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Vitamin D: Emerging Risk Factor for Acute Myocardial Infarction

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Abstract

Introduction: Current scientific evidence suggests a casual association between serum levels 25(OH)-D and an increase in risk for cardiovascular disease (CVD). Vitamin D supplementation establishes significant beneficial effects in reduction of risk factors associated with CVD. Current research also suggests that an increase of 25(OH)-D for at least 30 ng/mL, reduces the risk of CVD.

Methods: Between 2012 and 2016, we chose at random 226 patients assisted by the cardiology urgent care of Hospital de Clínicas Gaspar Viana Belem, PA-Brazil with clinical presentation, ECG and enzymes of myocardial necrosis compatible with Acute Coronary Syndrome. The patients were submitted to routines tests, including coronary cineangiography and vitamin D dosage.

Results: This sample was composed of 163 men (p<0.0001) and 63 women between 28 and 91 years of age, and the median age was 63.3 years. From the 226 patients under study, 220 (97%, CI 95%: 95.2-99.4) had a degree of coronary blockage above 70% (p<0.0001) and in 158 patients (70%; CI 95%: 63.9-75.9) the blockage was multiarterial (p<0.0001). There was significant association between the degree of obstruction above 70% and multiarterial obstruction (p=0.0214). As for the serum levels of 25-Hydroxy vitamin D, 107 (47%) had adequate levels (greater or equal to 30 ng/mL) and 119 (53%) had hypovitaminosis D, and among these patients, 23 had levels below 20 ng/mL, being considered with important deficiency for this vitamin (p<0.0001).

Conclusions: Our study showed high prevalence of low serum concentration of vitamin D in the tropical region of the Brazilian Amazon. Hypovitaminosis D, in particular, levels of vitamin D<30 nmol/L, may be associated with high rates of atherosclerotic blockage and predominance of multiarterial involvement, found in our population sample.

Keywords: Vitamin D; Risk factor; Atherosclerosis; Acute myocardial infarction; Cardiovascular Diseases

Introduction

Vitamin D is involved in cardiovascular diseases, and plays an important role in reducing CVD risk. It may be involved in the regulation of gene expression through the presence of vitamin D receptors in several cells, in the regulation of blood pressure (through the renin-angiotensin system (RAS)), and in the modulation of cell growth and proliferation, including vascular smooth muscle cells and cardiomyocytes [1].

The presence of vitamin D receptors has already been determined in vascular smooth muscle cells in cardiomyocytes [2], and vascular endothelium [3], besides the expression of 1-α-hydroxylase enzyme in cardiac myocytes and fibroblasts enabling the conversion for active metabolite 1.25-(OH)-2-vitamins D [4].

Observation done in the early 1980s and 1990s found geographic and seasonal differences in mortality caused by ischemic cardiopathy. The initial suggestion of vitamin D as a protective factor surged in a study done in the United Kingdom showing that mortality caused by ischemic heart disease was inversely proportional to hours of sun exposure [5].

Vitamin D active metabolite (1-α, 25-Dihydroxyvitamin D), is connected to the vitamin D receptor that regulates numerous genes involved in fundamental processes of potential relevance for cardiovascular disease, including the cell proliferation and differentiation, the apoptosis, oxidative stress, membrane transport and cell adhesion [6].

Recent studies [7] have shown that vitamin D deficiency is an independent factor associated with the prevalence of cardiovascular disease, demonstrating that the levels of the circulate form of Vitamin D are inversely associated with increase in mortality.

There is an indication of inverse relation between the level of 25-(OH)-vitamin D and cardiovascular risk, however the existing studies are not sufficient to assure relation between these facts and much less relation between Vitamin D supplements with reduction of cardiovascular risk either in experimental model [8], or in relation to plasmatic levels in human beings [9].

Research done in Central Europe show that high risk groups for vitamin deficiency include those people who spend most of the day inside their homes, such as pregnant women, lactating mothers,

newborns, breastfed infants without vitamin D supplementation, overweight people, patients with chronic or infectious disease, and those above 50 years of age [10].

Regulation of immune and inflammatory response is one of the mechanisms often associated with the antiatherogenic effect of vitamin D. It has protective effects against endothelial dysfunction, inflammatory process that precedes atherosclerosis, through several mechanisms, including the stimulation of nitric oxide production and inhibiting oxidative stress [11].

Vitamin D inhibits endothelium-dependent vasoconstriction through inhibition of the expression and production cyclooxygenase-1 and reactive oxygen species. Furthermore, 1.25 (OH)-2D3 can alter the macrophage function and the gene expression that is crucial to the formation of foam cells and vascular response to inflammation that promote the process of atherosclerosis [12].

Methods

Between January 2014 and January 2016, we performed a case study to evaluate Vitamin D levels in patients affected by Acute Myocardial Infarction (AMI). The target population in the research: Two hundred and twenty six (226) patients were randomly selected from the cardiology urgent care of Hospital de Gaspar Viana/Belém-Pará-Brazil Clinics, a reference institution of the Brazilian Unified Health System (SUS) for CVD treatment. It was a convenience sample and formed by men and women regardless of age group, with clinical, as well as laboratorial, eletrocardiographic (ECG) and angiographic diagnosis for coronary artery disease (CAD). The patients excluded were those below 21 years, patients with active infection, using antibiotics and anti-inflammatory immunosuppressant drugs for the last 30 days, and patients with neoplasia and considered terminal. All patients were subjected to optimized clinical treatment, routine laboratory exams, vitamin D dosage by chemiluminescence (Diasorin method LIAISON TMV (USA)), ECG, thorax X-ray, Doppler echocardiography, coronary angiography and angioplasty with intracoronary stent placement or Myocardial Revascularization Surgery. All information in the project was entered into a database using Excel. The data concerning the socio-demographic characteristics were treated using descriptive statistics, expressed in as Means ± SD and/or absolute and relative frequencies and their respective Confidence Interval (95%), as appropriate. The proportion of individuals according to gender, degree and type of coronary obstruction, and levels of vitamin D was tested using the Chi-square of Adhesion with Yates correction, when necessary. To evaluate the association between the levels of vitamin D and the main factors of coronary risk the g- test of independence was used. This test was also used to check the existence of association between the variables degree and type of coronary obstruction and levels of Vitamin to test the independence of the variables degree and type of coronary obstruction. The tests were performed using the BioEstat 5.4 software [13], and those results with $p \leq 0.05$ were considered significant.

Results

While the study took place, 497 patients that corresponded to the criteria of selection to participate in the research were admitted to the Cardiology Gaspar Viana/Belém-Pará-Brazil Clinics, with 226 of them randomly selected to form the sample. The major socio demographic variables of these patients are summed up in Table 1.

This sample was formed by 163 men ($p<0.0001$) and 63 women between ages 28-91, and the median age was 63.3 years. From the 226 patients under study, 220 (97%, CI 95%: 95.2-99.4) presented degree of coronary obstruction above 70% ($p<0.0001$) and in 158 (70%; CI 95%; 63.9-75.9) patients the obstruction was multiarterial ($p<0.0001$) in Figure 1.

Variables	n	%
Gender		
Male	163	72.1
Female	63	27.9
Race		
Brown	150	66.4
White	62	27.4
Black	10	4.4
No information	4	1.8
Occupation		
Retired	37	16.4
Housewife	26	11.5
Farmer	14	6.2
Professional driver	14	6.2
Self-employed	13	5.8
Construction worker	12	5.3
Other	102	45.1
No information	8	3.5
Education		
Illiterate	39	17.3
Less than 9th grade	93	41.2
Completed 9th grade	24	10.6
High school drop-out	14	6.2
High School Diploma	35	15.5
Some college	3	1.3
Bachelor's Degree	6	2.6
No information	12	5.3
Marital Status		
Single	33	14.6
Married	124	55
Cohabiting	32	14.3
Divorced	3	0.9
Widowed	32	14.3
No information	2	0.9

Family Income (monthly)		
Less than 3 Minimum Wages	205	90.7
Between 3 and 6 minimum wages	11	4.9
No information	10	4.4
Origin		
Urban Area	195	86.3
Rural Zone	29	12.8
No information	2	0.9

Table 1: Distribution of patients with Acute Myocardial Infarction, according to sociodemographic variables. Hospital de Clínicas Gaspar Viana – Pará, Brazil, 2016.

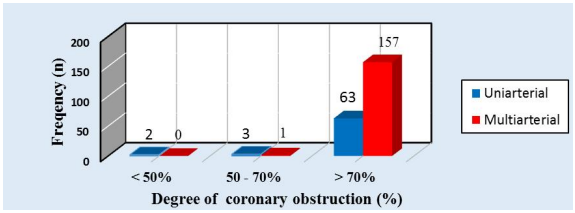

Figure 1: Degree and type of coronary obstruction defined by coronary cineangiography in patients included in the sample, Belem, Para, Brazil 2016.

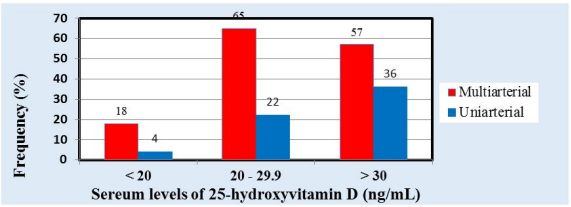

Figure 2: Relation of level of Vitamin D and involvement of multi or uniarterial in serum of patients with AMI. Belem, PA, Brazil, 2016.

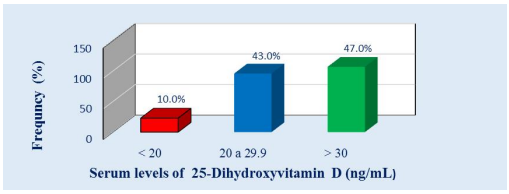

Figure 3: Levels of 25- hydroxyvitamin D in serum of patients with AMI. Belem, PA, Brazil, 2016.

There was a significant association between the degree of coronary obstruction above 70% and multiarterial obstruction (p=0.0214) (Figure 2). As for the serum levels of 25-hydroxyl vitamin D, 107 (47%) had adequate levels (greater or equal to 30 ng/mL) and 119 (53%) presented hypovitaminosis D and among these patients 23 had levels below 20 ng/mL, being considered with important deficiency of this vitamin (p<0.0001) in Figure 3.

Discussion

The role of vitamin D deficiency in cardiovascular decease (CVD) is a new field of interest. Well-founded experimental, epidemiological and observational data [14], describe in a convincing way the regulatory effects of vitamin D in relation to several factors of cardiovascular risk, such as hypertension and type II diabetes. And, they correlate vitamin D deficiency with incidence, degree and prevalence of cardiovascular risk factors.

In this work, done in a tropical region, the studied sample showed that most patients who had an AMI (53.0%) presented hypovitaminosis D, and 10% of them presented serum levels below 20 ng/mL, thus considered with an important deficiency of this vitamin (p<0.0001).

The findings above agree with most international studies [7-9,15,16]. In our review of the bibliography, we did not find studies or publications, whether experimental or in human beings on hypovitaminosis D, and acute myocardial Infarction in Brazil.

It was initially thought that Vitamin D deficiency was a problem of colder climates and high altitudes. In the Brazilian Amazon, with its hot and humid climate, even during periods of intense sunlight we found high rates of hypovitaminosis D in our sample. Such findings have also been documented in research done by the University of South Alabama, USA [17] that demonstrated the prevalence of vitamin D insufficiency in high temperatures with high rates of ultraviolet rays along the Southeast coast of the United States.

Recent studies [18] confirmed that vitamin D is a fat-soluble vitamin and is produced when ultraviolet rays from sunlight strike the human skin. Dark skin individuals are more predisposed to hypovitaminosis D. Since most of our post-infarct patients are dark, this condition associated with inadequate eating habits may be an excuse for our findings, similar to those found in studies done in migrating families in Australia, showing that dark skinned migrants who came to temperate climates are more at risk of Vitamin D deficiency and CVD [19].

Current scientific evidence suggests that a casual association between serum levels of 25-(OH)-D and an increase of risk for CVD. Vitamin D supplements determine significant benefits in the reduction of risk factor associated with CVD. Recent studies suggest that an increase in the levels of de 25(OH) D by at least 30 ng/ml reduce the risk of CVD.

Meta-analysis of prospective studies [20] show that vitamin D has pleiotropic effects that can favorably influence cardiovascular health through several mechanisms, including the negative regulation of the renin-angiotensin system, improvement of insulin secretion and insulin sensitivity, protection against angiogenesis and modulation of inflammatory response.

Arterial calcification is a common characteristic of arteriosclerosis that occurs in more than 90% of angiographically significant lesions. Current evidences [21] suggest that the development of atherosclerotic calcification is similar to the process of ossification. Those data suggest a possible role for vitamin D in the development of vascular calcification. In the tested sample of our study, most post-infarct patients (60%) with multi arterial obstruction had hypovitaminosis D.

Such high percentage may suggest a relation with greater gravity for coronary arterial disease in patients with hypovitaminosis D. The low levels of vitamin D in the serum levels are related to inflammation and severity of coronary atherosclerosis. Akin et al. [22], studied 239 patients who were subjected to coronary angiography coronary and found that 83% of the study population had plasmatic levels of vitamin D below 30 ng/ml. They concluded that lower levels of vitamin D are associated with a greater gravity of coronary artery stenosis.

Conclusions

We demonstrated in this study the potential of an epidemiological laboratorial and imaging evaluation for association of hypovitaminosis D with risk for coronary arterial disease. New studies are necessary to complement emerging evidences from international studies and better evaluate with more precision cardiovascular risks caused hipovitaminosis D.

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