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Original Article

Vitamin D Deficiency as an Independent Predictor of Myocardial Infarction in the Elderly

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Abstract

Cardiovascular diseases are among the most common causes of disability and death in the world, and the number of patients with this category of diseases is increasing every year. This study aimed to investigate the role of vitamin D and the problems caused by its deficiency on the cardiovascular system. Level of D-(25[OH]D) in blood was studied by enzyme immunoassay in 95 elderly patients with myocardial infarction (MI) (the main group) and 92 elderly patients with no history of MI. The level of lipid metabolism as an indicator was determined using a KoneLab 300 auto-analyzer. Based on the results of this study, it was found that the elderly group without MI had the highest amount of D-(25[OH]D)(24.5±1.2), compared to the elderly group with MI (14.8±1.3). The rates of expressed deficiency, deficiency, and insufficiency in the group of elderly with MI were 53.6±5.1, 23.2±4.4, and 12.6±3.4%, respectively. This experiment has shown that D-(25[OH]D) is involved in lipid metabolism and reduces the accumulation of cholesterol by macrophages. The content of vitamin D in blood plasma was a prognostic predictor of MI, which improved MI in the elderly. Regardless of pathological changes, the deficit level of D-(25[OH]D) should be considered a laboratory predictor of MI in the elderly.

Keywords: Lipid metabolism, Myocardial infarction, Old age Prognostic value, Vitamin D

1. Introduction

Heart disease is the leading cause of death in the United States. According to the Centers for Disease Control and Prevention, coronary heart disease is one of the most common types of this disease (1). Acute myocardial infarction (MI) is a scary, confusing, and stressful experience for patients. Although various therapeutic and preventive measures are being implemented, there has been no significant reduction in cardiovascular disease (CVD) worldwide. The World Health Organization (WHO) predicts that CVD mortality will increase worldwide from 17.1 million in 2016 to 23.4 million in 2030 (2). At the same time, the main contribution to the negative dynamics of CVD is due to MI. Studies have shown that the incidence of this complication in Russia is 3-4 times higher than that in the countries of the European Union and the United States (3).

According to the WHO, 76% of the 25 million deaths from CVD in developing countries will occur by 2020. Studies have shown that the prevalence of the CVD worldwide is an important cause of death and disability, especially in women, and national programs to reduce its associated complications and the risk factors are essential (4). Researchers have agreed that smoking, high low-density lipoprotein (LDL) cholesterol (5), low high-density lipoprotein (HDL) cholesterol (6), high blood pressure (7), and high blood sugar levels (8) are risk factors for CVD; moreover, the indirect affecting factors include low physical activity (9), obesity (10), diet (11), and low socio-economic status (12). There seem to be other risk factors that play roles in the development of CVD; however, they are currently unknown.

There is plenty of evidence that vitamin D deficiency may be an important factor in the development of CVD (9). Vitamin D deficiency occurs in an average of 50% of the world's population and is a common health problem. Vitamin D deficiency is one of the indirect risk factors; in addition, this vitamin enters the body through food (10), and sunlight (ultraviolet) (11) on the skin provides vitamin D and controls more than 200 genes. These genes are responsible for cell growth, proliferation, and differentiation. Therefore, deficiency of this substance may cause ventricular hypertrophy (12), narrowing and clogging of arteries (13), heart failure (14), and arrhythmias (15).

The classic traditional MI risk factors include heredity, obesity, hypodynamia, and lipid disorders (16). In recent years, vitamin D-(25[OH]D) has been considered one of the risk factors (17, 18). However, most of the studies on the role of vitamin D in the development of CVD had only review purposes (2, 16, 17) or contained conflicting data (19).

Various studies have evaluated the relationship between vitamin D deficiency and cardiovascular risk factors, such as high cholesterol, insulin resistance, hypertension, and diabetes (20). On the other hand, the relationship between serum vitamin D levels and cardiovascular events, including acute MI (21), CVD due to diabetes, peripheral arterial diseases, and heart failure have been studied in several cross-sectional, case-control, and prospective studies. In a systematic review conducted in 2010, a significant correlation was reported in seven out of 13 cohort studies that examined the association of serum D-(25[OH]D) (lower 25) with cardiovascular events in healthy adults (22).

In addition, in previous studies that are representatives of the elderly age (16, 23, 24), there is limited information about the relationship of vitamin D content and lipid metabolism with the risk of CVD, including MI, despite the presence of some data on the association of vitamin D deficiency with a high level of total cholesterol in healthy people (25). There is also limited data on comparative information on the predictive value of vitamin D and the parameters of the lipid transport system in elderly patients with MI. This study aimed to compare the predictive value of vitamin D levels and lipid metabolism indices for the development of MI in the elderly.

2. Material and Methods

2.1. Samples

This study mainly included a group of 95 patients with MI aged 60-74 years. The control group consisted of 92 patients of the same age with no history of MI during the study period. The study was conducted in compliance with the principles of the Declaration of Helsinki and Good Clinical Practice after obtaining written consent from the examined patients to process and use the results for scientific purposes.

2.2. Measurement of Vitamin D

The content of vitamin D-(25[OH]D) was measured in blood plasma by enzyme-linked immunosorbent assay during June-August 2019. The D-(25[OH] D) deficiency was considered a value over 30 ng/ml in accordance with the practical guidelines for the supplementation of vitamin D and the treatment of deficiency in Central Europe (10). The contents of D-(25[OH]D) less than 10 ng/ml and 10-19 ng/ml were regarded as severe deficiency and a deficiency, respectively. Furthermore, the amount of D-(25[OH]D) in blood plasma less than 20-29 ng/ml was considered a deficiency of vitamin D.

2.3. Measurement of Indicators of Lipid Metabolism

Among the indicators of lipid metabolism, the contents of total cholesterol, LDL, very low-density lipoprotein (VLDL), HDL, and triglycerides have been studied. The lipid content was determined in fasting blood serum using KoneLab 300 (an automatic biochemical analyzer).

2.4. Statistical Analysis

The prognostically significant level of D-(25[OH]D) in the development of MI in the elderly has been determined on the basis of calculating prognostic coefficients (PC) according to the following generally accepted formula:

$$PC = 10lg\left(\frac{P_1}{P_2}\right),$$

Where PC is the prognostic coefficient, P_1 signifies the prevalence of the level of D-(25[OH]D) in the control group, and P_2 presents the prevalence of the level of D-(25[OH]D) in the main group (11). Statistical data processing was performed using Statistica (version 10.0) and the non-parametric X^2 test.

3. Results

According to the data obtained from the present study, MI occurs more often in the elderly whose D-(25[OH]D) levels in their blood plasma are below average (Table 1). This indicates the relevance of determining the D-(25[OH]D) content in blood plasma for the diagnosis of MI. The distribution of patients in the groups also differed significantly regarding the level of deficiency and the reference content of D-(25[OH]D) in blood plasma. A statistically significant difference was established for all selected gradations of the D-(25[OH]D) level, except for patients with vitamin D deficiency. Among elderly patients with MI, the percentage of individuals with a reference level was significantly lower, and the number of patients with severe D-(25[OH]D) deficiency was significantly predominant. In the main group of patients, an excess of the proportion of persons with a deficiency of D-(25[OH]D) was revealed.

Table 1. Plasma concentrations of D-(25[OH]D) in elderly patients with and without MI

Level of 25(OH)D (units of measurement)	Elderly with myocardial infarction	Elderly without myocardial infarction	P-value
Average level (ng/ml)	14.8±1.3	24.5±1.2	<0.001
Expressed deficiency of 25(OH)D (%)	53.6±5.1	18.5±4.4	<0.001
Deficiency of 25(OH)D (%)	23.2±4.4	10.9±3.2	<0.05
Insufficiency of 25 (OH)D (%)	12.6±3.4	16.3±3.9	>0.05
Normal level of 25(OH)D (%)	10.6±3.2	54.3±5.2	<0.001

According to the above, D-(25[OH]D) in the blood plasma should be taken into account as clearly and objectively as an additional laboratory marker for the diagnosis of MI in older people. The presented data on the prognostic significance of the identified levels of D-(25[OH]D) deficiency (Table 2) indicate the highest predictive value of a severe D-(25[OH]D) deficiency in elderly patients with MI. A slightly lower predictive value was found for the D-(25[OH]D) deficiency, which ranked second for PC. D-(25[OH]D) deficiency, like normal vitamin D levels, does not affect the development of MI in the elderly.

Elderly patients with and without MI showed statistically significant differences in terms of the parameters of the lipid metabolism indicators (Table 3), except for VLDL. To the greatest extent, the studied lipid metabolism differs in the level of LDL, the content of which is 2 times higher than that in the control group. The same excess in elderly patients with MI is the characteristic of the level of triglycerides, compared to elderly patients without MI. The average total cholesterol value is also higher in the main group. Statistical analysis showed reliable differences in the groups regarding HDL.

The prognostic value of lipid metabolism indicators in the development of MI in the elderly varies significantly (Table 4). Moreover, LDL is characterized by the greatest prognostic value. Triglycerides with high PC rank second in terms of the significance of their influence on the development of MI among patients. Significantly lower PC values were also found for total cholesterol and HDL cholesterol. The content of VLDL had no significant effect on the development of MI in the elderly.

Table 2. Prognostic value of D-(25[OH]D) content in the development of myocardial infarction in the elderly

Level of 25(OH)D	Value of the prognostic coefficient	Rank position
Expressed deficiency of 25(OH)D	-4.6	1
Deficiency of 25(OH)D	-3.3	2
Insufficiency of 25 (OH)D	+1.1	3
Normal level of 25(OH)D	+7.1	4
Total for all levels of deficiency	-6.8	-

Table 3. Parameters of the lipid metabolism as indicators in elderly patients with and without MI (M±m)

Lipid indicator (units of measurement)	Elderly with myocardial infarction	Elderly without myocardial infarction	P-value
Total cholesterol (mmol/L)	6.9±0.3	4.7±0.3	<0.001
LDL (mmol/L)	5.6±0.4	2.8±0.3	<0.001
HDL (mmol/L)	1.0±.09	1.4±0.08	<0.001
Triglycerides (mmol/L)	2.9±0.2	1.4±0.1	<0.001
VLDL (mmol/L)	0.8±0.1	0.4±0.2	>0.05

Table 4. A prognostic value of lipid metabolism indicators in the development of MI in the elderly

Indicators	Value of the prognostic coefficient	Rank position
Total cholesterol	-2.6	3
LDL	-4.7	1
HDL	-1.5	4
Triglycerides	-4.0	2
VLDL	-0.5	5
In total	-13.3	-

4. Discussion

MI is more common in the elderly population with a low intake of vitamin D from food resulting in a decreased content of serum D-(25[OH]D) (26). A study on the concentration of D-(25[OH]D) in the serum of 239 patients with MI in 20 hospitals in the United States revealed a deficiency (vitamin D less than 30 ng/ml) in 229 patients. This correlation was observed in 90% of cases (27). The prevalence of vitamin D deficiency (D-(25[OH]D) less than 30 (ng/ml) was found in 8% of patients with MI treated at the Cardiovascular Research Institute in India (28).

A decrease in the level of vitamin D in the blood serum has a negative effect on the metabolism of the heart muscle. Experimental studies (29, 30) have shown that vitamin D affects the contractility of cardiomyocytes in the distribution of lysozyme chains and modulating the intake of calcium into cardiomyocytes. Vitamin D also affects growth, hypertrophy, collagen deposition, and cardiomyocyte differentiation (31, 32). In addition, vitamin D deficiency leads to vascular calcification. Studies on laboratory animals have shown that vitamin D slows down the aging process of cardiomyocytes, regulates their proliferation, inhibits hypertrophy (33), and reduces endothelial inflammation, which develops with a low level of vitamin D in the blood, thereby increasing the risk of MI and atherosclerosis (34). The protective role of vitamin D in reducing the incidence of atherosclerosis and MI is exercised by increasing the production of endothelial nitric oxide, reducing platelet adhesion and aggregation, oxidative stress, release of proinflammatory cytokines, vasoconstrictor metabolites, and regulation of muscle vascular tone (35).

A study conducted in the United Kingdom at the University of Leicester aimed at identifying the relationship between the development of post-infarction complications and low levels of vitamin D in the blood of patients with MI. Plasma levels of (D-(25[OH]D) were measured by mass spectrometry in combination with isotope dilution in 1,259 patients with acute MI (908 men, mean age of 65.7±2.8 years). Almost 74% of the patients suffered from vitamin D deficiency (D-(25[OH]D) less than 20 (ng/ml). The considerable point of the study were significant adverse events, mortality (n=141), subsequent hospitalization with heart failure (n=111), and recurrence of acute MI (n=147) on average within 550 days after admission for MI. The researchers concluded that vitamin D levels might also be used to predict future adverse events after MI using Cox multivariate regression models (36).

Despite the observed vitamin D deficiency in almost all patients with acute MI, researchers emphasize the need for further prospective studies due to the lack of an adequate control group with normal vitamin D levels.

To investigate the relationship between the risk of CVD and low levels of vitamin D, a study was conducted, which included 18,225 men aged 40-75 years without signs of CVD (37). The concentration of D-(25[OH]D) in blood plasma was determined, and the observation period was 10 years. During this period, 454 men developed non-fatal MI or fatal coronary heart disease. Considering the adjustment for the presence of such risk factors as heredity, obesity, alcohol use, physical inactivity, diabetes mellitus, hypertension, ethnicity, and lipid disorders, the relative risk of unfavorable cardiovascular outcomes increases in men with D-(25[OH]D) deficiency ($P<0.001$). Therefore, low concentrations of D-(25[OH]D) can be regarded as an independent risk factor for cardiovascular events. Scientists have concluded that vitamin D deficiency plays a negative role in the development of atherosclerosis and coronary heart disease in humans (36).

Our results indicate that serum D-(25[OH]D) levels significantly increase the risk of MI in the elderly. Increasing impact of D-(25[OH]D) levels increases with its deficiency, which is objectively confirmed by relative risk values that is significantly increased in elderly patients with severe D-(25[OH]D) deficiency (less than 10 ng/ml), compared to D-(25[OH]D) deficiency (less than 10-20 ng/ml) and D-(25[OH]D) deficiency (20-29 ng/ml). At the same time, single studies did not reveal a significant difference in patients with and without MI (control group) regarding the serum vitamin D (38).

Unlike other studies, correlations were not established between the serum D-(25[OH]D) content and the parameters of the lipid transport system in elderly patients with MI. Experimental studies have shown that D-(25[OH]D) takes part in lipid metabolism (39) and reduces the accumulation of cholesterol by macrophages. Vitamin D deficiency as had been shown earlier along with the induction of myocardial hypertrophy contributes to atherogenic changes in the lipid profile. It is assumed that vitamin D deficiency leads to an increase in serum lipids and the formation of insulin resistance. In healthy people, the content of D-(25[OH]D) is inversely proportional to the level of total cholesterol and LDL cholesterol (32). However, there are doubts about the reduction in vitamin D and LDL levels. Meanwhile, a correlation has been established between the content of vitamin D and metabolic risk factors in young men with no obesity, and the D-(25[OH]D) level correlates with the LDL level (40).

Vitamin D deficiency is an independent laboratory predictor of MI in the elderly. In addition, a severe D-(25[OH]D) deficiency and 25(OH)D deficiency are of the greatest prognostic significance in the prevalence of MI in the elderly. Among the indicators of the lipid metabolism indicators, LDL and triglycerides are the most predictive of MI in the elderly. The study of the content of vitamin D in blood plasma is of practical importance since it can serve as an important prognostic predictor of MI in the elderly. Determination of the D-(25[OH]D) content in blood serum along with the study of parameters of the lipid metabolism indicators will improve the verification of MI in the elderly.

Authors' Contribution

Study concept and design: N. I. Z.
Acquisition of data: S. S. B.
Analysis and interpretation of data: N. M. A.
Drafting of the manuscript: D. T. L.
Critical revision of the manuscript for important intellectual content: V. V. A.
Statistical analysis: N. I. Z.
Administrative, technical, and material support: S. S. B.

Ethics

The study was conducted in compliance with the principles of the Declaration of Helsinki and Good Clinical Practice after obtaining written consent from the examined patients to process and use the results for scientific purposes.

Conflict of Interest

The authors declare that they have no conflict of interest.

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