Functional Features of Modern Cardiological Patients

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Abstract

Context: Modern studies have shown that one of the risk factors for recurrent thrombosis, coronary heart disease and cerebrovascular pathology is the level of homocysteine in the blood. An analysis was made of the severity of homocysteinemia in patients with coronary heart disease with episodes of painless myocardial ischemia, and it was corrected with B vitamins. 84 patients with coronary heart disease with functional angina pectoris I-III were examined. It was found that the combination of hyperhomocysteinemia and frequent episodes of painless myocardial ischemia is recorded mainly in patients with a high functional class of angina pectoris. Reception of B vitamins can significantly reduce the concentration of homocysteine in blood plasma and the frequency of episodes of painless myocardial ischemia.

Keywords: *Hyperhomocysteinemia, coronary heart disease, angina pectoris, painless ischemia.*

Introduction

Currently, the pathology of the cardiovascular system occupies a leading position in the morbidity and mortality of the population worldwide[1]. Coronary heart disease has the status of the leading cause of death in most developed countries and accounts for about 30% of total mortality, with no tendency to decrease this indicator[2]. Moreover, back in 2001, cardiovascular diseases claimed the lives of about 16 million people, that is, a third of global world mortality, then by 2025 it is predicted that this figure will be 25 million and in almost half of the cases will be caused by coronary heart disease[3,4].

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In this regard, the search for new risk factors continues, the identification of which would allow to influence the mortality rate from cardiological causes. Today there is no doubt that inflammation factors and procoagulants circulating in the blood play an important role in the pathogenesis of vascular lesions and atherosclerosis[5,6]. It has been established that hyperhomocysteinia is an important risk factor for recurrent thrombosis, coronary heart disease and cerebrovascular pathology[7,8].

Homocysteine is a sulfur-containing amino acid that is not involved in the synthesis of protein. It is a demethylated derivative of the essential amino acid methionine, which in humans and animals is the only metabolic precursor of homocysteine. Foods in a normal diet contain an insignificant amount of homocysteine. The low content of this potentially cytotoxic amino acid in the cells is ensured by its remethylation to methionine, by its transulfonation to cysteine, or by the formation of its oxidized forms[9].

Normally, the level of homocysteine in blood plasma is 5-15 μmol/l. In children and adolescents, this indicator is approximately 5 μmol/l. During life, the average level of homocysteine increases by 3-5

micromol/l and it is slightly higher in men compared with women. Hyperhomocysteinemia is diagnosed if the level of homocysteine in the blood exceeds 15 μmol/l. Its plasma concentration of 15-30 μmol/l indicates moderate hyperhomocysteinemia, from 30 to 100 μmol/l - intermediate, and more than 100 μmol/l - heavy[7,8].

Hyperhomocysteinemia negatively affects endothelial and smooth muscle cells of blood vessels, platelets, blood lipids, nitric oxide and coagulation factors[9]. This is manifested even with moderate hyperhomocysteinemia. In addition, it stimulates atherosclerosis, disrupts the vasomotor function and anticoagulant properties of endothelium[10,11].

For patients with coronary heart disease, regardless of the clinical form, elevated plasma homocysteine levels and episodes of painless myocardial ischemia are very characteristic[12,13]. According to modern concepts, the phenomenon of painless myocardial ischemia is found in 2–5% of the healthy population, in 30% of patients with post-infarction cardiosclerosis, and 40–100% of patients with stable and unstable angina[14]. The proportion of episodes of painless myocardial ischemia reaches 75–89% of the total number of cases of myocardial ischemia in these patients[15,16]. The detection of painless myocardial ischemia in combination with other high-risk criteria in a patient with coronary heart disease and confirmed angina pectoris is an indication for surgical treatment, since it significantly increases the likelihood of fatal cardiac complications in the near future[17,18].

Along with hyperhomocysteinemia, the presence of painless myocardial ischemia is now regarded as one of the risk factors for the development of complications of coronary heart disease, including myocardial infarction and prognostically unfavorable heart rhythm disturbances[3,19]. It is believed that the combination of hyperhomocysteinemia and episodes of painless myocardial ischemia worsens the course of coronary heart disease. A relationship was suggested between the level of homocysteine in blood plasma in patients with coronary heart disease and the incidence of episodes of painless myocardial ischemia due to the presence of moments in their pathogenesis and the point of application that damages the effects of hyperhomocysteinemia[20,21].

It is believed that metabolic elimination of hyperhomocysteinemia is possible with the help of vitamins[22,23]. When they are prescribed, there is a decrease in the initially elevated level of homocysteine in all cases[24]. Particularly effective injections of B vitamins[25,26].

The purpose of the study was to analyze the severity of homocysteinemia in patients with coronary heart disease with episodes of painless myocardial ischemia and its correction with a combination of vitamins B_1, B_6 and B_{12}.

Materials and Method

The research was approved by the local ethical committee of the Russian State Social University on September 9, 2018 (protocol №9).

84 patients (62 people – the main group and 22 – the control group) who had a diagnosis of coronary heart disease with functional angina pectoris I-III, were examined at a clinic in Kursk State Medical University. The average age of the patients was 53.8±1.45 years, of which 58 were men and 26 women. The study did not include patients with acute myocardial infarction, valve defects, and chronic heart failure stage III (according to the classification of Strazhesko-Vasilenko), myocardiopathy and endocrine pathology, with any kidney pathology and oncology.

To study the frequency and characteristics of painless myocardial ischemia, electrocardiography was used according to the standard method, two-dimensional echocardiography, bicycle ergometry, electrocardiography with dosed physical activity after canceling antianginal therapy, except nitroglycerin, which was used in case of an angina attack.

All patients with coronary heart disease were determined the concentration of homocysteine in plasma on the first and on the fourteenth day of observation. Blood sampling was carried out on an empty stomach after 12-hour fasting from a cubital vein in an amount of 10 ml. For quantitative determination of total homocysteine in blood plasma by enzyme-linked immunosorbent assay, a test system from Axell Biochemicals (Oslo, Norway) was used.

In addition to standard antianginal therapy, for the correction of hyperhomocysteinemia, patients additionally received B vitamins: B_1 at a dose of 150 mg/day, B_6 - 150 mg/day and B_{12} - 3 mg/day.

The effectiveness of treatment was evaluated by re-determining the concentration of homocysteine in

blood plasma on the 14 day, as well as the frequency and intensity of angina attacks and exercise tolerance.

Statistical processing of the data obtained in the studies was carried out using variation statistics based on the program Statistica 5.0 for Windows, including the determination of t-student criterion and correlation analysis. Differences starting from $p<0.05$ were considered statistically significant.

Results and its Discussion

For the convenience of comparative characteristics of patients with coronary heart disease of the main group, they were divided into 3 groups, depending on the functional class of angina pectoris. The 1st group (n=20) included patients with the I functional class, the 2 group (n=21) - the patients with the II functional class and the 3rd group (n=21) were the patients with the III functional class. Patients of group 1 showed a milder course of coronary heart disease, fewer complications than in groups 2-3. The presence of postinfarction cardiosclerosis in the first group was noted in 11.5% of cases, and episodes of painless myocardial ischemia in 11.7% of cases; in patients of the 2nd group, postinfarction cardiosclerosis was in 32.6% of cases, episodes of painless myocardial ischemia in 38.4%, in patients of group 3 postinfarction cardiosclerosis was recorded in 69.6% of cases, and in 72.3% - episodes of painless myocardial ischemia. When analyzing homocysteinemia in patients with coronary heart disease, it was taken into account in combination with concomitant pathology, taking into account previous myocardial infarction. Thus, the highest concentration of homocysteine was observed in patients with coronary heart disease with post-infarction cardiosclerosis and averaged 18.5±1.8 μmol/l compared with patients with coronary heart disease without complications - 15.2±0.9 μmol/l ($p<0.05$). Patients with coronary heart disease, who also had hypertension — 17.6±1.7 μmol/l — were distinguished by a rather high level of homocysteine compared with patients without arterial hypertension. With a combination of coronary heart disease with post-infarction cardiosclerosis and hypertension, the level of homocysteine remained elevated - 16.8±1.4 μmol/l.

Among patients included in group 2 and 3, the highest percentage of concomitant pathologies, such as hypertension, was noted - 31.9% and 55.6%, respectively.

Painless myocardial ischemia was diagnosed in 28 patients (33.3%) of the total number examined with coronary heart disease in the form of stable angina pectoris of functional class III, with a history of post-infarction cardiosclerosis in 30 (35.7%) cases (table 1).

Table 1: The dynamics of the level of homocysteine in the plasma of patients with coronary heart disease while taking vitamins of group B

Patient groups	The level of homocysteine, μmol/l, M±m		p
	for 1 day	for 14 days	
1 group (n=20)	11.9±1.3	9.1±0.8	<0.05
2 group (n=21)	15.6±0.5	13.1±0.7	<0.05
3 group (n=21)	19.5±0.6	15.0±1.2	<0.05
Control group (n=22)	16.6±0.8	17.2±0.8	

The duration and frequency of episodes of painless myocardial ischemia directly depended on the severity of the course of coronary pathology and occurs in patients with coronary heart disease with a high functional class of stable angina pectoris, that is, in the 2-3 group, as well as in people who have suffered myocardial infarction. After myocardial infarction, 44% of patients with coronary heart disease who had had angina attacks before, ceased to feel pain typical of angina pectoris, therefore, the study of the frequency of detection of painless myocardial ischemia in these patients is of no small importance. When conducting physical exercise tests in patients with coronary heart disease in the late post-infarction period, despite the absence of angina attacks in most patients, almost 45.2% of them revealed episodes of painless myocardial ischemia.

An analysis of homocysteinemia in patients with coronary heart disease revealed a tendency to significantly increase homocysteine levels as the functional class of exertional angina increases. So in patients of 1 group the average level of homocysteinemia was 11.9±1.3 μmol/l, in 2 group the concentration of homocysteine reached 15.6±0.5 μmol/l, in 3 group 18.5±0.6 μmol/l ($p<0.05$). That is, in patients with tension angina of functional class III, the concentration of homocysteine was higher than in functional class I by 63.8%. When re-determining the concentration of homocysteine after taking B vitamins, a significant decrease in homocysteine was noted ($p<0.05$). So, its average level in group 1 after 14 days decreased to 9.1±0.8 μmol/l. In 2 group after 14 days it decreased to 13.1±0.7 μmol/l and in group 3 to 15.0±1.2 μmol/l ($p<0.05$). In the control group homocysteine levels did not experience dynamics (table 1).

The results obtained indicate that with the additional intake of vitamins B1, B6 and B12 in combination with antianginal therapy, the level of homocysteine in plasma in patients with coronary heart disease significantly decreases. Moreover, in patients with initial hyperhomocysteinemia, the decrease is more pronounced.

Against the background of a decrease in the level of homocysteine in patients, the quality of life improved by reducing the number of angina attacks and thereby reducing the use of nitroglycerin per week, compared with the control group. So in the 2 group, the number of nitroglycerin tablets consumed by patients after 14 days decreased by 25.8%, in the 3rd group this amounted to 36.1%. In the control group, the dynamics of nitroglycerin consumption were not detected ($p<0.05$). Also, against the background of the treatment, all patients noted an improvement in overall health, a decrease in the frequency and intensity of angina attacks, as well as increased tolerance to physical activity. In this regard, the need for early diagnosis of painless myocardial ischemia and correction in such patients with hyperhomocysteinemia should be recognized. This will help to slow the progression of angina pectoris and reduce the number and duration of episodes of painless myocardial ischemia[27].

Conclusion

The level of plasma homocysteine is directly proportional to the functional class of angina pectoris. The more pronounced homocysteinemia, the more severe the clinical manifestations of stable exertional angina. An additional intake of B vitamins statistically significantly reduces the level of total homocysteine in blood plasma in most patients. This is accompanied by a decrease in the number and duration of episodes of painless myocardial ischemia. There is reason to hope that the optimization of homocysteine will inhibit the progression of coronary heart disease and lower the functional class of angina pectoris.

Conflict of Interest: No conflict of interest is declared.

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Ethics Committee Resolution: The study was approved by the local ethics committee of the Russian State Social University on September 9, 2018 (protocol №9).

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