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The Leading Pathogenic Mechanism of Endothelial Dysfunction in Patient with Acute Coronary Syndrome

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Abstract The problem of ischemic heart disease (IHD) remains important among cardiovascular diseases. The problem of diagnostics and treatment of acute coronary syndrome (ACS) and its complications are also considered to be vital questions. Between 2009 and 2012, 80 patients (69 males and 11 females) who had acute coronary syndrome with elevation of ST segment admitted to the Cardioresuscitation Department of RSCEMA were enrolled in the study. All patients were divided into 2 groups: the 1st - group included 80 ACS patients with ST segment elevation, and the 2d - group included 40 ACS patients without ST segment elevation. During the study we observed that increase of stable nitric oxide (NO3, NO2+NO3) metabolites is noted in patients with acute coronary syndrome without ST segment elevation, unlike ACS patients with ST segment elevation. On the basis of these findings it is possible to make a conclusion that in the development of unfavorable coronary events in ACS patients without ST segment elevation vasoconstructive mechanism (endothelia-1) takes place and in ACS patients without ST segment elevation the findings of changes are not so clearly marked. Thus, at present the study of markers of endothelial dysfunction and no specific inflammation is of great interest for estimation prognosis and follow-up outcomes in ACS patients.

Keywords: *acute coronary syndrome, nitric oxide, endothelial dysfunction, endothelin-1*

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1. Introduction

Every year, approximately 1.2 million Americans survive an acute coronary syndrome (ACS) event, and many have clinically significant and persistent depression [1,2,3].

Patients with post-ACS depression have significantly more ambulatory medical appointments, emergency department visits, and higher health care costs than similar patients without depression. Post-ACS depression is also associated with a 150% increased risk of ACS recurrence and a 100% increase in the relative risk of all-cause mortality and persistent depression as ACS event is associated with an even higher morbidity and mortality risk [4,5,6]. Reducing persistent post-ACS depression is therefore an important public health objective.

The problem of ischemic heart disease (IHD) remains important among cardiovascular diseases. The problem of diagnostics and treatment of acute coronary syndrome (ACS) and its complications are also being vital questions. At present critical revision of lots of ideas concerning causes and mechanisms of development and treatment of both ischemic heart disease on the whole and acute coronary syndrome in particular takes place.

The purpose of the study – To study the chief pathogenetic mechanism of endothelial dysfunction (ED) depending on acute coronary syndrome.

2. Material and Methods

Between 2009 and 2012, 80 patients (69 males and 11 females,) who had acute coronary syndrome with elevation of ST segment admitted to Cardio resuscitation department of RSCEMA were enrolled in the study. All patients were hospitalized no later than 12 hours from the beginning of pain syndrome development, the average time (M±s) from the begining of the disease to diagnosis made 5. 01±2.45 hours (from 50 min. to 11 hours). The average age (M±s) of ACS patients with ST elevation corresponds to 56.7±8,7 years (from 34 to 73 years), for ACS patients without ST elevation corresponds to 58.8±7.0 (years 38 to 75 years).

Rapid and exact diagnosis of pain syndrome in the thoracic cavity was based on the adequately taken case history analysis of patient's complaints and ECG taken at rest. As a result of the initial examination the patient can already be attributed to one of four diagnosis categories:

- Absence of coronary diseases;
- Stable angina pectoris;

- Unstable angina pectoris;
- Myocardial infarction.

Among examined patients males predominated 85% in ACS with ST elevation and 72.5% with ACS without ST elevation. All patients underwent clinical and laboratory instrumental examination.

The criteria for exceptions were – cardiogenic shock, background pathology like diabetes mellitus, blood creatinine level of more than 200 MKmol/l, signs of acute and chronic hepatic insufficiency, developed on the background of infectious damage to respiratory organs (pneumonia, chronic obstructive lung disease at the stage of exacerbation) signs of acute infection of kidneys and urinary duct, inflammatory disease of gastrointestinal tract, C-reactive blood protein (CRP) concentration of more than 10. ACS diagnosis is made on the basis of subjective findings and electrocardiographic examination (ECGE). There was determined the level of stable blood NO-metabolites: nitrites ($N0_2$-) and nitrates ($N0_3$-) for indirect determination of NO level. NO metabolites concentration was estimated by means of quantitative method of hard phase IFA total NO/Nitrite/Nitrate Assay, (ELISA, USA) [7].

Measuring of NO molecule contents was performed on immunofermental plane table. Statistic processing of the material was carried out making use of applied programmes statistica 6.0 packet.

3. Results

Laboratory indicators of patients endothelial functions during first 24 hours from development of ACS symptoms were presented in Table 1.

Table 1. Laboratory indicators of endotheliae function in ACS patients during the first 24 hours begining from the development of symptoms

Indicators	Groups of patients		P
	With elevation of ST segment Group I Patients - 80	Without elevation of ST segment Group II Patients - 40	
	25% < median < 75%	25% < median < 75%	
Endothelia -1 mmol/ml	0.1 <0.4 < 1.1	0.5 < 0.7 < 1.4	0.041
N02, мkmol/l	5.9 < 7,0 < 8,2	6.5 < 7.3 < 8.6	0.338
N03, мkmol/l	13.0 < 17.7 <25.8	13.2 < 18.4 <20.4	0.827
NO2+NO3, мkmol/l	19.8 < 25.4 < 32.6	20.7 <25.5 <31.3	0.879
sP- selectine ng/ml	57.5 < 108.0 < 166.4	19.8 < 85.0 < 133.4	0.232

Notes: N02 – nitrite, N03 – nitrate – stable metabolites of nitric oxide.

Reliability of indicator differences in the studied groups was estimated by means of unparametric criterion and Manna-Uitni test. From the findings given in the table it is necessary to notice reliable (p=0.041)more powerful synthesis of endotheline - 1, having vasoconstrictive effect in ACS group of patients without elevation of ST segment in comparison with the first group of patients with lower concentration of endotheline - 1. Indicated reliable difference in endothelines level in ACS groups of patients can testity to various force of vasotonic response.

Since in ACS group of patients without ST segment elevation concentration of this marker was higher, more marked spasm of KA may be supposed in such patients. The period of endotheline - 1 half life is 10-20 min. but this marker is responsible for a number of pathological processes: AIM, damage to cardiac rhythm, pulmonary and systemic hypertension, atherosclerosis [8].

Endotheline effects are determined by properties of receptors which are connected with endothelines. Connection with endotheline - A receptors inhibits NO sythesis in the vessels and causes their constriction, connection with B-1 receptors causes dilatation of vessels (inhibition of cyclic adenosinmonophosphate and elevation of NO synthesis take place). Endothelines concentration is also significant: endothelines are also formed in physiological conditions but a small number. They dilate the vessels reacting to B-1 receptors. However impaired endothelines cause vasoconstriction that could take place in ACS patients without ST elevation. Reliable differences concerning concentration of stable NO metabolites (nitrite [NO2] and nitrate [NO3) were not received between the studied groups. Moreover, concentration of total stable NO metabolites in both studied groups during the first 24 hours beginning from ACS symptoms was lower than referent meaning that can testify to reduce NO synthesis by endothelial cells during the first 24 hours from the moment of ACS symptoms development. At the same time it must be taken into account that NO is produced not only by endotheliocytes but by the cells of the other organs.

4. Discussion

Any group of clinical signs can be interpreted under the term of acute coronary syndrome (ACS) with stable ST segment elevation on the with stable ST segment elevation on the background of available ST segment elevation with 1 mm ECG amplitude for no less than 20 min. making suspicion of coronary catastrophe [9,10].

It should be noted that ACS term is not the diagnosis. ACS determination makes it possible to recognize the presence of coronary catastrophe, requiring strict complex therapeutic and diagnostic methods and necessary hospitalization of patients to an adequate inpatient department.

Together with impairment of atherosclerotic plaque with the following intracoronary thrombosis ACS may be caused by sharply increased need in oxygen (cocain intoxication, the thyroid gland pathology and anemia), coronary vasospasm and more rare causes (coronary arteries dissection in pregnant women. At the same time more than 95% of ACS cases with stable ST segment elevation are association with the processes of impairment of plaque membrane safety.

Significant attention in stydying ACS pathogenesis is payed to endothelium dysfunction as the earlest phase of

damage to the vascular wall. Each of endothelal functions determining thrombogenity of the vascular wall, inflammatory changes, vasoreactivity and stability of atherosclerotic plaque (ASP), is connected directly or indirectly with IHD progression and complications. That is why the conception about endothelium as a target for ACS prevention and treatment became uniting. Endothelial dysfunction (ED) evaluation by means of NO blood quantity levels is a limit of the study is first of all a dysbalance between production of vasodilating, angioprotective, antiproliferative factors (nitric oxide (NO), prostacycline, plasminogen tissue activator, C-type sodiouretic peptide and others) on the one hand and vasoconstructive, thrombotic, proliferative factors (endotheline, thromboxan A, inhibitor of plasminogen tissue activator) on the other hand [11].

In addition to these indicators some substances are studies as potential ED markers as their production can reflect endothelial function.

These indicators are the following:

Antiinflammatory cytokines like interleukins (IL- 1, IL-6, IL -8), a factor of tumour – a necrosis (ΦНО –a), factor of Villebrand, selectines, C-reactive blood protein (CRP) and others [12,13,14]. By now the role of upper mentioned factors is not monosemantic in development of unfavourable cardiovascular events in ACS patients in partucular in those who underwent transcutaneous coronary interventions. There is no single opnion concerning the terms of laboratory results determination. In particular the problem of prognosis and prevention of stent thrombosis and coronary artery restenosis in ACS patients is of great importance [15]. In addition the urgency of the paper is motivated also due to the fact that it is directed to the patients with various clinical ACS variants related both to high and average risk of cardiovascular complications development. Thus, at present the study of markers of endothelial dysfunction and nospecific inflammation is of great interest for estimation of prognosis of follow-up outcomes in ACS patients.

5. Conclusion

Increase of stable nitric oxide (NO3, NO2+NO3) metabolites is noted in patients with acute coronary syndrome without ST segment elevation, unlike ACS patients with ST segment elevation. On the basis of these findings it is possible to make a conclusion that in the development of unfavorable coronary events in ACS patients without ST segment elevation vasoconstructive mechanism (endothelia-1) takes place and in ACS patients without ST segment elevation the findings of changes are not so clearly marked.

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