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PREVENTION OF DISTURBANCES OF ELECTRICAL STABILITY OF THE HEART IN EXPERIMENTAL MYOCARDIAL INFARCTION BY ADAPTATION TO ANOXIA

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UDC 616.127-005.8-092.9.-092:
612.273.2.01.4.49

KEY WORDS: adaptation to anoxia; myocardial infarction; electrical stability of the heart.

Recent investigations have shown that adaptation to periodic anoxia in a pressure chamber can prevent or limit disturbances of the electrical stability of the heart arising during stress and cardiac arrhythmia and fibrillation associated with acute ischemia, and can also abolish established disturbances of contractility and electrical stability of the heart due to postinfarction cardiosclerosis [4, 5]. However, the question of how adaptation to periodic anoxia affects the electrical stability of the heart in acute myocardial infarction (MI) has remained unstudied until recently. Accordingly, it was decided to compare the effect of preliminary adaptation to anoxia on disturbances of electrical stability and contractility of the heart usually observed in MI.

EXPERIMENTAL METHODS

Male Wistar rats weighing 320-350 g were divided into four groups: 1) control animals, 2) animals with experimental MI, 3) animals adapted to anoxia, 4) adopted animals with experimental MI. Adaptation to anoxia was carried out in pressure chamber at an "altitude" of 5000 m for 6 h daily for 5 days a week for 6 weeks. Experimental MI was produced by the method in [9] by ligaton of the descending branch of the left coronary artery. The animals were used in the experiments 2 days after coronary occlusion.

The experiments to evaluate the parameters of electrical stability of the heart was done on animals anesthetized with pentobarbital (50 mg/kg). In the first stage the reaction of the heart to stimulation of the peripheral end of the divided vagus nerve (pulse duration 2 msec, delay 5 msec, frequency 20 Hz) by means of an ÉSL-2 electronic stimulator, was investigated. After determination of the threshold strength of current inducing bradycardia, the responses to stimulation with a strength of 1, 2, 3, and 4 thresholds were determined consecutively. The ECG was recorded on a Mingograf-34 (Siemens-Elema, Sweden) and the effect

Research Institute of General Pathology and Pathological Physiology, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR A. D. Ado.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 105, No. 4, pp. 401-403, April, 1988. Original article submitted April 13, 1987.

 0007-4888/88/0004-0474$12.50

Table 1. Effect of Adaptation to Anoxia and of Myocardial Infarction on Parameters of Electrical Stability of the Heart (M ± m; n = 7)

Group of animals	HR, beats/min	VFT, mA	Threshold of vagal effect, V	Effect of vagal stimulation (ΔHR, %)				Total No. of extrasystoles
				1 thres.	2 thres.	3 thres.	4 thres.	
1- (Control)	360±15	5,3±0,2	0,42±0,08	20±3	39±7	42±7	50±7	0
2-	368±15	5,2±0,3	0,60±0,07	14±4	20±2*	31±8	32±9*	0
3-	382±14	2,0±0,3*	0,71±0,08*	21±2	54±4*	64±2*	65±4*	124
4-	399±13	4,6±0,4**	0,50±0,08**	24±4	48±7	59±6	61±6	54

Legend. Here and in Table 2: *) significant difference from control, **) significant difference from group 3.

of vagus nerve stimulation was estimated as the difference between the heart rate before and during stimulation, as a percentage of its initial rate, and the number of extrasystoles arising in the animals of each series against the background of vagal bradycardia during 30 sec was counted, by summation of the four values of stimulation.

In the next stage the electrical threshold of ventricular fibrillation (VFT) was determined. For this purpose thoracotomy was performed and the heart stimulated with single square pulses, 10 msec in duration, by an SEN 1101 stimulator (Nihon Kohden, Japan) through a coaxial electrode, inserted into the myocardium at the apex of the right ventricle. The value of VFT was estimated as the minimal strength of current at which fibrillation developed.

The contractility of the heart was evaluated by recording the interventricular pressure by means of a catheter introduced into the chamber of the left ventricle through the apex of the heart, and recorded electromanometrically on the Mingograf-34. The systolic, diastolic, and pulse pressure, heart rate (HR), and intensity of functioning of structures (IFS – a parameter reflecting the quantity of function performed by unit mass of the organ, and equal to the product of the pulse pressure and HR, divided by the absolute weight of the left ventricle) were determined. After the end of the experiment the heart and its ventricles were weighed.

EXPERIMENTAL RESULTS

It will be clear from Table 1 that MI lowered the threshold of ventricular fibrillation of the heart by 2.5 times. Adaptation to anoxia itself had no effect on this parameter, but lowering of the threshold in adapted animals by infarction was not significant ($p > 0.05$).

MI increased the vagal effect to stimulation with a strength of 2-5 thresholds by 35-52%. Adaptation to anoxia, on the other hand, led to some reduction of the negative chronotropic effect of the vagus nerve. The negative chronotropic effect of the vagus nerve stimulation in adapted animals with MI was about as strong as that in unadpated animals. The essential fact discovered at this stage of the experiment was that preliminary adaptation of animals to anoxia led to reduction by more than 50% of the number of extrasystoles, usually arising in animals with MI against the background of vagal bradycardia. Taken together these two facts – prevention of the fall of VFT and the reduction of ectopic activity of the heart during infarction in the adapted animals – are evidence that adaptation to anoxia prevented disturbance of the electrical stability of the heart during infarction.

The results of the study of cardiac contractility (Table 2) confirmed those of previous investigations [1] and showed that preliminary adaptation to anoxia, which itself had no significant effect on the contractile function of the heart, limited the fall of pulse pressure in infarction, but did not affect HR. Correspondingly, IFS of the adapted animals with MI was 50% higher than in the rats unprotected by adaptation.

It has been shown with respect to contractility that adaptation to anoxia, by increasing the capacity of the coronary bed and the myoglobin concentration in the myocardium [10, 11], regularly restricts the area of necrosis and the reduction of myocardial contractility in experimental infarction [1].

The protective effect of adaptation to anoxia with respect to disturbances of electrical stability of the heart in MI may be realized at the level not only of neurohumoral regulation, but also of the myocardium itself. We know, for instance, that adaptation to anoxia leads

Table 2. Effect of Adaptation to Anoxia and of Myocardial Infarction on Parameters of Cardiac Contractility (M ± m; n = 7)

Group of animals	Pulse pressure, mm Hg	HR, beats/min	IFS
1- (Control)	110±9	308±8	46±6
2-	117±8	310±10	52±9
3-	52±10*	275±10*	17±2*
4-	77±7**	274±14	26±3**

to a decrease in the noradrenalin concentration in brain structures, combined with an increase in the affinity of β-adrenoreceptors for ligands, and also to an increase in the dopamine concentration [6-8]. These changes may give rise to limitation of the stressor-induced adrenergic effect, and thereby help to maintain electrical stability of the myocardium. Consequently, effects of adaptation to anoxia at the neurohumoral regulatory level may themselves lead to an increase in electrical stability of the heart.

At the myocardial level adaptation to anoxia also gives rise to a number of changes which may help to maintain electrical stability of the heart in infarction. Adaptation to anoxia prevents activation of lipid peroxidation in the myocardium in infarction [2], and this may directly cause disturbances of the cardiac rhythm [3]. It has also been shown that adaptation to anoxia leads to a decrease in the density of adrenoreceptors in the myocardium and to a fall in their adenylate cyclase activity [12]. The decrease in the number of β-adrenoreceptors under these circumstances is accompanied by an increase in their affinity for the ligand [8]. On the whole this creates a situation in which effective adrenergic regulation of the heart is ensured by the release of only small quantities of catecholamines and that this regulation can continue for a longer time when they are exhausted. Meanwhile massive catecholamine release in stress situations, infarction, and other lesions of the heart is limited to the level of their binding with receptors, and in that way adaptation to anoxia can limit an excessive damaging effect. These changes in adrenergic regulation will also help to maintain the electrical stability of the heart in MI.

The results as a whole are evidence that adaptation to periodic anoxia can prevent disturbances of the contractile function and electrical stability of the heart in infarction basically on account of the same mechanisms as those by which the principal cardiotropic drugs in use today, such an vasodilators and adrenoblockers, act.

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