**STUDY OF HUMORAL MECHANISMS IN THE DEVELOPMENT OF ACUTE MYOCARDIAL INFARCTION WITH CONCOMITANT OBESITY ANDTYPE 2 DIABETES MELLITUS**

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**Abstract**

The article investigates the development of acute myocardial infarction with concomitant obesity and type 2 diabetes mellitus. The study involves the assessment of pathogenic roles of FABP4, CTRP3, adropin, irisin - reg-ulatory proteins related to regulation of adipogenesis, response to insulin, and the development of acute myocardial infarction with concomitant obesity and type 2 diabetes mellitus. The findings showed that FABP4, CTRP3, adropin, irisin could be regarded as new markers for the development and progression of acute myocardial infarc-tion with concomitant obesity and type 2 diabetes mellitus.

**Keywords:** acute myocardial infarction, humoral indices, obesity, diabetes mellitus.

**Problem statement.** Ischemic heart disease (IHD) ranks high among cardiovascular diseases and is one of the leading causes of disability and mortality in the countries of Western Europe and Ukraine [1, p.197-202].

The risk of mortality increases in patients with myocardial infarction (MI) with concomitant obesity and type 2 diabetes mellitus. Complications of MI in patients with concomitant obesity and type 2 diabetes are the actual issues of internal medicine [6]. Despite numerous studies, the humoral mechanisms of the de-velopment of MI with comorbid pathology remain dis-putable issues.

To date, there are many issues that require detailed consideration for a new assessment of the diagnosis of MI in patients with concomitant obesity and type 2 DM.

**The purpose of the study** is to investigate the pathogenic role of humoral indices: FABP4, CTRP3, adropin, irisin and their employment in diagnosis of acute myocardial infarction with concomitant obesity and type 2 DM.

Over the last decade, there have been findings sug-gesting integration of metabolic and inflammatory pathways of metabolic syndrome development. A fatty acid binding agent 4 (FABP4), also known as adipocyte FABP (A-FABP) or aP2, is predominantly expressed in adipocytes and macrophages, and plays an important role in the development of resistance to insulin and ath-erosclerosis. Despite the absence of a typical secretory signal peptide, it has been shown that FABP4 is se-creted from adipocytes in the nonclassical pathway as-sociated with lipolysis, possibly acting as adipokin. In-creased circulating levels of FABP4 are associated with obesity, insulin resistance, diabetes, hypertension, car-diac dysfunction, atherosclerosis, and cardiovascular events. In addition, ectopic expression and the function of FABP4 in several types of cells and tissues cannot be detected. Scientists discuss the significant role of FABP4 in the pathophysiological sense and its useful-ness as a biomarker of metabolic and cardiovascular diseases [10, p. 23-33].

Several studies showed a significant correlation between circulating FABP4 and norepinephrine in trial tests. Moreover, FABP4 was found to be secreted from adipocytes by β-adrenergic mediated lipolytic mecha-nisms [15, p. 896-902].

The authors have confirmed that FABP4 is iso-lated from macrophages and adipocytes cultured in vitro. Exogenous FABP4 affects macrophages and hu-man coronary arteries derived from smooth muscle cells and endothelial cells in vitro. Treatment of cells with recombinant FABP4 significantly increases the expression of genes of inflammatory markers depend-ing on the dose. Finally, researchers measured serum FABP4 levels in the aorta and coronary sinuses with suspected or known coronary artery disease. The eval-uation of coronary stenosis considered using the modi-fied Gensini score, weakly correlated with FABP4 de-tected in coronary sinuses, but did not correlate with FABP4 detected in the aorta. Stronger correlation was observed between coronary stenosis baseline and coro-nary vein-arterial difference in FABP4 level, indicating local production of FABP4 during coronary circulation in the heart. The analysis of the study showed that FABP4 was an independent predictor of coronary ste-nosis after adjusting traditional risk factors [10, p. 23-33].

Scientists [7, c. 74-81] found differences in the ex-pression of genes between macrophages isolated from stable and discontinuities of human atheromatic plaques. The results indicate that FABP4 and leptin are involved in the progression of atherosclerosis and Danish Scientific Journal No10, 2018 39

plaque rupture, and believe that reducing the regulation of PPAR / adipocytokine signals in plaques may have therapeutic potential.

Scientists report that FABP4 is also expressed in cardiomyocytes and plays an important role in the reg-ulation of cardiac function. In the experimental model, FABP4 had an effect on hypertrophy of the heart under increased pressure at overload. The circulating level of FABP4 is an independent risk marker of the heart, and exogenous FABP4 secreted with adipose tissue or mac-rophages may suppress contraction of cardiomyocytes and may directly regulate the cardiac function. Conse-quently, inhibition of FABP4 in humans may have a positive effect on cardiac hypertrophy and cardiac events associated with PPARγ agonist preparations [6].

The level of FABP4 in atherosclerotic lesions is associated with an unstable plaque phenotype and an increased risk of cardiovascular events during the ob-servation. In addition to the risk of adverse future car-diovascular events, the study confirms the relevance of the study of FABP4 antagonists as a potential pharma-ceutical intervention for the treatment of progression of atherosclerotic disease [16, p. 1758-1768].

Circulating levels of CTRP3 are significantly re-duced in patients with obesity and hypertension. CTRP3 protein is closely linked to insulin resistance, glycolipid metabolism and sex. It can play a significant pathophysiological role in the mechanism of obesity and hypertension. Scientists have observed close rela-tionships between CTRP3, insulin resistance and arte-rial hypertension, as well as systemic chronic inflam-mation, but the molecular mechanisms between these relationships require confirmation in future studies. Adipokin CTRP3 has cardio-protective properties, and its level of circulation is reduced in obesity and in pa-tients with high blood pressure and is inversely related to the parameters of insulin resistance [18]. Scientists indicate that the level of CTRP3 has a negative relation-ship with the levels of leptin [11, p. 691-701].

Today, it is known that adropin and irisin affect the development of MI and its complications, but their predictive value of MI development has not been fully studied, thus representing a scientific interest [4, p. 9-12; 5, p. 46-49].

Studies of recent years have shown a significant humoral role of adropin and irisin in patients with type 2 DM [13, p. 510; 14, p. 544-556]. It is believed that adropin and irisin are closely associated with the pro-gression of atherogenesis in the development of cardi-ovascular diseases, namely, MI [2, p. 119-124], which requires further detailed study of these indices in pa-tients with comorbid pathology.

Scientists have shown that energy expenditure is regulated by adropin, which is expressed in the endo-cardium, myocardium and epicardium. Scientists have hypothesized that adropin is secreted into the blood-stream during a myocardial injury, caused by MI, there-fore the level of adropin rises. The authors of the exper-imental model investigated the relationship between the expression of adropin and MI induced by isoproterenol. The results showed that heart muscle cells synthesize adropin, and its synthesis increases in 1-24 hours after MI. The results highlight MI pathogenesis, and a grad-ual increase in serum adropin may become a new diag-nostic marker and serve as an alternative to measuring troponin I for the diagnosis of MI [3, p. 91-97].

The level of adropin in serum was significantly lower in patients with MI than in the control group. Multifactor logistic regression showed that the lower level of adropin was an independent prognostic factor for the presence of MI. The level of adropin in serum was negatively related to the body mass index and lev-els of triglycerides in patients with MI [5, p. 46-49; 9, p. 185-192].

It is known that diabetes increases the risk and se-verity of atherosclerosis. Adropin is associated with metabolic homeostasis. The researchers examined the relationship between serum adropin and angiographic severity of coronary atherosclerosis in patients with and without DM [17, p. 751-758].

It is well-studied that energy metabolism under-goes changes in MI. Irisin is a hormone with a peptide structure that contains 112 amino acids and is involved in energy metabolism. The main function of irisin is the transformation of fat of white tissue into brown fat tis-sue that produces energy in the form of heat. Irisin is fundamentally synthesized from muscle tissue. To date, changes in the level of irisin in the heart muscle during the acute MI period are observed. Scientists have proven that isoproterenol is a corresponding agent for inducing experimental MI. The levels of irisin are in-creased in cardiac tissue at the first and second weeks after MI. In the future, research is planned on the use of irisin as a biological marker, which can predict tissue damage, assist in prognosis, determine the role of irisin in pathophysiology, diagnosis and treatment of MI [4, p. 9-12].

Scientists have researched that irisin can stimulate energy expenditure and alleviate insulin resistance in an experimental model. It has been found that insulin resistance is often associated with endothelial dysfunc-tion. Scientists believe that circulating levels of irisin are associated with endothelial dysfunction in type 2 DM [8, p. 328-333; 12, p. 152-155].

It is known that irisin is a protein that is of interest as a potential new strategy for controlling obesity and related disorders, such as type 2 DM. Scientists evalu-ated circulating levels of irisin in serum in obesity and type 2 DM and found out possible relationships be-tween levels of irisin in serum and anthropometric and metabolic indices of obesity and type 2 DM. The study found that serum irisin was significantly lower in pa-tients with type 2 DM compared with patients without type 2 DM. In patients with obesity with a lack of DM 2, the level of irisin in serum was significantly higher compared to the control group. In patients with type 2 DM and without type 2 DM, the level of irisin posi-tively correlated with body mass index and HOMA-IR and negatively correlated with insulin sensitivity. Sci-entists have shown that the level of irisin increases in patients with obesity without type 2 DM, whereas in patients with type 2 DM it diminishes. In addition, the levels of irisin correlated with anthropometric and met-abolic markers of obesity and type 2 DM [14, p. 544-556]. 40 Danish Scientific Journal No 10,2018

**Conclusions**. Consequently, further study of FABP4, CTRP3, adropin, and irisin allows to employ them as predictors of unfavorable course of acute myo-cardial infarction with concomitant obesity and type 2 diabetes mellitus.

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