The prognostic value of serum 25-hydroxyvitamin D level in patients with ST-segment elevation myocardial infarction

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Received 01 Octobber 2014
Accepted 01 December 2014

Egyptian Journal of Obesity, Diabetes and Endocrinology
2015, 1:49–52

Background
Low serum level of vitamin D has been shown to be associated with cardiovascular diseases as well as the presence of diabetes, dyslipidemia, and hypertension. Vitamin D deficiency is prevalent in Egypt as well as worldwide. We aimed to assess vitamin D status in patients with acute ST-segment elevation myocardial infarction (STEMI) and its correlation with hospital length of stay, in-hospital complication, in-hospital mortality, and 6-month mortality.

Patients and methods
In a prospective study, 53 patients with acute STEMI were included. The patients' 25-hydroxyvitamin D levels (ng/ml) were determined and the associations with clinical characteristics, laboratory data, in-hospital outcomes, and 6-month mortality were investigated. The study also included 20 healthy adult volunteers.

Results
Almost 70% of the patients in the STEMI group were vitamin D deficient (<30 ng/ml). Patients with a history of hypertension had significantly lower vitamin D levels ($P < 0.001$). Moreover, there was a significant positive relationship between hospital length of stay and levels of vitamin D ($P < 0.003$). Also, hospital length of stay was significantly shorter in patients who had undergone a primary percutaneous intervention ($P < 0.008$).

Conclusion
Vitamin D deficiency is highly prevalent in patients with acute STEMI. Vitamin D deficiency is highly prevalent in patients with a history of hypertension. Vitamin D deficiency is associated with longer length of hospital stay.

Keywords:
deficiency, prognosis, ST-segment elevation myocardial infarction, vitamin D

Egyptian Journal of Obesity, Diabetes and Endocrinology 1:49–52

2356-8062

Introduction

The link of vitamin D deficiency to cardiovascular disease has only recently been suggested as it was traditionally recognized as the cause of musculoskeletal pathology. Lower vitamin D status (VDS) in healthy individuals has been associated with incident cardiovascular disease, hypertension, and diabetes in several studies. 25-Hydroxyvitamin D [25(OH)D] is the major circulating form in blood and is considered the measure of an individual's VDS [1].

Receptors for vitamin D are present in a wide variety of tissues, including cardiomyocytes vascular endothelium, and lymphocytes [2]. Generation of left ventricular (LV) hypertrophy, extracellular matrix changes, and activation of plasma renin are all the result of decreased vitamin D receptors [3]. Vitamin D has many other functions such as suppression of the renin–angiotensin system [4], and it also affects endothelial function and exerts anticoagulant effects by upregulating thrombomodulin and downregulating tissue factor [5]. Vitamin D also regulates macrophage activity to reduce responsiveness to pathogen-associated molecular patterns. These effects may have direct relevance to cardiovascular disease [6].

Patients and methods

Study population

In a prospective cohort study, we enrolled 53 adult patients of both sexes with a diagnosis of ST-segment elevation myocardial infarction (STEMI) who were admitted to the units of the Critical Care Department, and coronary care unit in Alexandria Main University Hospital; in addition to coronary care units experienced in percutaneous coronary intervention. Approval of the Medical Ethics Committee of Alexandria Faculty of Medicine and an informed consent from the patients or their next of kin were obtained before the study. The study also included 20 healthy adult volunteers as controls.

Patients were divided into two groups: group A included individuals who had a normal serum level

of 25(OH)D, that is, above 30 ng/ml [7] and group B included individuals who had a low serum level of 25(OH)D, that is, below 29.9 ng/ml. Patients who had chronic kidney diseases, advanced liver cirrhosis, malabsorption syndrome, and active orthopedic diseases were excluded from the study. In addition, patients taking vitamin D supplements, patients taking certain drugs affecting serum 25(OH)D level, for example, phenytoin, carbamazepine were also excluded. Patients' demographic data, including sex, age, and risk factors for cardiac events including high-risk age (men >45, women >55 years old), smoking history, medical history of hypertension, hyperlipidemia, diabetes, and a positive family history, drug history, presence of arrhythmia, laboratory data, ECG, and echocardiography findings, were recorded. Echocardiographic studies were performed for all of the patients including evaluation of LV systolic function by estimating patients' ejection fraction or any regional wall motion abnormalities.

Collection of samples

Peripheral venous blood (10 ml) samples were collected from each patient upon admission to determine the 25(OH)D serum level. Serum level of 25(OH)D was measured by electrochemiluminescence. In this study, 25(OH)D levels greater than 30 ng/ml were considered normal; 25(OH)D concentrations of equal to or less than 30 ng/ml were considered deficient.

Statistical analysis

Data were analyzed using the SPSS software package, version 18.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed using range, mean, SD, and median, whereas qualitative data were expressed as frequency and percentage. Qualitative data were analyzed using the χ^2-test; also, exact tests such as Fisher's exact were used to compare the two groups. Non-normally distributed quantitative data were analyzed using the Mann–Whitney test to compare the two groups. The Pearson coefficient was used to analyze the correlation between any two variables. *P* value was assumed to be statistically significant at 0.05.

Results

This prospective cohort study enrolled 53 patients with acute STEMI admitted to the units of the Critical Care Department, and coronary care unit in Alexandria Main University Hospital. A total of 63% of the participants were men. The mean age of the participants was 51.82 ± 9.70 years. 25(OH)D serum level in the STEMI group had a mean ± SD of 25.13 ± 5.42, whereas in the control group, it was 33.23 ± 1.99 ng/ml. Vitamin D level was significantly lower in the STEMI group ($P < 0.001$). There was no significant difference in the 25(OH)D levels of men and women. There was no relationship between the patients' age and the level of vitamin D. The presence of a history of hyperlipidemia, drug history of antiglycemic and antihyperlipidemic agents, a history of smoking, and a family history of ischemic heart disease did not contribute toward lower levels of vitamin D. However, there was a significant relationship between a medical history of hypertension and low vitamin D level ($P < 0.001$). On evaluating the association between vitamin D level and the patients' laboratory data, it was found that serum hemoglobin, white blood count, platelet count, blood urea nitrogen, serum creatinine, and random blood glucose level did not have a significant relationship with vitamin D levels (Table 1).

Hospital stay was significantly longer in patients with deficient vitamin D levels ($P = 0.003$). There was no significant relationship between patients' echocardiographic data, including LV systolic function regional wall motion abnormality, and 25(OH) D concentration. In terms of complications, there was no significant difference among the STEMI groups. Among the participants, five died during the hospitalization period. Also, three patients died during the 6-month follow-up. All the patients who died had low vitamin D levels, but this was not a statistically significant difference ($P = 0.307$ and 0.541, respectively) (Table 2).

Discussion

In our study, vitamin D level was significantly lower in the STEMI group than the control group. Similarly, Khalili *et al.* [8] reported that the level of 25(OH)D was low in the majority of patients admitted with acute myocardial infarction. Melamed *et al.* [9] concluded that the lowest quartile of 25(OH)D level (<17.8 ng/ml) is associated independently with all-cause mortality in the general population.

In the present study, we found that history of hypertension was more prevalent.

Vitamin D can suppress rennin [10], and an inverse relationship between vitamin D level and plasma renin activity has been reported [11]. Moreover, vitamin D can inhibit the nuclear factor-jB pathway directly, which regulates genes that contribute toward inflammation, cell proliferation, fibrogenesis, and increased oxidative stress [12]. The prevention of secondary hyperparathyroidism and the direct effect

Table 1 Comparison between the groups studied according to demographic data, vitamin D level, risk factors, and some laboratory investigations

	Total cases 'STEMI' (*n* = 53)	STEMI		Control (*n* = 20)	*P*
		Group A (*n* = 16)	Group B (*n* = 37)		
Sex					
Male	—	10 (62.5)	23 (62.2)	13 (65.0)	0.977
Female	—	6 (37.5)	14 (37.8)	7 (35.0)	
Age (years)	—	51.44 ± 7.83	54.05 ± 10.58	48.0 ± 8.40	0.077
Vitamin D	25.13 ± 5.42	—	—	33.23 ± 1.99	<0.001*
≥30 ng/ml	16 (30.2)	—	—	19 (95.0)	<0.001*
<30 ng/ml	37 (69.8)	—	—	1 (5.0)	
Hypertension	30 (56.6)	3 (18.8)	27 (73.0)	—	<0.001*
Diabetes	16 (30.2)	7 (43.8)	19 (51.4)	—	0.748
Family history	16 (30.2)	4 (25.0)	12 (32.4)	—	0.748
Dyslipidemia	8 (15.1)	3 (18.8)	5 (13.5)	—	0.625
Smoking	15 (28.3)	5 (31.3)	10 (27.0)	—	0.754
History of IHD	13 (24.5)	3 (18.8)	10 (27.0)	—	0.731
CK-MB (ng/ml)	—	36.19 ± 19.36	38.84 ± 23.19	—	0.808
Troponin I (ng/ml)	—	1.56 ± 0.75	1.87 ± 1.35	—	0.663
Hemoglobin (g/dl)	—	11.12 ± 1.70	12.22 ± 2.54	—	0.071
White blood count (10^3/μl)	—	9.77 ± 1.89	11.02 ± 4.52	—	0.635
Platelet count (10^3/μl)	—	246.94 ± 67.62	282.32 ± 106.83	—	0.388
Blood urea nitrogen (mg/dl)	—	23.50 ± 5.62	28.19 ± 14.38	—	0.342
Serum creatinine (mg/dl)	—	1.0 ± 0.19	1.03 ± 0.19	—	0.646
Random blood glucose level (mg/dl)	—	123.31 ± 25.98	139.86 ± 37.74	—	0.128

Data were expressed as mean ± SD for normally distributed data or as *n* (%); CK-MB, creatine kinase MB; IHD, ischemic heart disease; STEMI, ST-segment elevation myocardial infarction; *Statistically significant at $P \leq 0.05$.

Table 2 Comparison between STEMI groups according to reperfusion therapy, ejection fraction, hospital stay, complications, and mortality

	STEMI		*P*
	Group A (*n* = 16)	Group B (*n* = 37)	
Thrombolytic therapy	11 (68.8)	28 (75.6)	
Success	5 (31.3)	12 (32.4)	
Fail	6 (37.5)	16 (43.2)	
Percutanous coronary intervention	5 (31.3)	9 (24.3)	
Ejection fraction (%)	49.56 ± 8.02	46.62 ± 11.15	0.346
Hospital stay (days)	3.69 ± 1.01	5.14 ± 1.67	0.003*
Complications	2 (12.5)	10 (27.0)	0.307
Need for inotropic drugs	1 (6.3)	4 (10.8)	
Arrythmia	2 (12.5)	8 (21.6)	
Reinfarction	0 (0.0)	2 (5.4)	
Shock	1 (6.3)	3 (8.1)	
Hospital mortality	0 (0.0)	5 (13.5)	0.307
6-month mortality	0 (0.0)	3 (9.4)	0.541

Data were expressed as mean ± SD for normally distributed data or as *n* (%); STEMI, ST-segment elevation myocardial infarction; *Statistically significant at $P \leq 0.05$.

on vascular and endothelial cells can also explain the mechanisms by which vitamin D could play a role in preventing hypertension [13].

The results of our study are that length of hospital stay was significantly longer in patients with low vitamin D. In agreement with our study, Hélard *et al.* [14] reported that lower serum 25(OH)D concentrations were associated linearly with longer hospital stay in a cohort study carried out in critical care units.

This may be explained by the role of vitamin D in regulating cellular growth, differentiation, and function. Lower vitamin D status leads to multiple organ dysfunction, disability, and unstable health status, which lead to deconditioning, and longer length of hospital stay [15].

In terms of hospital mortality and 6-month mortality, there was no significant difference in hospital mortality between the two groups. In agreement with our study, Mahdavi *et al.* [16] did not find any relationship

between hypovitaminosis D and short-term mortality in patients with acute coronary syndrome. However, Melamed *et al*. [9] reported that patients with low 25(OH)D levels had significantly higher all-cause mortality rates compared with individuals with high 25(OH)D levels. This discrepancy can be attributed to dissimilar thresholds used for the definition of vitamin D deficiency as well as inconsistent methodologies used in different studies.

Conclusion

Vitamin D deficiency is highly prevalent in patients with acute STEMI. Vitamin D deficiency is highly prevalent in patients with a history of hypertension. Vitamin D deficiency is associated with longer length of hospital stay.

Acknowledgements

Conflicts of interest

None declared.

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