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Association of 25 (OH) vitamin D levels with carotid intima media thickness in elderly north Indians

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Abstract

Background: Atherosclerosis is a major factor for cerebrovascular disease development and involves complex interplay between different cell types of the immune system with cells of the vessel wall. It can be measured by assessing the carotid intima media thickness (CIMT). A number of studies have shown variable results on the relationship between 25 (OH) D deficiency and subclinical atherosclerosis. The objectives of the present study were therefore to investigate the relationship between CIMT and Vitamin D status in the North Indian population ≥ 60 years.

Methods: Patients aged ≥ 60 years who visited hospital for health check-up were enrolled and analyzed in present study.

Results: 61.2 % of the subjects under study were Vitamin D deficient with mean Vitamin D level of 25.1 ± 15.6 ng/mL. The average C-IMT was 0.81 ± 0.27 mm. A significant inverse relationship was found between 25(OH) D concentration and CIMT with p = 0.003.

Conclusion: Our data shows an inverse association of 25 (OH) Vitamin D concentration with CIMT in elderly subjects ≥ 60 years. These findings suggest a potential role Vitamin D deficiency in the development of subclinical atherosclerosis.

Background

Atherosclerosis is a major factor for development of cardiovascular disease and is a process involving complex interplay among different factors and cell types including cells of the immune system (T cells, B-cells, Natural killer cells, monocytes/macrophages and dendritic cells) along with cells of the vessel wall including endothelial cells, vascular smooth muscle cells etc. The atherosclerotic process initiates from endothelial dysfunction and can progress to plaque vulnerability and rupture [1]. 25(OH) Vitamin D plays an important role in bone metabolism. There is an increasing interest in its association with atherosclerosis disease. A growing body of evidence shows low levels of Vitamin D to be related with increased risk of stroke, myocardial infarction and total cardiovascular events [2-7]. Vitamin D receptors have a broad tissue distribution that includes vascular smooth muscle,endothelium, and cardiomyocytes [8-10]. In vitro, activated 1, 25-dihydroxyvitamin D (1, 25-OH D) directly suppresses renin gene expression, regulates the growth and proliferation of vascular smooth muscle cells and cardiomyocytes, and inhibits cytokine release from lymphocytes [11-14]. Studies in knockout mice confirm that the absence of vitamin D receptor activation leads to tonic up regulation of the renin-angiotensin system, with the development of hypertension and left ventricular hypertrophy [12,15,16]. Emerging data has shown high prevalence of vitamin D deficiency among Indians despite the availability of abundant sunshine in large parts of India. This is true for both urban and rural populations and, in men and women, with reported population of prevalence of 70-99%, with severe deficiency (<10 ng/ml) being reported as 62% in studies from Delhi [17-20]. Lo et al. [21] reported that Asian Indians require twice as much UV-B exposure to produce 25(OH)D levels equal to Caucasians due to increased skin pigmentation. In addition, a cultural tendency to avoid direct sunlight may contribute to suboptimal vitamin D status in spite of sunny climate throughout the year.

Carreli et al. [22], in his study on 203 subjects more than 50 years found low 25 (OH) D levels to be associated with increased carotid intima media thickness (CIMT). Similar results were found by Reiss et al. [23], in his study of adults aged 55-96 years in which low 25 (OH) D levels were inversely associated with CIMT among those with hypertension. Imran et al. [24] in his study of 45 elderly women ≥ 60 years also found a significant inverse relationship between 25 (OH) D level and CIMT. However, Deleskog et al. [25] in his study on 3430 adult and elderly subjects found no association between 25 (OH) Vitamin D and increased CIMT. The results of various studies studying relationship of 25 (OH) Vitamin D with CIMT are contradictory. There are also very few reports on the relationship between 25 (OH) D and CIMT in the Indian population.

Objectives

In view of this the present study was therefore aimed to investigate the relationship between CIMT and Vitamin D status in the North Indian population ≥ 60yrs.

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Methods

The present study was a retrospective cross-sectional study conducted in the Department of Biochemistry and Cardiology at Medanta-The Medicity Hospital. Gurgaon. The study included 49 elderly patients ≥ 60 years with a male-female ratio of 3:1 visiting the executive health check-up services from 1st January till 31st May 2015. We excluded subjects who were on wheelchair, those taking vitamin D or calcium supplementation in the last 6 months and those with diseases related to vitamin D metabolism (for instance liver or kidney disease) and diabetes mellitus. A questionnaire-based direct interview was used to collect information on disease profile, demographic variables, risk factors and medications used. BMI was calculated as (weight (kg)/height ($m^{2)}$). The World Health Organization (WHO) has recommended lower BMI thresholds for Asians, therefore obesity was defined using WHO new guidelines. Participants with BMI <23 kg/m^2 were classified as normal weight, BMI between 23-27.5 Kg/m^2 were classified as over-weight and BMI >27.5 kg/m^2 as obese. Blood pressure was measured twice after a five-minute seated rest period with the participant's feet flat on the floor. Hypertension was defined as SBP >130 and/or DBP>80 mm Hg. In addition, participants who referred to taking medicines for hypertension were also considered as having high blood pressure. Criteria for diabetes mellitus were a fasting blood glucose >126 mg/dL or HbA1C >6.5 % or use of insulin or hypoglycemic agent. Dyslipidemia was defined as either of serum triglycerides (TG) >150 mg/dL or high-density lipoprotein cholesterol (HDL-C) <40 mg/dL in men and 50 mg/dL in women or low-density lipoprotein (LDL-C) >100 mg/dL. Lipid profile and fasting blood sugar were analyzed on Vitros 5600 routine chemistry analyzer by Ortho Clinical Diagnostics. HbA1C was measured on Biorad D10 analyzer. Serum levels of 25-hydroxy vitamin D [25(OH) vit D] were estimated by electrochemiluminescence method on Architect ci4100 analyzer (Abbott, Max-PlanckRing 2, Germany).

Ultrasonography measurements

A single qualified trained technician blinded to individual's previous disease histories carried out all ultrasound examinations. Patients were examined while they were in the supine position using B mode ultrasonography (Terason 3000; Terason, Burlington, Massachusetts, USA) with a 5–12-MHz linear array transducer. CIMT at the near and far walls of the common carotid artery were measured on the left and right, and three values were obtained: the maximum CIMT, minimum CIMT and average CIMT. Images were obtained and digitally stored according to a standard protocol.

Statistical analysis

Continuous variables were presented as means with standard deviations. Pearson's regression analysis was used to evaluate the associations between traditional risk factors and CIMT. P-values <0.05 was considered statistically significant. SPSS for Windows (version 18.0; SPSS Inc., Chicago, Illinois, USA) was used for analysis.

Results

The mean age of the patients under study was 65.31 ± 4.89 years with a male: female ratio of 3:1. The subjects under study had a mean BMI of 27.9 ± 5.68 kg/m^2 and average systolic blood pressure of 139.35 ± 16.5 mm Hg and diastolic blood pressure of 81.6 ± 10.1 mm Hg. The mean cholesterol levels of the subjects were 174.6 ± 43 mg/dL, mean triglyceride levels was 138.51 ± 65 mg/dL, mean LDL cholesterol was 103.44 ± 40.9 mg/dL and HDL cholesterol 45.47 ± 9.86 mg/dL. The average fasting blood sugar was 110.4 ± 28 mg/dL. The mean 25 (OH) Vitamin D concentration was 25.1 ± 15.6 ng/mL and 61 % of the patients under study were Vitamin D deficient. The average carotid intima-media thickness was 0.81 ± 0.27 as shown in table 1.

On correlating CIMT with other variables with simple linear regression a significant inverse relationship was found with 25 (OH) D concentration (p = 0.003) as shown in table 2. Since no other variable was found to correlate with CIMT with p < 0.05 therefore a multiple logistic regression between variables and CIMT could not be performed.

Discussion

The key finding of the present study was that elderly subject's ≥ 60 years showed a decreasing trend in serum 25 (OH) Vitamin D level that was associated with carotid intima-media thickness. Similar findings were observed by Hao et al[26] in his study of 926 post-menopausal Chinese women. Imran et al. [24] also found a negative association of vitamin 25 (OH) D and CIMT in elderly women. Carreli et al. [22] in their study along with Reiss et al. [23] also showed similar findings. However contradictory findings were observed in a study by Monteiro Junior et al. [27] who initially showed significant inverse relationship between serum 25 (OH) D concentrations and CIMT which became non-significant after the inclusion of variable age in the multivariate analysis model. Deleskog et al. [25] also found levels of serum 25 (OH) D to be inconsistently related to measures of carotid IMT. They argued against protective role of Vitamin D against subclinical atherosclerosis in high risk individuals and concluded that Vitamin D did not play a role in combating subclinical atherosclerosis. Our study showed 30 (61.2%) of the elderly subjects to be vitamin D deficient. Similar findings were found by Kweder et al. [28] in his study who found 43 % vitamin D deficiency in elderly >75 years. Similar results were obtained by Setiali et al. [29] who found 35.1% women to be vitamin D deficient in age group of 60-75 years. Lack of physical activity and sun exposure are important factors leading to vitamin D deficiency in the elderly population [30]. Vitamin D shows a cardio-protective role by inhibiting

Table 1. Characteristics of elderly subjects ≥ 60 years

Characteristic (N=49)	Mean ± SD
Age	65.31 ± 4.89
Male: Female	3:1
BMI	27.9 ± 5.68
Systolic Blood Pressure	139.35 ± 16.5
Diastolic Blood Pressure	81.6 ± 10.1
Total Cholesterol	174.6 ± 43
Triglyceride	138.51 ± 65
LDL Cholesterol	103.44 ± 40.9
HDL Cholesterol	45.47 ± 9.86
Fasting Blood Sugar	110.4 ± 8.3
25 (OH) D Concentration	25.1 ± 15.6
25 (OH) D Deficiency (N, %)	30 (61.2%)
Average CIMT	0.81 ± 0.27

Table 2. Correlation between CIMT with cardiovascular risk factors and 25 (OH) Vitamin D

Variable	r- value	p-value
Age	0.65	< 0.05
BMI	0.08	0.584
Total Cholesterol	0.136	0.351
Triglyceride	0.148	0.310
HDL – Cholesterol	0.0134	0.929
LDL – Cholesterol	0.078	0.594
25 (OH) D Concentration	-0.42	0.003

cholesterol uptake and formation of foam cells [31]. Its deficiency might activate the rennin-angiotensin system, increase serum levels of Parathormone and Insulin like growth factor-1 (IGF-1) [32,33]. Low 25 (OH) D concentration influences activity of lymphocytes and macrophages causing chronic inflammation of the arterial wall. In a study by Mheid et al. [34] low 25 (OH) D was associated with blood vessel rigidity and endothelial dysfunction in 554 healthy individuals. The results of the present study indicate that elderly subjects have low serum Vitamin D levels. A nutritious diet with increased intake of Vitamin D rich foods along with regular exercise and exposure to ultraviolet rays of the morning sun are essential in order to delay the thickening of the carotid artery intima and media. Further longitudinal studies on a larger sample size are required to substantiate our findings.

Conclusion

A significant inverse relationship between 25 (OH) Vitamin D and C-IMT in elderly subjects ≥ 60 years was observed in our study. These findings suggest a potential role Vitamin D deficiency in the development of subclinical atherosclerosis.

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