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Original article

Association of vitamin D with blood pressure and obesity in prinzmetal angina

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Summary. Vitamin D deficiency is a main risk factor for cardiovascular disease. Low serum vitamin D can increase blood pressure and weight in person. A case–control study was conducted on 69 matched pairs, aged 40-60 years. Vitamin D was measured by Chemi-luminescence immunoassay method. There was significant difference in serum 25- Hydroxy vitamin D between groups of study (P= 0.0001). The mean ± SD of 25-Hydroxy vitamin D in prinzmetal angina was 12.16 ± 5.21 and in healthy persons was 23.44 ± 2.52 ng/ml. Between vitamin D and waist circumference there was significant association in prinzmetal patients (p= 0.04, ß= 0.236). There was not significant relation between vitamin D with blood pressure and BMI in study participants (P≥0.05). Vitamin D can effect on obesity in prinzmetal angina patients.

Key words: vitamin D, obesity, blood pressure

Introduction

Prinzmetal variant angina (PVA) is an unusual syndrome of cardiac pain secondary to myocardial ischemia, which is not intensified by physical exertion or emotional stress, and is associated with transient ST (one section of Electrocardiogram) segment elevation (1). Many studies indicated that vitamin D deficiency is a main risk factor for cardiovascular disease (CVD), because the cardiac tissue has vitamin D receptor (VDR). Since 2008, more than 30 cohort studies have been published, with meta-analyses of their results showing that low baseline levels of blood 25-hydroxy-vitamin D (25(OH)D) predict increased risk of CVD and all-cause mortality during follow-up. Hypertension (HTN) is a chronic condition that can lead to renal disease, CVD, stroke, and mortality (2). Moreover, previous cross-sectional and cohort studies have shown an inverse association between 25(OH)D concentration and blood pressure (3). A previous meta-analysis including eight prospective studies reported that the level of 25(OH)D was inversely associated with the incidence of HTN (RR: 0.70; 95% CI: 0.58e0.86) (4). Obesity is one of main risk factor for cardiovascular disease. In addition, several prospective studies reported that low 25(OH)D plasma levels may determine the incidence of obesity (5). The reported prevalence of vitamin D deficiency in obese individuals ranges from 21% to 87% (5, 6) depending on the severity of obesity, country of residence, ethnicity, skin pigmentation, clothing customs, and use of vitamin supplementation. Recently, a large genetic study reported that genes associated with reduced 25(OH)D levels have very small effects on obesity (7). Despite importance of coronary heart diseases in Ardebil, no risk factor study has ever been conducted; therefore, we decided to conduct a case-control study to investigate the hypothesis that whether there is any relation between serum vitamin D with blood pressure and obesity in prinzmetal angina patients.

Material and method

A case-control study was conducted on 69 matched pairs, aged 40-60 years, and persons that

referred to Emam Khomeini hospital of Ardebil. To recruit controls, 100 households were visited and 70 eligible controls (70% of eligible controls) agreed to participate in the study. Control group was sought for each case, frequency matched to the case group based on age and gender. Control group was selected randomly from households of the same region depending of being visited by health professionals. The aims and study protocol were explained to the both groups and a written consent was taken prior to filling a questionnaire. Exclusion criteria included: Persons that had other metabolic diseases, were pregnant, or had used calcium or vitamin D supplement in the past 6 month. In the study start, a general questionnaire about persons' health condition and confounder risk factors was completed to assess. Anthropometric parameters including height, weight and body mass index (BMI) at the baseline and end of the study were measured. Using a pretested questionnaire, a trained interviewer collected information, which included demographic data, job, age, medication use, and education level. Arterial blood pressure was measured between 7:00 a.m. and 11:00 a.m. after a rest of at least 5 min via a sphygmomanometer with a cuff and a stethoscope to detect the Korotkoff sound. Each person was asked to take a seated position, and their arm was supported at heart level. The first sound was defined as systolic blood pressure (SBP), while the last sound was defined as diastolic blood pressure (DBP).

Serum 25- Hydroxyl vitamin D assessment

Serum 25-Hydroxyl vitamin D was determined by Chemi-luminescence immunoassay method. This automated immunoassay is the previous version of the new follow-up IDS-iSYS 25(OH)D^{s} CLIA as listed below. It is based on chemiluminescence technology. The assay was performed on the IDS-iSYS Multi-Discipline Automated Analyzer. 10 µL of serum aliquots were automatically pipetted and subjected to a pre-treatment step with NaOH (part of the reagent used for CLIA and ELISA methods) to denature the DBP inside the IDS-iSYS Multi-Discipline Automated Analyzer. The extraction procedure of 25(OH) D from the DBP was followed by analysis. This assay is not aligned to the NIST SRM (NIST, Gaithersburg, Maryland). The measurement range of this assay is 5-140 ng/mL (information of the manufacturer). The IDS-iSYS 25(OH)D control set (IS-2730) (Immunodiagnostic Systems Ltd, Boldon, United Kingdom) was used for quality control (QC) (8).

Statistics analysis

To correlate variables with normal and non-normal distribution, Pearson's and Spearman's correlations respectively were used. Normally distributed continuous variables are reported as the mean ± SD. Pearson Chi-Square test was used to compare qualitative variables, independent sample t-test was used to compare quantitative variables means. Statistical analyses were performed using SPSS version 16.0. For relation evaluating vitamin D with obesity and blood pressure liner regression was used. In all of analyses $p< 0.05$ was significant.

Results

The characteristics of the sample population are summarized in Table 1. No significant differences between groups were observed in age, weight, height, age and sex ($p>0.05$). The prinzmetal angina patients had higher values for blood pressure. Systolic and diastolic blood pressure mean± SD in prinzmetal angina patients was 13.60± 0.56 and 8.98 ± 0.46. There was significant difference between groups in SBP and DBP ($p<0.05$).

Table 2 indicates vitamin D status in prinzmetal angina patients and health persons. There was significant difference in serum 25- Hydroxy vitamin D between groups of study ($p= 0.0001$). Vitamin D status in 2.9% of patients and health persons was normal.

Table 3 indicates relation of vitamin D with blood pressure and obesity in study participants. There was significant relation between serum vitamin D with Waist circumference in prinzmetal angina patients ($p= 0.04$, ß= 0.236). There was not significant relation between vitamin D with blood pressure and BMI in study participants ($P\geq0.05$).

Table 1. Baseline Characteristic of the study population

Variables	Case group (n=34)	Control group (n=35)	Pv*
Age (y)	51.26± 0.86	51.20 ± 0.96	0.356
Weight (kg)	88.30 ± 2.29	88 ± 2.60	0.390
Height (m)	1.70 ± 0.007	1.70 ± 1.006	0.410
BMI	26.25 ± 2.35	25.28 ± 2.05	0.084
Systolic blood pressure (mmHg)	13.60± 0.56	11.61 ± 0.93	0.039
Diastolic blood Pressure (mmHg)	8.98 ± 0.46	8.16 ±0.26	0.001
Sex(%) Male Female	 50 50	 50 50	 0.079
Waist circumference (cm)	92.15± 5.80	84.93± 7.43	0.001

**:based on independent sample T - test*

Table 2. Serum 25 Hydroxy vitamin D statue in study participants

Vitamin D	**case group**	**control group**	**p**
Mean± SD (ng/ml)	12.16 ± 5.21	23.44 ± 2.52	0.0001
30≤ (%)	1(2.9)	1(2.9)	
20-30	2(5.9)	33(94.3)	
10-20	20(58.8)	1(2.9)	
10	11(32.4)	0	

Table 3. Regression coefficients (B) from the linear model with 25-Hydroxy vitamin D as independent variable

	Case group		Control group	
	P	ß	P	ß
Systolic blood pressure	0.48	0.007	0.20	0.090
Diastolic blood pressure	0.09	0.229	0.08	0.682
BMI	0.36	-0.062	0.27	0.093
Waist circumference	0.04	0.236	0.085	0.22

Discussion

In our results there was significant association in serum 25-Hydroxy vitamin D between patients and healthy persons. About 3% of prinzmetal patients had normal vitamin D status, 5.9% had insufficient vitamin D, 58.8% had moderate vitamin D deficiency, 32.4% had severe vitamin D deficiency. Just 2.9% of healthy persons had moderate vitamin D deficiency. Kienreich in one study indicated that there is a significant association between low vitamin D level with cardiovasulare disease prevalence (9). Possible mechanisms underlying this association include increased inflammation, renin–angiotensin system upregulation, insulin resistance, altered lipid metabolism, and altered vascular smooth muscle growth and function that lead to hypertension, diabetes, dyslipidemia and atherosclerosis (10). For first in the present study, we reported the relation between serum 25-Hydroxy vitamin D with blood pressure in prinzmetal angina patients and health persons; there was not any relation between vitamin D with blood pressure. Evidence from randomised controlled trials to assess the effectiveness of vitamin D supplementation in reducing blood pressure have not provided consistent evidence of a benefit (11). In subgroup analyses done within meta-analyses of these trials (12, 13), some reductions in diastolic blood pressure were reported for participants with hypertension or cardiometabolic diseases, and when studies had used higher doses were compared with those that used lower doses of vitamin D (14). Although the investigators of one study (15) reported dose-dependent reductions in systolic blood pressure after 3 months of supplementation with 1000 IU, 2000 IU, and 4000 IU of vitamin D per day (0·66, 3·4, and 4·0 mm Hg, respectively), no effect was seen in another trial (16).

Vitamin D metabolites could also exert antihypertensive effects through various other molecular mechanisms. Vitamin D is indirectly related to blood pressure through its regulation of calcium absorption from the gut and its interaction with parathyroid hormone in the maintenance of calcium homeostasis. The renoprotective and anti-inflammatory actions of vitamin D metabolites and their analogues suggest a possible role for vitamin D deficiency in cardiovascular morbidity and mortality in patients with chronic kidney disease. Furthermore, adipocyte inflammation has a crucial role in hypertension: in an in-vitro study, $1,25(OH)_2D$ inhibited lipopolysaccharide-stimulated cytokine secretion in two human adipocyte models through direct inhibition of nuclear factor-κB (17, 18) . Small sample size is one of the reasons of our different results. We did not measure the stress level in persons, this can be another reason for our different results. Our study indicated that there was significant relation between waist circumference with vitamin D in prinzmetal angina patients, this relation was not significant in health persons. There was not significant relation between vitamin D with body mass index. Low serum 25(OH) D concentrations are inversely associated with insulin resistance and metabolic syndrome, especially in those who are overweight and obese. The exact molecular mechanisms at the origin of fatty acid oxidation remain to be identified VDR appears as a good candidate of such regulation. It would have been interesting to verify whether this nuclear receptor is involved by using genetically modified mice. However, VDR/ mice are resistant to high fat diet-induced obesity (19) Gonzalez in one study indicated that obese person had vitamin D dificiency comparioson with person with normal weight (20). Vitamin D stimulates adiposity tissue cells so it can increase fat oxidation (21). To conclude, our data did not indicate any relation between serum vitamin D and blood pressure, body mass index, but there was relation between vitamin D with waist circumference in prinzmetal patients. Our sample size was small, we did not measure stress level, and these are our study limitations. Our results may not be generalizable to other racial/ethnic groups or may not be generalizable to others living indifferent geographical latitudes and altitudes.

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