ORIGINAL ARTICLE

THE DYNAMICS OF NEUROHUMORAL MEDIATORS OF VASOCONSTRICTION AND VASODILATION AND TROPONIN I IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION DEPENDING ON THE DEGREE OF CONCOMITANT OBESITY

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ABSTRACT

The aim: Is to evaluate copetin's, MRproADM's and troponin's I dynamic in patients with acute myocardial infarction depending on the degree of concomitant obesity.

Material and methods: The study included 105 patients with AMI. There were formed 2 groups: 1st group of patients with AMI and concomitant obesity (n=75), 2nd group – patients with AMI without obesity (n=30). 37 patients had obesity of the I degree, 38 patients - II degree. The groups were comparable in age and gender. Copeptin, MRproADM, troponin I were determined by enzyme immunoassay method. Data are presented as mean values and the error of the mean (M±m). Differences were considered statistically significant at $p<0,05$.

Results: It was found an increased copeptin's level by 73,8 % ($p<0,001$) in obesity I degree and by 205,9 % in obesity II degree compared with group with isolated AMI, MRproADM - by 30,68 % ($p<0,001$) and 54,5 % ($p<0,001$) respectively. Concentration of copeptin was higher by 76 % ($p<0,001$) in patients with AMI and II degree obesity comparing to patients with obesity of I degree, and MRproADM - by 18,3% ($p<0,001$) respectively. Troponin I value fully corresponded the comparison group both in obesity of I degree and II degree ($p>0,05$).

Conclusions: The present study provides evidence that a high activity of copeptin and MRproADM in patients with AMI and obesity of I degree with an excessive activity of a marker of vasoconstriction copeptin in conditions of moderate inadequate to the needs MRproADM functioning in patients with obesity of II degree.

KEY WORDS: acute myocardial infarction, obesity, vasoconstrictors, vasodilators, copeptin, MRproadrenomedulin

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INTRODUCTION

Cardiovascular diseases (CVD) occupies the first place in the structure of morbidity, disability and mortality worldwide. Priority in the structure of the cardiovascular disease belongs to coronary artery disease (CAD) and especially to its acute form - acute myocardial infarction (AMI). The destabilization of CAD in the form of the development of AMI remains an important cause of disability and mortality worldwide [1-3]. Every year in the world there are more than 15 millions of new cases of AMI. By 2030, it is projected that about 23.6 million people will die due to heart attacks and mainly from heart disease and stroke. The leading nosological form in the structure of CAD is the AMI with elevation of ST segment (STEMI) for many years [4-5].

According to World Health Organization (WHO), obesity is recognized as a non-infectious «epidemic of the 21st century» and is one of the five major risk factors of death. In addition, obesity is a risk factor for the development of CVD, progression and destabilization of CAD [6, 7]. As a result of the INTERHEART study, it has been proved that obesity is an independent risk factor for CAD [8]. Obesity is not only an independent factor in the risk of cardiovascular complications, but also is a trigger mechanism for the development of CVD [9]. Despite the existence of a close relationship between obesity and cardiovascular disorders, the molecular genetic bases remain not fully defined. It is known that adipose tissue secretes a large number of biologically active substances - adipocytokines, which can provide either local auto- and paracrine effects or systemic endocrine and pro-inflammatory effects, as well as to promote and counteract the development of cardiovascular disease [10, 11, 12]. Additionally, adequate therapy for hyperglycemia leads not only to lowering insulinemia, but also to a decreasing in the content of sCD40-ligand, which contributes to inhibition of immune-inflammation and thrombosis [13-16].

In accordance with European and Ukrainian guidelines increased concentration of troponin I is a diagnostic criteria for ST segment elevation myocardial infarction (STEMI) and non-ST segment elevation myocardial infarction (nonSTEMI) [17, 18]. But searching for new, more specific, prognostically valuable markers today takes the attention of the world medical community. Activation of neurohumoral systems plays an important role in the pathogenesis of AMI under conditions of comorbid obesity [19]. Most

Table 1. The levels of copetin, MRproADM and troponin I in patients with acute myocardial infarction depending on the degree of concomitant obesity (M±m)

Indicator, units	Patients with AMI and obesity		Patients with AMI and obesity
	Obesity of I degree	Obesity of I degree	
	1	2	3
Copeptin, ng/ml	145,86±3,76	256,73±11,37	83,9±5,38 $p_{1 \text{ and } 2}$<0,001 $p_{1 \text{ and } 3}$<0,001 $p_{2 \text{ and } 3}$<0,001
MRproADM, ng/ml	586,4±12,12	694,06±19.99	449,03±6,49 $p_{1 \text{ and } 2}$<0,001 $p_{1 \text{ and } 3}$<0,001 $p_{2 \text{ and } 3}$<0,001
Troponin I, ng/ml	6,53±1,48	6,44±1,37	6,98±1,91 $p_{1 \text{ and } 2}$>0,05 $p_{1 \text{ and } 3}$>0,05 $p_{2 \text{ and } 3}$>0,05

neurohumoral shifts are mediated by vasoconstrictor and vasodilator responses. Given this fact, it is interesting to study the C-terminal part of the prohormone vasopressin (vasoconstriction mediator) - copeptin and midregional proadrenomedullin (MRproADM) (vasodilator mediator).

THE AIM

The aim of the present research is to evaluate copetin's, MRproADM's and troponin's I dynamic in patients with acute myocardial infarction depending on the degree of concomitant obesity.

MATERIALS AND METHODS

SUBJECT RECRUITMENT

Between 2013 and 2015, eligible people were identified and recruited from the electoral roll, and invited to attend a screening clinic close to their home. On arrival at the clinic, the trial was explained to each participant and written consent was obtained. A risk factor questionnaire covering aspects of medical history and lifestyle relevant to CVD was completed. Height, weight, girth at hips and waist, and blood pressure were measured. The study included 105 patients with AMI and obesity, who were treated at the intensive care unit and cardiological department at the hospital No 27. We formed 2 groups: 1st group of patients with AMI with concomitant obesity (n=75), 2nd group – patients with AMI and without obesity (n = 30). 37 patients had obesity of the I degree, the 38 patients - II degree according to the body mass index (BMI). The average age of patients in group 1 was 65,96±1,11 years, and 2 groups - 63,46±1,76 years (p>0,05). The groups were comparable in gender. The exclusion criteria were acute and chronic inflammatory processes, diffuse connective tissue diseases, oncological diseases, concomitant diseases of the thyroid gland, and the presence of symptomatic hypertension. Diagnosis of AMI verified according to ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation [9]. The presence of obesity was established according to the classification of WHO, 1997 [19] under the BMI >30 kg/m^2 according to the formula: BMI (kg/m^2) = body weight/(height)^2.

IMMUNOASSAY METHOD

Copeptin was determined using the Human Copeptin (Copeptin) ELISA Kit (Shanghai, China). MRproADM was determined using «Human mid-regional pro-adrenomedullin (MRproADM)» (Biological Technology, Shanghai). Troponin I was determined using «Troponin I» with an enzyme immunoassay method in the blood serum (Ham, Russian Federation).

STATISTICAL METHODS

Data are presented as mean values and the error of the mean (M±m). Statistical analysis of the difference between dispersions in the groups was evaluated using F-Fisher's criterion. An assessment of the differences between groups in a distribution close to normal was carried out using the Student's criteria. Differences were considered statistically significant at p<0,05.

RESULTS

Copeptin and MRproADM showed significant differences in patients with AMI and obesity of I and II degree, comparing with group represented by AMI patients without obesity. It was found an increased copeptin's level by 73,8 % (p<0,001) in obesity I degree and by 205,9 % in obesity II degree compared with the comparison group, MRproADM - by 30,68 % (p<0,001) and 54,5 % (p<0,001), respectively (Table I).

Concentration of copeptin was higher by 76 % (p<0,001) in patients with AMI and II degree obesity comparing to patients with AMI and obesity of I degree, and MRproADM - by 18,3% (p<0,001) respectively. As for the content of troponin I, its value fully corresponded the comparison

group both in obesity of I degree and II degree (p>0,05). Comparison of the concentrations of this parameter in obesity of I degree and II degree in patients with AMI did not reveal any significant differences (p>0,05). The ranking of indicators according to the degree of their differences in obesity of 1st degree from the comparison group using the F-criterion determined that the cluster of pronounced disorders included both parameters - copeptin (F=77,9; p<0,001) and MRproADM (F=82,5; p<0,001). Thus, in patients with AMI and obesity of I degree, it was found high activity of both markers (copeptin and MRproADM) - that is confirmed by approximately the equivalent degree of deviation (F=77,9 and F=82,5 respectively). The obtained data prove opinion about work of system of vasoconstrictors and vasodilators in the form of adaptive stress due to the adequate compensatory mechanisms presented by MRproADM. According to the obtained results while comparison of indicators deviation by the degree of their differences in obesity of the II degree (according to the F-criterion), it can be distinguished that a cluster of very expressive changes (F=100) included increased level of copeptin (F=177,9; p<0,001). The significant growth was noted for MRproADM (F=99,5; p<0,001). In order to evaluate the changes in copeptin and MRproADM with varying degrees of overweight in patients with AMI, a ranking was conducted for the degree of their deviation in obesity of II degree from the group of patients with obesity of I degree. According to the obtained results, it can be distinguished a cluster of very expressive changes (F=100) and moderate changes (50>F>10). Very significant deviations were found for copectin (F=107,9; p<0,001), where as it was detected moderate deviations (F=21,2; p<0,001) for MRproADM.

DISCUSSION

The obtained results of indicators deviation comparison by the degree of their differences in obesity of the II degree indicate that the presence of II degree obesity in patients with AMI is accompanied by a disproportionate increase in the concentrations of vasoconstrictors and vasodilators with a lower activity of last one, which are represented by MRproADM, while the vasoconstrictive activity (due to copeptin) occupies the first rank position. The obtained results of evaluation the changes in copeptin and MRproADM with varying degrees of overweight in patients with AMI indicate that the appearance of AMI in patients with concomitant obesity of II degree comparing with obesity of I degree was excessive activity of copeptin, which are the stress marker, indicator of platelet aggregation and vasoconstriction in conditions of moderate increase of MRproADM, which indicates an inadequate vasodilator system functioning. Thus, the imbalance in the work of vasoconstrictors and vasodilators in patients with AMI clearly manifests itself at the obesity of the II degree. The findings are in line with the findings of the specialists of the world medical community. Thus, according to Morgentaler N., the activity of copeptin increases in patients with cardiovascular events, including AMI and heart failure [20]. Similar results were obtained in the LAMP study [21]. On the other hand, body mass growth is accompanied by an increase in the activity of copeptin, which some authors consider as a predictor of obesity [22]. However, there is evidence that copeptin has a strong association with insulin resistance and, as a result, displays indicative properties in patients with obesity [23, 24, 25]. This fact explains the results obtained in our study on the maximum activity of copeptin in a cohort of patients with AMI and obesity of II degree, since the progression of the severity of obesity is associated with a proportional increase in the incidence of insulin resistance [24].

CONCLUSIONS

In conclusion, the present study provides evidence that a high activity of mediator of vasoconstriction copeptin and mediator of vasodilation MRproADM in patients with acute myocardial infarction and concomitant obesity of I degree. The feature of the development of acute myocardial infarction in patients with obesity of II degree compared with obesity of I degree is an excessive activity of a marker of vasoconstriction - copeptin in conditions of moderate inadequate relative to the needs of the functioning of MRproADM.

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