL-C).

Analysis of variance (ANOVA) was used to evaluate differences between BP categories. Associations of 25(OH)D and PTH with covariates were examined using Pearson's correlation.

In secondary analysis, we also investigated whether the associations among vitamin D status, iPTH, and BP were confounded by physical activity, sunscreen use, and other clinical conditions, for example dyslipidemia (TC, LDL-C, and triacylglycerol) and obesity (BMI and WC). For this, two models were built: model 1 included adjustments for physical activity, sunscreen use, blood lipids (TC, LDL-C, and triacylglycerol) and BMI; in model 2, WC replaced BMI. To evaluate possible interference of pharmacologic treatment in these analyses, we performed the same correlations without participants under antihypertensive medication. Finally, to better display the associations between PTH and BP, we performed the correlation analysis without individuals with high PTH.

Multiple linear regression models were used for testing 25(OH)D and iPTH as continuous variables for predicting SBP and DBP with the whole sample and then without individuals under hypertension treatment.

Results

High BP was present in 34% of the whole sample, and another 16% were taking medication for hypertension. Overweight and obesity (WHO, 1997) was present in 75% of the individuals. Only 23% of whole sample reported practice regular physical exercise and the use of sunscreen was present in 22% of individuals. The general characteristics of the whole sample and in the different subsamples are presented in Table 1. As expected, BMI, WC, glucose, and triacylglycerol were significantly higher in individuals with high BP and in those who were under hypertension treatment. No differences were observed regarding the prevalence of vitamin D insufficiency and high PTH among the BP groups.

Table 2 shows the serum concentrations of 25(OH)D and other calcemic hormones in the whole sample and in each BP group. The serum iPTH concentrations were significantly higher in individuals with high BP than in individuals with normal BP.

No significant association was observed between the concentrations of 25(OH)D and BP. However, vitamin D status was positively associated with TC ($r = 0.479$; $P = 0.000$), LDL-C ($r = 0.360$; $P = 0.000$) and log triacylglycerol ($r = 0.491$; $P = 0.000$). From analysis on associations between 25(OH)D and BP with adjustments, no correlation was observed either in model 1 or in model 2.

On the other hand, positive correlations were observed between iPTH and the following: SBP ($r = 0.168$; $P = 0.002$), DBP ($r = 0.168$; $P = 0.002$), BMI ($r = 0.125$; $P = 0.023$), WC ($r = 0.172$; $P = 0.002$), and %FM ($r = 0.158$; $P = 0.004$). There was a negative

Table 1
General characteristics of the whole sample

Variable	Whole sample	Normal blood pressure	High blood pressure	Normal blood pressure through medication	*P*-value
Participants (n)	332	166	112	54	
Age (y)	50 (15)	42 (13)	57 (14)*	59 (11)*	0.000
BMI (kg/m^2)	29 (6)	27 (5)	30 (6)*	31 (6)*	0.000
%FFM	68 (10)	69 (10)	67 (9)	65 (9)*	0.015
%FM	32 (10)	31 (10)	33 (9)	35 (9)*	0.015
Waist circumference (cm)	97 (13)	92 (13)	101 (14)*	100 (12)*	0.000
Gender (%)					
Male	38	38	45	24	
Female	62	62	55	76	
Systolic BP (mm Hg)	129 (18)	118 (11)	148 (14)*	125 (9)*,†	0.000
Diastolic BP (mm Hg)	80 (11)	74 (8)	89 (11)*	77 (7)*,†	0.000
Total cholesterol (mg/dL)	190 (41)	184 (41)	198 (42)*	193 (39)	0.022
LDL-C (mg/dL)	120 (37)	117 (37)	125 (37)	118 (36)	NS
HDL-C (mg/dL)	43 (12)	43 (11)	43 (12)	44 (11)	NS
Triacylglycerol (mg/dL)	134 (76)	122 (77)	146 (79)*	148 (57)*	0.009
Glucose (mg/dL)	93 (11)	91 (11)	94 (13)	97 (12)*	0.006
Vitamin D insufficiency (%)	86	88	84	87	NS
High PTH (%)	12	10	14	13	NS

%FM, percent body fat mass; %FFM; percent body fat-free mass; BMI, body mass index; BP, blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; PTH, parathyroid hormone

Data are mean (SD) for continuous variables and % for categorical variables. High PTH was defined as > 65 pg/mL; vitamin D insufficiency was defined as < 75 nmol/L

* Significant when compared with normal BP group ($P < 0.05$).

† Significant when compared with high BP group ($P < 0.05$).

Table 2
Mean serum concentration of calcemic hormones in the whole sample and in each blood pressure group

Variable	Whole sample (N = 332)	Normal blood pressure (n = 166)	High blood pressure (n = 112)	Normal blood pressure through medication (n = 54)	*P*-value
25(OH)D_3 (nmol/L)	55.8 (17.1)	55.6 (17.7)	56.4 (17.4)	55.3 (15.0)	NS
PTH (pg/mL)	40.8 (18.7)	37.7 (17.7)	44.3 (18.6)*	43.0 (20.4)	0.006
Serum calcium (mg/dL)	9.3 (0.5)	9.2 (0.5)	9.4 (0.4)*	9.4 (0.5)	0.004
Serum phosphorus (mg/dL)	3.7 (0.7)	3.7 (0.7)	3.6 (0.8)	3.7 (0.9)	NS

25(OH)D_3, 25-hydroxyvitamin D_3; PTH, parathyroid hormone
Data are means (SD)
* Significant when compared with normal blood pressure group ($P < 0.05$).

correlation between iPTH and %FFM ($r = -0.158$; $P = 0.004$). Furthermore, when the data were adjusted, in model 1, the associations between PTH and SBP ($r = 0.157$; $P = 0.005$) and between PTH and DBP ($r = 0.139$; $P = 0.014$) were maintained, and a negative association was observed between PTH and vitamin D status ($r = -0.137$; $P = 0.015$). After adjustment, in model 2, the same associations occurred: positive with SBP ($r = 0.146$; $P = 0.010$) and DBP ($r = 0.126$; $P = 0.026$) and negative with vitamin D status ($r = -0.133$; $P = 0.019$).

In a multiple linear regression model (Table 3), iPTH and BMI could only account for 5% of the variation in SBP and 10% of the variation in DBP.

When individuals taking medication for hypertension (n = 54) were excluded from the analysis, significant correlations were found between iPTH and SBP ($r = 0.194$; $P = 0.001$), DBP ($r = 0.211$; $P = 0.001$), and WC ($r = 0.147$; $P = 0.015$). In the secondary analysis, including adjustment for BMI (model 1), vitamin D status was negatively correlated, but not significantly, with SBP ($r = -0.114$; $P = 0.067$), whereas iPTH remained essentially unaltered, with positive correlations with SBP ($r = 0.185$; $P = 0.003$) and DBP ($r = 0.188$; $P = 0.002$). The same correlations appear when analysis was adjusted for WC (model 2).

Thus, in a multiple linear regression (Table 4), the model can explain approximately 6% of the variation in SBP and 13% of the variation in DBP, of the individuals who were not under hypertension treatment.

In the last analysis, individuals with high PTH (n = 40) were excluded and the same correlations between iPTH and SBP ($r = 0.175$; $P = 0.003$) and DBP ($r = 0.151$; $P = 0.009$) were observed. These correlations remain significant when the analysis was performed with adjustments.

Discussion

In the present study, PTH was associated with elevated BP, whereas vitamin D status was not correlated with BP even after exclusion of individuals under treatment for hypertension and adjustment for physical activity, sunscreen use, blood lipids, and BMI or WC. Hellstrom et al. (1958) first described the association between elevated serum concentrations of PTH and hypertension in individuals with hyperparathyroidism [15]. Over the years, the contribution of PTH toward raised BP has been observed even in individuals with PTH within the normal range [16–18]. Another study [19] reported that individuals with higher PTH also were at greater risk for cardiovascular mortality, even when the data were adjusted for established cardiovascular risk factors. Moreover, this association remained present in individuals with PTH within the normal range. Like these studies, PTH in our study was positively correlated with BP, and this association also was observed among individuals with PTH within the normal range even after adjustments. Additionally, all individuals had serum calcium within the normal range. However, in a study performed with Chinese population [20], PTH was associated with BP and risk for hypertension, but this association became non-significant after adjustments.

More recently, in cross-sectional data from National Health and Nutrition Examination Survey (NHANES) 2003–2006, researchers [21] found that PTH was positively correlated with BP and, when PTH was divided into quintiles, the SBP and DBP were 5.9 and 4.5 mm Hg higher, respectively, in the highest quintile of PTH (≥ 59 ng/L) than in the lowest quintile (≤ 27 ng/L). These authors suggested that PTH might modulate the relationship between vitamin D status and BP. Among older Chinese men, one study [22] reported that increased PTH

Table 3
Regression coefficients (B) for PTH (pg/dL), 25(OH)D_3 (nmol/L) and BMI (kg/m^2) regressed against blood pressure in whole sample (N = 332)

	Systolic BP			Diastolic BP		
	B (SE)	B	R^2	B (SE)	B	R^2
Step 1						
Constant	55.39 (18.10)			11.53 (10.50)		
Vitamin D	0.06 (0.06)	0.06		0.05 (0.03)	0.08	
iPTH	13.70 (4.76)	0.16*		7.36 (2.76)	0.14*	
BMI	33.62 (11.97)	0.15*	0.06	36.88 (6.94)	0.28*	0.11
Step 2						
Constant	57.71 (18.00)			13.48 (10.45)		
iPTH	13.11 (4.73)	0.15*		6.87 (2.75)	0.13†	
BMI	35.07 (11.90)	0.16*	0.05	38.10 (6.92)	0.29*	0.10

BMI, body mass index; BP, blood pressure; iPTH, intact parathyroid hormone; PTH, parathyroid hormone
* $P < 0.01$.
† $P < 0.05$.

Table 4
Regression coefficients (B) for PTH (pg/dL), 25(OH)D_3 (nmol/L) and BMI (kg/m^2) regressed against blood pressure in the individuals without medication for hypertension (n = 278)

	Systolic BP			Diastolic BP		
	B (SE)	β	R^2	B (SE)	B	R^2
Step 1						
Constant	40.06 (20.92)			0.06 (11.95)		
Vitamin D	0.06 (0.07)	0.05		0.04 (0.40)	0.07	
iPTH	16.92 (5.58)	0.18*		10.07 (3.19)	0.18*	
BMI	41.75 (14.01)	0.18*	0.06	42.35 (8.00)	0.30*	0.11
Step 2						
Constant	40.85 (20.89)			1.21 (11.94)		
iPTH	16.54 (5.56)	0.18*		9.77 (3.18)	0.17	
BMI	43.78 (13.80)	0.18*	0.06	43.93 (7.89)	0.32	0.13

BMI, body mass index; BP, blood pressure; iPTH, intact parathyroid hormone; PTH, parathyroid hormone
* $P < 0.01$.

concentrations were associated with higher BP. Men in highest quartile of PTH presented SBP and DBP, respectively, 3.4 and 2.8 mm Hg higher than men in lowest quartile.

Vitamin D insufficiency present in our sample, 86%, should reflect besides the low outdoor activity, the low vitamin D intake, once that, in our country, the food fortification with vitamin D is not mandatory and the principal foods that contains this vitamin is not present in our dietary habits.

Although several studies have suggested that low concentrations of 25(OH)D are associated with higher BP [5,23], no association was observed between vitamin D status and BP in our sample. In older Chinese men [22] no associations were found between vitamin D and BP, however, in this study, the participants evaluated had optimal vitamin D concentrations.

Also in relation to data from NHANES 2003–2006 [21], the authors found values for SBP and DBP that were respectively 3.5 and 1.8 mm Hg lower in the highest quintile of vitamin D (25[OH]D $\geq$ 75 nmol/L) than in the lowest quintile (25[OH]D $\leq$ 32.5 nmol/L). These findings are similar to the results from a previous study also performed with participants from NHANES III [6]. This negative relationship between serum concentration of 25(OH)D and hypertension was also demonstrated in the Nurses' Health Study and the Healthy Professional Follow-up Study [24]. In the present analysis, a tendency toward a negative association between vitamin D status and SBP was only present in individuals who were not using medication for hypertension and with adjustment for blood lipids and BMI or WC. This could indicate some kind of interaction between these medications and mechanisms for vitamin D metabolism, thus confounding the association between it and BP. Although our sample was composed of many obese individuals, adjustments for blood lipids and WC removed the effect of obesity (factor that is well established as leading to development of hypertension).

There are three main mechanisms that may explain the role of PTH in regulating BP. It could act on cardiomyocytes to promote left ventricular hypertrophy [25,26] and chronotropic effects on pacemaker cells [27] producing immediate and sustained rise in heart beats [28]. Intracellular calcium seems to be involved in this mechanism, but the evidences are conflicting [27,29]. Furthermore, the high serum concentrations of PTH seem to lead the exposed cardiac cells to premature death [28]. Another mechanism through which PTH can interfere in BP consists of structural and functional modifications to the vascular wall, promoted by PTH through alterations in endothelium and vascular smooth muscle cells, given that PTH receptor have been described in these cells [30]. Finally, some evidence has shown that PTH could be involved in inflammatory response mediated production of interleukin-6 by osteoblasts and, possibly, by adipocytes [31]. Additionally, PTH has been positively correlated with fibrinogen, C-reactive protein, [31] and leptin [32].

The role of PTH in regulating mineral metabolism is well recognized. Increases in PTH could be indicative of other disorders such as vitamin D deficiency [33], hyperphosphatemia, hypercalcemia, or chronic kidney disease (conditions that are known to lead to cardiovascular complications and higher risk for mortality). In our study, we sought to remove the patients who presented such conditions, except for vitamin D insufficiency. In addition the negative correlation between PTH and vitamin D status observed, 10% of our sample presented both high PTH and low vitamin D status.

It is important to emphasize that the prevalence of overweight and obesity among the participants was found to be very high (75%). Likewise, the WC measurements were large (such measurements have been linked with abdominal obesity) and the TC, LDL-C, and triacylglycerol concentrations were high. These conditions, as well as hypertension, are strong risk factors for CVD, and together reflect a serious problem in our environment that deserves attention.

The present study has some limitations. Because it had a cross-sectional design, these results do not allow us indicate causality and temporal associations. Furthermore, low concentrations of 25(OH)D in all groups may have been the cause of null interactions between them. These concentrations of 25(OH)D and the lack of association with BP lead us to question the real cutoff point that should be considered for classifying individuals with vitamin D insufficiency when the aim is to establish a predictor for CVD in our population. From this point of view, the number of participants, and their conditions, like the high percentage of overweight and obese, as well the vitamin D classification based on bone metabolism effects, may not have been sufficient to establish the association between vitamin D status and BP. Additionally, the role of inflammation through increased PTH should be further investigated.

Conclusions

In summary, the association between PTH and BP observed in this study contributes to the understanding of calcemic hormones and BP regulation. The metabolic pathway that causes this disorder needs further investigation in clinical and prospective studies in order to better characterize and elucidate the relationship between them.

References

[1] Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, et al. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension 2003;42:1206–52.
[2] Sociedade Brasileira de Hipertensão. Diretrizes Brasileiras de Hipertensão VI. Rev Hipertensão 2010;13:1–66.
[3] World Health Organization. Cardiovascular diseases (CVDs) Fact Sheet 317. Fact Sheets 2011. Available from http://www.who.int/mediacentre/factsheets/fs317/en/index.html# [accessed 24 November 2011].
[4] Melamed ML, Michos ED, Post W, Astor B. 25-hydroxyvitamin D levels and the risk of mortality in the general population. Arch Intern Med 2008;168:1629–37.
[5] Forman JP, Curhan GC, Taylor EN. Plasma 25-hydroxyvitamin D levels and risk of incident hypertension among young women. Hypertension 2008;52:828–32.
[6] Scragg R, Sowers M, Bell C. Serum 25-hydroxyvitamin D, ethnicity, and blood pressure in the Third National Health and Nutrition Examination Survey. Am J Hypertens 2007;20:713–9.
[7] Martini LA, Wood RJ. Vitamin D and blood pressure connection: update on epidemiologic, clinical, and mechanistic evidence. Nutr Rev 2008;66:291–7.
[8] Kendrick J, Targher G, Smits G, Chonchol M. 25-Hydroxyvitamin D deficiency is independently associated with cardiovascular disease in the Third National Health and Nutrition Examination Survey. Atherosclerosis 2009;205:255–60.
[9] Reis JP, von Mühlen D, Michos ED, Miller ER III, Appel LJ, Araneta MR, et al. Serum vitamin D, parathyroid hormone levels, and carotid atherosclerosis. Atherosclerosis 2009;207:585–90.
[10] Giovannucci E, Liu Y, Hollis BW, Rimm EB. 25-hydroxyvitamin D and risk of myocardial infarction in men: a prospective study. Arch Intern Med 2008;168:1174–80.
[11] Garcia VC, Martini LA. Vitamin D and cardiovascular disease. Nutrients 2010;2:426–37.
[12] Lips P, Duong T, Oleksik A, Black D, Cummings S, Cox D, 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 2001;86:1212–21.
[13] Genaro PS, Pereira GA, Pinheiro MM, Szejnfeld VL, Martini LA. Relationship between nutrient intake and vitamin D status in osteoporotic women. Int J Vitam Nutr Res 2007;77:376–81.
[14] Dawson-Hughes B. Racial/ethnic considerations in making recommendations for vitamin D for adult and elderly men and women. Am J Clin Nutr 2004;80:1763S–6S.

[15] Hellströum J, Birke G, Edvall CA. Hypertension in hyperparathyroidism. Br J Urol 1958;30:13–24.
[16] Snijder MB, Lips P, Seidell JC, Visser M, Deeg DJ, Dekker JM, et al. Vitamin D status and parathyroid hormone levels in relation to blood pressure: a population-based study in older men and women. J Intern Med 2007;261:558–65.
[17] Jorde R, Svartberg J, Sundsfjord J. Serum parathyroid hormone as a predictor of increase in systolic blood pressure in men. J Hypertens 2005;23:1639–44.
[18] Taylor EN, Curhan GC, Forman JP. Parathyroid hormone and the risk of incident hypertension. J Hypertens 2008;26:1390–4.
[19] Hagström E, Hellman P, Larsson TE, Ingelsson E, Berglund L, Sundström J, et al. Plasma parathyroid hormone and the risk of cardiovascular mortality in the community. Circulation 2009;119:2765–71.
[20] Li L, Yin X, Yao C, Zhu X, Wu X. Vitamin D, parathyroid hormone and their associations with hypertension in a Chinese population. PLoS One 2012;7:e43344.
[21] He JL, Scragg RK. Vitamin D, parahtyroid hormone, and blood pressure in the National Health and Nutrition Examanation Surveys. Am J Hypertens 2011;24:911–7.
[22] Chan R, Chan D, Woo J, Ohlsson C, Mellström D, Kwok T, et al. Serum 25-hydroxyvitamin D and parathyroid hormone levels in relation to blood pressure in a cross-sectional study in older Chinese men. J Hum Hypertens 2012;26:20–7.
[23] Zhao G, Ford ES, Li C, Kris-Etherton PM, Etherton TD, Balluz LS. Independent associations of serum concentrations of 25-hydroxyvitamin D and parathyroid hormone with blood pressure among US adults. J Hypertens 2010;28:1821–8.
[24] Forman JP, Giovannucci E, Holmes MD, Bischoff-Ferrari HA, Tworoger SS, Willett WC, et al. Plasma 25-hydroxyvitamin D levels and risk of incident hypertension. Hypertension 2007;49:1063–9.
[25] Saleh FN, Schirmer H, Sundsfjord J, Jorde R. Parathyroid hormone and left ventricular hypertrophy. Eur Heart J 2003;24:2054–60.
[26] Nappi S, Saha H, Virtanen V, Limnell V, Sand J, Salmi J, et al. Left ventricular structure and function in primary hyperparathyroidism before and after parathyroidectomy. Cardiology 2000;93:229–33.
[27] Shimoyama M, Ogino K, Furuse Y, Uchida K, Kinugasa Y, Tomikura Y, et al. Signaling pathway and chronotropic action of parathyroid hormone in isolated perfused rat heart. J Cardiovasc Pharmacol 2001;38:491–9.
[28] Bogin E, Massry SG, Harary I. Effect of parathyroid hormone on rat heart cells. J Clin Invest 1981;67:1215–27.
[29] Wang R, Wu L, Karpinski E, Pang PK. The changes in contractile status of single vascular smooth muscle cells and ventricular cells induced by bPTH-(1-34). Life Sci 1993;52:793–801.
[30] Usdin TB, Bonner TI, Harta G, Mezey E. Distribution of parathyroid hormone-2 receptor messenger ribonucleic acid in rat. Endocrinology 1996;137:4285–97.
[31] McCarty MF. Secondary hyperparathyroidism promotes the acute phase response—a rationale for supplemental vitamin D in prevention of vascular events in the elderly. Med Hypotheses 2005;64:1022–6.
[32] Maetani M, Maskarinec G, Franke AA, Cooney RV. Association of leptin, 25-hydroxyvitamin D, and parathyroid hormone in women. Nutr Cancer 2006;61:225–31.
[33] Holick MF, Chen TC. Vitamin D deficiency: a worldwide problem with health consequences. Am J Clin Nutr 2008;87:1080S–6S.