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SOME INTERCONNECTIONS OF PATHOGENETIC MECHANISMS OF EARLY POST-INFARCTION ANGINA

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The complex survey of 80 AIM patients was conducted. The first group included EPIA III C class 60 patients with high and intermediate risk, according to E.Braunwald (1994) classification. For comparison it was made the group of 20 patients with uncomplicated macro focal IM. Survey of autonomic nervous system condition and nitric oxide concentration was conducted. Results testify that at early postinfarctial stenocardia patients detected expressed contraventions of all links of autonomic nervous system, appeared by rather low sympathetic tone with excessive reactance. At acute myocardial infarction complicated with early postinfarctial angina patients the histic adrenergic receptors' density is increased and simultaneously paradoxical increase of nitric oxide's metabolites concentration.

Keywords: *myocardial infarction, early post-infarction angina, autonomic nervous system, adrenergic receptors, nitrogen oxide*

Проведено комплексное обследование 80 больных ОИМ. Первую группу составили 60 человек с РПИС III C класса высокого и промежуточного риска, согласно классификации Е.Браунвальд (1994). В группу сравнения вошли 20 больных с неосложненным течением крупноочагового ИМ. Проведено обследование состояния вегетативной нервной системы и концентрации оксида азота. Полученные результаты свидетельствуют о том, что у больных ранней постинфарктной стенокардией выявлены выраженные нарушения всех звеньев вегетативной нервной системы, проявляющиеся относительно низким симпатическим тонусом с чрезмерной реактивностью. У больных инфарктом миокарда, осложненного ранней постинфарктной стенокардией, повышена плотность тканевых адренорецепторов и, одновременно парадоксальное повышение концентрации метаболитов оксида азота.

Ключевые слова: *инфаркт миокарда, ранняя постинфарктная стенокардия, вегетативная нервная система, адренорецепторы, оксид азота*

One of the actual problems in modern cardiology is unstable angina, in particular an early post-infarction [1]. It explains the fact that this category of patients has a very high risk of sudden death and other myocardial infarction complications (AMI). In pathogenesis of early post-infarction angina (EPIA) the leading role plays the derangements of homeostasis [2].

There are numerous researches of autonomic nervous system condition (ANS) in acute AMI patients. In the overwhelming majority of AMI patients occurs a sharp decrease of heart rate variability (HRV), which can be served as a prognostic criteria [3,4]. In most AMI cases sympathetic impacts and a sharp decrease of HRV are predominant [5,6]. Dovgalevsky P.Y with his co-

authors (1999) made a research of the ANS measures and its connection to the coronarography data. Authors come to conclusion that sympathetic influences affects on clinical manifestations of ischemic heart disease (IHD) considerably [7,8]. At the beginning of 90's the idea that the of heart rate variability presents a steady predictor of death AMI patients was confirmed [9,10]. In first weeks after AMI development, sharp decrease of parasympathetic impacts occurs, that concurs with the highest development period of heart rate fatal disorder [11,12]. The disorders in autonomic regulation of cardio hemodynamic are less researched on patients with EPIA.

In recent studies which have been devoted to nitrogen oxide concentration in IHD patients' blood are presented the data about its level decrease among the patient groups with acute manifestations in particular — Acute coronary syndrome (ACS) [13,14]. At the same time according different authors' data NO concentration in acute IHD patients is different and depends on the time factor. In 1995 Wildhirt S.M. [15] in his experimental works with artificially induced IM rabbit detected that iNOS level considerably increased after 48 hours coronary artery ligation. In another work [16] after rat coronary artery ligation the iNOS level stayed invariable during first 2 hours. After 3 hours there was the essential reduction, and 5 hours later — a quick double time level increase. During 24 hours the NO level was stable. The patients with coronary arteries atherosclerosis had increased iNOS level [17]. In intact coronary arteries the iNOS activity was invariable and in atherosclerotic plaque region its highest activity was detected.

In spite of a lot of works, concerning an early post-infarction angina pathogenesis there are still uninformed questions of interconnection of vegetative system regulation disorder with myocardium endothelial dysfunction.

The research materials and methods

The complex survey of 80 AIM patients was conducted. The first group included EPIA III C class 60 patients with high and intermediate risk, according to E.Braunwald (1994) classification. The average age was 55.1 ± 0.9 years. 52 men (86.7%) and 8 women (13.3%) were in this group. The second group included 22 inter-

mediate risk patients (36.7%) and 38 (63.3%) high risk patients. The average age was 56.2 ± 7.9 years.

For comparison it was made the group of 20 patients with uncomplicated macro focal IM. Average age was 53.8 ± 2.2 years.

The diagnose was verified on the basis of adopted examination methods, including general clinic data, Troponin and Myoglobin tests, ECG in dynamics.

For homeostasis and nitrite (NO) tests the blood was taken from patient ulna vein on empty stomach after hospital admission 24 hours later.

The study of the ANS values was conducted on patients in lying position, under cold exposure. In the morning after antianginal and antiarrhythmic drug discontinuation in order to determine ANS tonus and reactivity the ECG values were recorded for one minute in lying patients. Then the ice was put on the left hand and the ECG values were recorded simultaneously. After one minute without the ice contact the recordings were repeated again for one minute. The RR interval was calculated. The digital dynamic sequence was made at rest, with the ice contact and without it. The studied results were following: Moda — The commonest RR interval value (Mo); the variation range (VR) — the min and max RR interval value; the moda amplitude (AMo) — the Mo frequency in %; the ratio between AMo/VR and strain index (SI) that can be calculated according formula $SI = AMo/VR \times Mo$ [18].

The adrenergic receptor lymphocyte activity was estimated by reaction of rosetta formation with the sheep erythrocytes, which were sensitized with Glutar

Aldehyde and loaded with Norepinephrine (Noradrenaline) according Veber V.R. and etc method (1987). As a result the rosetta cells percentage is considered.

The NO blood metabolite study is being made according Navarro J.A.'s and Molina J.A.'s method, 1993, which has been modified by Karpuk V.B. and co-authors. (1998).

Results and discussion

The ANS reaction on cold test is presented on table 1. The examined parameters dynamics in macro focal IM patients was considerable and practically unidirectional with parameter deviation in the control group at the

Table 1

The vegetative tonus and reactivity results of EPIA III C class patients

Values	Healthy persons, n = 30			Macro focal IM, n = 20			EPIA IIIC class, n = 60		
	Original	Cold exposure	Restoration	Original	Cold exposure	Restoration	Original	Cold exposure	Restoration
VR, c	$0,18 \pm 0,02$	$0,10 \pm 0,002$	$0,17 \pm 0,02$	$0,066 \pm 0,005^{**}$	$0,060 \pm 0,009^{***}$	$0,062 \pm 0,007^{**}$	$0,048 \pm 0,006^{*}$	$0,039 \pm 0,007^{***}$	$0,041 \pm 0,010^{*}$
AMo, %	$18,6 \pm 1,9$	$44,6 \pm 2,3$	$21,7 \pm 1,8$	$31,09 \pm 2,79^{*}$	$35,1 \pm 5,2^{*}$	$33,09 \pm 4,58^{*}$	$28,9 \pm 4,2$	$39,2 \pm 3,7^{*}$	$41,6 \pm 4,2^{*}$
AMo/VR, %/c	$103,3 \pm 43,2$	$446,0 \pm 102,3$	$135,5 \pm 11,9$	$471,6 \pm 60,8^{**}$	$585,78 \pm 74,13^{***}$	$536,15 \pm 64,19^{***}$	$602,1 \pm 82,5^{*}$	$1004,9 \pm 53,0^{***}$	$1029,0 \pm 60,8^{***}$
SI	$80,2 \pm 10,3$	$272,0 \pm 32,6$	$117,0 \pm 10,3$	$205,0 \pm 44,92^{***}$	$498,5 \pm 74,41^{***}$	$436,34 \pm 61,77^{***}$	$381,1 \pm 52,9$	$975,2 \pm 57,4^{***}$	$1016,7 \pm 49,4^{***}$

Note: * — the authentic differences with healthy people group;

• — the authentic differences with macro focal IM patients (1 sign — $p < 0,05$, 2 signs — $p < 0,01$, 3 signs — $p < 0,001$).

initial period. The VR level differences from control group was 2,9 times more ($p < 0,01$), AMo — 1,8 times, AMo/VR level was 1,3 times more than the healthy people level and SI — 1,8 times more ($p < 0,05$). At the same time these changes have occurred basically due to the control value dynamics, in addition the macro focal IM patients' ANS reaction to cold was quite limited and was mainly expressed by SI increase.

Similarly, no considerable VR, AMo and AMo and AMo/VR changes were registered during the restoration period, besides that SI value kept the tendency to increase. Its size exceeded a control value ($p < 0,01$) in 3, 7 times. The EPIA patients after macro focal IM from a general group had similar vegetative reactions. The AMo, AMo/VR and SI levels were higher in initial condition, than in healthy people 55,3% more ($p < 0,05$), in 5,8 and 4,7 times ($p < 0,01$), but VR was lower in 3,7 times ($p < 0,001$).

The variational intervalogram measurement ratio in comparison with patients not complicated and complicated EPIA with cold tests during AMI changed. The complicated EPIA patients dynamics of VR occurred to decrease considerably (in 2,5 times lower than in control group, $p < 0,01$), AMo/VR (in 2,2 times higher, than control measure, $p < 0,05$), SI (in 3,5 times, $p < 0,001$). The SI gained in 2,5 times ($p < 0,01$) in compare with initial conditions. The considerable increase of integrated parameters, in comparison with patients with uncomplicated macro focal AMI was detected. AMo/VR gained to 71,6% ($p < 0,05$) and SI — to 90,1% ($p < 0,05$).

The restoration period was characterized by preservation high-authentic differences with healthy persons. The AMo/VR and SI gained level results in relation to not complicated macro focal AIM patient's results attracts attention.

E-POK (peripheral blood lymphocytes) content study results with noradrenaline at various forms of IHD patient's examination are presented in table 2.

Table 2

The E-POK content comparative characteristic with noradrenaline in healthy persons' blood and various forms of IHD patients

Healthy persons, n=30	AMI patients without EPIA, n=20	AMI patients with EPIA, n=60
$6,3 \pm 1,1$	$9,2 \pm 0,6^*$	$15,3 \pm 1,5^{**\bullet}$

Note: * — the authentic differences with healthy people group;
 • — the authentic differences with macro focal IM patients
 (1 sign — $p < 0,05$, 2 signs — $p < 0,01$, 3 signs — $p < 0,001$).

From the data presented in table 2, AMI patients' authentic value exceeding over control group has been registered. And if the EPIA patients excess degree was only 46,0% ($p < 0,05$), then in EPIA development — reached up to 142,9% ($p < 0,01$).

Thereby, the analysis results testify about the most expressed cardiovascular system vegetative regulation segmentary level's changes at acute myocardial infarction patients. At the same time the EPIA presence gives unexpectedly sharp increase in myocardium sensibility degree to catecholamines. It is connected with compensatory increase of receptors' density.

There was adrenergic receptors' density values and an autonomic nervous system tone comparative analysis done in acute myocardial infarction patients groups with and without EPIA. Detected data testify that AMI patients with EPIA histic adrenergic receptors' have a raised density, lowered VR and AMo and SI are increased in comparison with healthy persons, that confirms the known data about role of SNS' raised tone and histic adenosensibility in myocardial infarction and unstable angina (UA) pathogenesis. The histic adrenergic receptors' activity analysis in various AMI verified patient groups has revealed its statistically authentic increase in group with EPIA in comparison with 2nd group without EPIA.

During the ANS tonus analysis in EPIA patients' group the VR decrease, the AMo and SI increase is observed in comparison with macro focal IM patients without EPIA. The studies testify decrease of parasympathetic and increase of sympathetic tonus of the patients with IHD. Age-related and more expressed because of IHD exhaustion of humoral sympathetic influences on myocardium is accompanied with general activity increase of supersegmental and segmental SNS components. It is shown by tonus and compensatory density increase.

The nitrogen oxide metabolite concentration study results revealed clear regularity of nitrite concentration in patients with different forms IHD — this value increase mostly at acute and heavy coronary disease. Reliable differences were registered at EPIA presence, the exceeding over the uncomplicated IM course group average value was 69,2% (1,3 and 2,2, accordingly, $p < 0,01$).

Thereby, at EPIA patients we can see reliable adrenergic receptor density increase in comparison as with healthy persons as with IM patients without EPIA. It testify about SNS segmental level compensatory capabilities exhaustion. Simultaneously the variation intervalometria AMo and SI value increase appears at this patient category that confirms assumption about CVS regulation level express centralization. The paradoxical nitrogen oxide metabolite concentration increase revealed at early post infarction angina patients. Usage of these methods gives ability to prognosticate EPIA development at AMI patients and to take timely preventive arrangements to correct treatment and patient management.

Conclusions

1. All SNS components derangements revealed at early post infarction angina.
2. Relatively low sympathetic tonus with excessive reactivity characterize suprasegmental level condition.
3. Histic adrenergic receptor density in IM patients with EPIA is increased.
4. The paradoxical nitrogen oxide metabolite concentration increase revealed at early post infarction angina IM patients.

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