EFFECT OF EMOTIONAL-PAINFUL STRESS ON RESISTANCE OF THE HEART TO ISCHEMIA

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Stress is known to play an essential role in the onset and development of ischemic heart disease [14]. It has recently been shown that one of the mechanisms responsible for this pathogenetic effect of stress is a poststress reduction in the resistance of the myocardium to oxygen deficiency. However, experiments in which this phenomenon was discovered for the first time were conducted on isolated ventricles and atria of animals subjected to stress, and the myocardium in these experiments was exposed to hypoxic hypoxia [2, 9].

The object of the present investigation was to discover how the post-stress reduction in resistance of the heart to ischemia is brought about in the intact organism.

EXPERIMENTAL METHOD

Two series of experiments were carried out on male Wistar rats: In series I control rats were used, in series II rats were subjected to emotional-painful stress (EPS) by Desiderato's method [16] for 1.5-2 h before the experiment. The animals were anesthetized with urethane (160 mg/kg), thoracotomy was performed, and artificial ventilation with air was commenced. The pressure was recorded in the left ventricle and carotid artery by means of electromanometers, and the cardiac output (CO) and stroke volume of the heart were determined by an ultrasonic method [4]. An ultrasonic transducer 2 mm long, with internal diameter of 2-2.5 mm, was placed on the ascending aorta and the momentary linear and volume velocity of the blood flow were recorded, whereas the stroke volume of the heart and CO were recorded by electronic integrators. These parameters were recorded on a Mingograf-34 apparatus (Siemens-Elema, Sweden). The total peripheral resistance (TPR) and external work of the heart were calculated by the usual formulas.

In the first stage of the experiment the reaction of the heart to transient regional myocardial ischemia lasting 30 min was evaluated. Ischemia was created by ligation of the upper third of the descending branch of the left coronary artery. Ischemia produced by ligation in this way affects about 50% of the area of the left ventriole. In the second stage of the experiment the ligature on the coronary artery was released and the reaction of the heart to reperfusion also was evaluated for 30 min. The location of the ligature was verified at the end of the experiment by injecting a suspension of chalk into the left ventricle. The coronary arteries under these circumstances stained white. The results of only those experiments in which arteries with the standard position and branching pattern were ligated were taken into consideration.

EXPERIMENTAL RESULTS

The experimental results (Table 1) are evidence that stress by itself caused no significant changes in cardiac function or TPR of the vessels. Considerable poststress disturbances of contractile function, which we observed on isolated hearts and papillary muscles [7], were compensated in the intact organism and so did not appear. Ischemia for 30 min caused a fall of pressure in the left ventricle, the mean arterial pressure, and the external work of the heart on average by 30% compared with their initial level, whereas the change in CO by the

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TABLE 1. Effect of EPS on Contractile Function of the Heart during Transient Ischemia and Reperfusion

Parameter studied	Experimental conditions	Before ischemia	Ischemia		Reperfusion	
			1 min	30 min	15 min	30 min
Pressure developed in left ventricle, mm Hg	Control	116±4,4	87±4,1	83±2,5	81±3,5	72±5,6
	Stress	107±6,3	73±6,4	64±5,2***	63±5,5**	49±6,9*
Mean pressure in carotid artery, mm Hg	Control	77±4,7	60±4,2	54±3,9	51±4,1	45±4,0
	Stress	67±6,8	54±5,1	37±1,3***	38±3,1*	31±3,0**
Heart rate, beats/min	Control	388±19	383±17	379±17	368±14	349±18
	Stress	415±16	400±15	418±18	384±20	310±20
Stroke volume, ml	Control	0,09±0,008	0,10±0,006	0,09±0,005	0,07±0,005	0,05±0,003
	Stress	0,09±0,006	0,11±0,006	0,08±0,004	0,06±0,006	0,03±0,004**
CO, ml/min	Control	34,2±2,9	40,7±3,4	33,4±2,9	27,3±2,5	19,7±2,7
	Stress	37,2±3,2	43,2±3,0	35,0±3,9	24,9±3,2	10,5±1,3**
TPR, dynes·sec·cm^{-5}	Control	3174±309	1950±181	2181±214	2517±230	3286±304
	Stress	2717±260	1674±180	1599±190	2025±217	3779±234
External work of the heart J/min	Control	0,35±0,03	0,33±0,02	0,23±0,01	0,18±0,02	0,12±0,02
	Stress	0,33±0,03	0,31±0,03	0,18±0,02*	0,14±0,02	0,04±0,01***

Legend. Number of experiments on control rats and on rats subjected to stress was 10 and 7 respectively. *P < 0.05, **P < 0.02, ***P < 0.001.

end of ischemia was not significant. In stressed animals at the 30th minute of ischemia CO also showed little change compared with its initial value, whereas the pressure developed in the left ventricle, TPR, and the external work of the heart were less in the poststress period than in the control, by 23, 27, and 21% respectively.

Significant differences between the parameters for control animals and animals subjected to stress were found in the reoxygenation period: Reoxygenation disturbances of cardiac function were more marked in animals subjected to stress. The data in Table 1 in fact show that the pressure developed by the left ventricle, the mean pressure in the carotid artery, the stroke volume and, in particular, CO were significantly reduced by the 30th minute of reoxygenation in animals subjected to stress, and as a result the external work of the heart done by these animals was only one-third that of the control. EPS thus potentiates postischemic (reoxygenation) disturbance of the contractile function of the heart to a high degree.

An interesting feature of the reaction of the heart to ischemia also was noted (Table 1). The initial period of action of ischemia was characterized by a marked fall (by 40% of the initial level) of TPR and a paradoxical rise of the stroke volume of the heart and CO (by 20% above the initial value). This fact has been observed also by clinicians during the first day of acute myocardial infarction [3]. The fall in TPR in response to ischemic heart damage is one of the factors of coordinated unloading of the heart [12], which is aimed at maintaining CO under conditions when the weight of functioning myocardium is reduced by the action of ischemia. As a result not only does CO not fall, but to begin with it rises, and thereafter is kept for some time at its initial level, maintaining intensive functioning of the heart and of the body as a whole. It is important to note, however, that during reperfusion after ischemia the cardiac output, like all other parameters of the pumping function of the heart, was significantly reduced, and this reduction was greater in animals subjected to stress.

Two circumstances must be borne in mind when the mechanism whereby stress aggravates the disturbance of the pumping function of the heart caused by ischemia and, even more, by postischemic reoxygenation is evaluated.

First, stress causes disturbances in the glycolysis system, and in particular, it reduces the reserves of glycogen in the myocardium and its resynthesis [13]. Since the glycolysis system helps to maintain the functioning of the membrane apparatus of the cardiomyocytes and helps to maintain their resistance to hypoxia [5, 15], this disturbance may reduce the resistance of the heart to ischemia and may impair restoration of the contractile function of the heart during postischemic reoxygenation.

Second, excess of catecholamines in stress and rapid recovery of the partial pressure of oxygen in the tissues during reoxygenation are two factors which, more than any others, activate the process of lipid peroxidation (LPO). This phenomenon has been proved in relation to the heart on the model of EPS which we used [11], and also during reoxygenation after prolonged hypoxia [10]. It can be postulated that as a result of summation of stress and reoxygenation activation of LPO the intensity of this process in the myocardium of the experimental animals reaches a degree at which it damages the cardiomyocyte membranes and, con-

sequently, disturbs the transport of calcium and other cations [6], and so increases the depression of the contractile function during postischemic reoxygenation.

Besides activation of LPO in myocardial injury, in a stress + reoxygenation situation a definite role may perhaps be played also by activation of lipases and phospholipases [1]. These arguments are in agreement with the fact that LPO inhibitors, and also inhibitors of lipases and phospholipases protect the heart both against stressors [8, 9] and against reoxygenation injuries [7].

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