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Original Research Article

Vitamin D and functional arterial parameters in postmenopausal women with metabolic syndrome

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ABSTRACT

Purpose: Our cross sectional study aimed to identify the relation between vitamin D level and functional arterial parameters in postmenopausal women with metabolic syndrome.
Material and methods: 100 postmenopausal women at age 50–65 with diagnosed metabolic syndrome were included in this study. Laboratory tests were performed to determine lipid profile, serum glucose, creatinine, C-reactive protein, serum levels of 25(OH) D, ionized calcium and urine albumin/creatinine ratio. Also non-invasive assessment of arterial function (arterial stiffness, flow-mediated dilatation and carotid artery ultrasound examinations) was performed.
Results: The mean vitamin D blood concentration was 47.4 ± 16.9 nmol/l. The prevalence of modest insufficiency and deficiency of vitamin D was 62%. Vitamin D concentration in samples assembled from January to March was significantly lower than concentration levels from September to November. No significant relationship was observed between vitamin D and endothelial function, arterial stiffness, carotid intima-media thickness. Week negative correlation was stated between mean arterial pressure and 25(OH) D concentration ($p = 0.04$). A positive correlation was found between high density lipoprotein cholesterol and vitamin 25(OH) D ($r = 0.3$, $p < 0.05$). No significant difference between 25(OH) D and other lipoproteins, calcium ions, glucose, albumin/creatinine ratio and C-reactive protein blood concentrations were found.
Conclusions: The prevalence of vitamin D deficiency in postmenopausal women with metabolic syndrome is high. No relation was found between vitamin D levels and parameters that indicate atherosclerotic vascular lesions. Nevertheless our study revealed the relation between concentrations of vitamin D and mean blood pressure and high density lipoprotein cholesterol.

1. Introduction

It is widely recognized that vitamin D is responsible for keeping healthy bone structure and for maintaining acceptable serum calcium and phosphate concentrations. However, vitamin D plays other important roles in the human body, including immune function, modulation of cell growth, neuromuscular and reduction of inflammation.

Presently there is a growing interest in the extra-skeletal roles of vitamin D. Lack of vitamin D has been related not only to bone mineral density, but also to cardiovascular disease, diabetes mellitus, cancer, cystic fibrosis and mental health [1]. Nevertheless parallel between vitamin D and overall health is unclear until now.

Some authors reported that vitamin D' deficiency increases risk of cardiovascular diseases [2]. Several experimental studies with animals and cell cultures show pathogenically based evidence that vitamin D receptors activation may protect against cardiovascular diseases. However, it is not clear if this is relevant in clinical practice [3]. Large prospective observational studies demonstrate a higher incidence of cardiovascular events in individuals with vitamin D deficiency [4]. Systematic review and meta-analysis performed by Chowdhury et al. [5] described similar results which show inverse associations of 25(OH) D with risk of death due to cardiovascular disease and other causes. Despite these findings, meta-analyses of clinical trials have not shown evidence of

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beneficial effects of vitamin D supplementation on cardiovascular outcomes [6]. In systematic review conducted in 2010 researchers analyzed longitudinal cohort studies that reported associations between vitamin D status and cardiometabolic outcomes in generally healthy adults, including randomized trials of vitamin D supplementation and found that the association between vitamin D status and cardiometabolic outcomes is uncertain. Lower 25(OH) D concentration was associated with incident cardiovascular disease in 5 of 7 analyses and 4 trials found no effect of supplementation on cardiovascular outcomes [7]. Despite enormous number of studies published, there is still a controversy regarding the vitamin D deficiency and cardiovascular diseases.

In this study we hypothesize that vitamin D' deficit is related to atherosclerotic vascular injury in postmenopausal women with metabolic syndrome. For this reason protective functions of vascular endothelium become weaker. Consequently the adhesion of low density lipoproteins to vascular endothelium occurs faster and it primarily affects the function of vessels. The after coming structural changes convert to the first signs of early atherosclerosis.

2. Material and methods

2.1. Study design

The aim of this cross sectional study was to identify the relation between vitamin D level and atherosclerotic vascular injury. The inclusion criteria were: women in age between 50 and 65 years diagnosed metabolic syndrome and postmenopausal period. Metabolic syndrome was diagnosed if at least 3 out of 5 symptoms were present: waist circumference >88 cm; systolic blood pressure (SBP) ≥130 mmHg and/or diastolic blood pressure (DBP) ≥85 mmHg; glucose concentration before food >5.6 mmol/l or type 2 diabetes mellitus; triglycerides (TG) concentration >1.7 mmol/l or special treatment is administered in order to reduce TG concentration; high density lipoprotein (HDL) cholesterol <1.2 mmol/l [8]. Exclusion criteria were: diagnosed coronary heart disease, malignant disease (stage IV), kidney or liver failure, permanent arrhythmias, drug-resistant tuberculosis, acute rheumatic fever or rheumatic disease (acute phase), pulmonary arterial hypertension (greater than grade 2), decompensate heart disease, lymphatic vessels and lymph node diseases with expressed lymphostasis, advanced stage of mental illness. Approval was obtained from the Lithuanian Bioethics Committee (nr. 158200-14-720-240), and each participant gave written informed consent. One hundred women, from those who came to Vilnius University Hospital according to Lithuanian High Cardiovascular Risk primary prevention program, were included in this study until the end of year 2014.

2.2. Study variables

All participants filled in the structured questionnaire about demographic and social characteristics, including age, living place (town or countryside) and addictions (smoking, alcohol consumption). All patients underwent measurements of height, weight, waist circumference and arterial blood pressure. Waist circumference was measured midway between the top of the hip bone and the bottom of the ribs. Body mass index (BMI) was calculated as body weight (kg) divided by height (m) squared and categorized to normal, overweight and obese. Arterial hypertension was determined when SBP was ≥140 mmHg and/or DBP was ≥90 mmHg, or diagnosis of hypertension was documented in a medical record. Arterial hypertension was classified as grade 1 hypertension when SBP was 140–159 mmHg and/or DBP 90–99 mmHg, as grade 2 hypertension when SBP – 160–179 mmHg and/or DBP 100–109 mmHg, as grade 3 hypertension when SBP ≥180 mmHg and/or DBP ≥110 mmHg [9]. All laboratory tests were performed in the morning after 12 h fasting, and the following variables were determined: total cholesterol, low-density lipoprotein (LDL) cholesterol, HDL cholesterol, triglycerides, serum glucose, creatinine, C-reactive protein, serum levels of 25(OH) D, ionized calcium, urine albumin/creatinine ratio was calculated. 25(OH) D values 25 nmol/l or less were considered as vitamin D deficiency, while 25–50 nmol/l and 50–75 nmol/l were considered as modest and mild insufficiency. 75 nmol/l up to 125 nmol/l reflect adequate Vitamin D status as it is suggested by Endocrine Society clinical practice guideline [10].

2.3. Non-invasive assessment of arterial stiffness

The participants were refrained from eating and drinking alcohol, coffee, or tea for at least 12 h prior to the study. The test of arterial stiffness was performed in the supine position in a quiet, temperature-controlled room (22–24 °C). Pulse wave velocity (PWV) was determined by measuring the carotid-to-radial and carotid-to-femoral pulse wave transit time. Carotid–radial or carotid–femoral pulse waves were obtained non-invasively by applanation tonometry using high-fidelity micromanometer (Sphygmocor (v.7.01) AtCor Medical Pty. Ltd 1999–2002, Sydney, Australia). Pulse waves obtained consecutively from the radial or femoral and carotid arteries were referenced to a simultaneously recorded ECG, and transit time was computed from the time difference between the carotid and radial or femoral waveforms. The distance between the surface markings of the sternal notch and the radial or femoral artery was used to estimate the difference in path length between the carotid and radial or femoral arteries, and PWV adjusted for mean blood pressure was calculated. Aortic augmentation index (AIx adjusted for heart rate 75 bpm) was calculated from radial pulse waves of non-dominant arm [11,12]. Validated transfer function from peripheral pulse wave analysis was used to generate a corresponding central waveform. From this, aortic AIx was calculated by using the integrated software. The systolic part of the central arterial waveform is characterized by two pressure peaks. The first peak is caused by left ventricular ejection, whereas the second peak is a result of pulse wave reflection. The difference between both pressure peaks reflects the degree to which central arterial pressure is augmented by wave reflection. AIx, a measure of systemic arterial stiffness, is calculated as the difference between the second and first systolic peaks expressed as a percentage of the pulse pressure [13]. Blood pressure was recorded in the left arm using an automatic blood pressure monitor (HEM-757; Omron Corporation, Kyoto, Japan).

2.4. Flow-mediated dilatation (FMD) measurement

The endothelium-dependent flow-mediated dilatation test in a brachial artery was performed according to the method described by Celermajer et al. and adapted according to international recommendations [14,15] and technical equipment of Cardiology and Angiology center [16]. The brachial artery diameter was measured on B-mode imaging by the ultrasound system (Logiq 7, General Electric, Solingen, Germany) with a high resolution 12-MHz linear-array transducer. The computerized software program for image acquisition (CVI Acquisition) and semi-automatic analysis software were used (Vascular Analysis Tools, Vascular Converter CVI and Brachial Analyzer, Medical Imaging Application, 1998–2003 LLC Iowa City, IA 52246, USA). The arterial diameter was measured between the intima/lumen interfaces of the anterior and posterior wall at the end of diastole (synchronized with the beginning of the *R* wave on the continuously recorded ECG).