PREVENTION OF DISTURBANCES OF CONTRACTILITY OF THE NONISCHEMIC HEART IN INFARCTION BY PRELIMINARY ADAPTATION TO SHORT-TERM STRESS

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UDC 616.127-005.8:616.127-009.1-084]:[616-003.96:613.863-07

KEY WORDS: heart; atrium; stress; myocardial infarction; adaptation.

In experimental infarction disturbances of the structure, metabolism, and function of the nonischemic portions of the heart are observed [5, 10-13] and, in particular, there is a marked decrease in extensibility, developed tension, and resistance of the myocardium of the right atrium to hypoxia [4, 6]. This last phenomenon is the result of stress-induced injury of adrenergic nature, and it can be very effectively prevented by the β-adrenoblocker inderal [2, 3], and can be reproduced completely in emotional-painful stress even in the absence of myocardial infarction [9]. Disturbances of myocardial contractility of this kind, arising as the result of severe emotional-painful or immobilization stress, can be prevented by preliminary adaptation to short periods of stress [8]. It seems likely that such adaptation can prevent the above-mentioned disturbances of contractility of the nonischemic heart after infarction, for these disturbances are stressor in origin.

The aim of this investigation was to study the effect of preliminary adaptation to short periods of stress on contractility of the right atrium and its resistance to hypoxia and Ca^{++} excess in experimental infarction of the left ventricle.

EXPERIMENTAL METHOD

Experiments were carried out on male Wistar rats weighing 200-250 g in four groups: animals of group 1 were controls; animals of group 2 were adapted to frequent short periods of stress, in animals of group 3 a myocardial infarct was created in the left ventricle, and animals of group 4 were adapted to short periods of stress, after which a myocardial infarct was created in them. Each group consisted of 10-12 rats. The animals were adapted to short periods of immobilization stress for 18 days by fixing them in the supine position: for 15 min on the first day, 30 min on the second, 45 min on the third day, and 1 h on the next 15 days. Experimental myocardial infarction was produced by ligation of the descending branch of the left coronary artery by Selye's method [15]. The animals were decapitated 24 h after creation of the infarct. The area of the infarct (in mm^2) was more than 60% of the total area of the left ventricle on its outer surface and about 45% on its inner surface. Animals undergoing thoracotomy but without ligation of the coronary artery, and intact animals served as the control. The atria were isolated immediately after decapitation of the animals and placed in a constant-temperature bath containing oxygenated Krebs–Henseleit solution (95% O_2, 5% CO_2, pH 7.4, 34°C): The base of the atrium was fixed rigidly, and the apex of the auricle was attached to the F-50 myograph of a "Physiograph DMR-4B" ink-writing instrument (Narco Biosystems, USA). Contractility of the isolated atrium and its resistance to hypoxia and to excess of Ca^{++} were determined by the method described previously [1].

EXPERIMENTAL RESULTS

It will be clear from Table 1 that under aerobic conditions depression of the parameters of contractility of the right atrium caused by the infarct was quite definitely present. Preliminary adaptation to short-term

Institute of General Pathology and Pathological Physiology, Academy of Medical Sciences of the USSR, Moscow. Vitebsk Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR P. D. Gorizontov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 99, No. 6, pp. 667-669, June, 1985. Original article submitted April 2, 1984.

 0007-4888/85/9906-0712$09.50

TABLE 1. Effect of Preliminary Adaptation to Short-Term Stress on Disturbance of Contractility of Right Atrium and on Decrease in Its Resistance to Hypoxia in Experimental Left Ventricular Infarction

Parameter	Experimental conditions	Initial value	Hypoxia		Reoxygenation	
			1 min	5 min	1 min	5 min
Maximal developed tension, mg	Control	353,1±32,7	77,0±9,6	20,0±0	85,0±12,7	298,0±32,9
	Adaptation	265,7±32,9	83,6±17,5	22,7±2,9	77,7±29,6	243,2±38,3
	Infarct	153,1±7,4**	30,0±6,3**	14,3±3,7	57,5±15,2	122,5±10,1**
	Adaptation + infarct	261,8±32,5*[4]	55,6±6,9***	37,5±8,2***	98,9±13,5	224,4±30,0*[4]
MIFS, g/mg·min	Control	4,8±0,10	0,9±0,1	0,2±0,01	1,1±0,1	4,2±0,4
	Adaptation	3,7±0,02	0,8±0,1	0,2±0,03	1,1±0,3	2,8±0,4
	Infarct	1,7±0,2**	0,3±0,04**	0,1±0,03**	0,6±0,1*	1,5±0,2**
	Adaptation + infarct	3,4±0,6*[4]	0,6±0,5*[5]	0,2±0,02***	1,2±0,2***	3,2±0,6***
Index of contracture, %	Control	—	9,3±1,9	46,4±4,4	24,9±6,3	5,3±1,5
	Adaptation	—	11,8±3,6	50,4±5,9	17,4±7,0	1,7±0,2
	Infarct	—	34,5±7,4*	71,2±5,6**	60,7±13,4*	41,1±13,2*
	Adaptation + infarct	—	12,1±3,3*[4]	46,8±3,3*[5]	15,7±4,9*[4]	3,6±1,9*[4]

Legend. Significance of differences from control (group 1): $*P < 0.01$, $**P < 0.001$, $***P < 0.05$, $*^{4}P < 0.01$, $*^{5}P < 0.001$.

stress itself had no significant effect on contractility of the right atrial myocardium, but largely prevented depression of its contractility in the presence of left ventricular infarction. In unadapted animals, infarction led to a decrease in the maximal tension developed by the atrium and the maximal intensity of functioning of structure (MIFS) by about 2-2.5 times, whereas in the adapted animals the decrease was under one-third of the control value. In hypoxia, just as in previous investigations [1], there was a marked decrease in resistance of the right atrial myocardium to oxygen insufficiency in animals with left ventricular infarction. Adaptation itself had no significant effect on resistance to hypoxia but largely prevented the decrease in resistance of the myocardium to this factor caused by infarction. For instance, at the 5th minute of hypoxia the maximal developed tension and MIFS of the atria in rats with infarction, adapted beforehand to stress, was about twice as high as in unadapted animals with infarction, whereas the index of hypoxic contracture, on the other hand, was significantly lower than in unadapted animals. After the end of exposure to hypoxia, atrial contractility during reoxygenation in animals adapted to stress and with experimental infarction also was about twice as high as in unadapted animals. Consequently, adaptation to short-term stress largely prevents depression of contractility of the nonischemic part of the heart (right atrium) and the decrease in its resistance to hypoxia which is usually observed in left ventricular infarction.

The next experiments on the atria showed that adaptation to short-term stress itself had no significant effect either on the positive inotropic effect, usually developing under the influence of an increased Ca^{++} concentration, or on the appearance of hypercalcium contracture. Meanwhile this adaptation largely prevented the almost complete abolition of the positive inotropic effect of calcium and activation of the development of hypercalcium contracture of the atria due to the myocardial infarction.

Preliminary adaptation to short-term stress thus largely prevents the stress-induced disturbances of function of the nonischemic parts of the heart in myocardial infarction. An essential role in the mechanism of the protective effect of this adaptation is played by prevention of disturbances of functioning of the Ca^{++} transport mechanisms arising in nonischemic parts of the myocardium during infarction.

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EFFECT OF α-TOCOPHEROL ON RESPONSE OF THE ADRENALS TO COLD STRESS

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UDC 616-001.18-092.9-07:616.45-008.6-02:615.356:577.161.3

KEY WORDS: cold stress; adrenocortical functions; lipid peroxidation; α-tocopherol.

The protective action of antioxidants during exposure to extremal factors is associated with their ability not only to inhibit lipid peroxidation (LPO) reactions in target organs, but also to inhibit the generalized neuroendocrine response of the body [1, 2]. This last fact suggests that antioxidants may have an antistress action. Meanwhile, the writers have shown that a single dose of ionol or tocopherol can cause a sharp rise of the plasma corticosteroid level [3]. Hence the need for an investigation of these properties of antioxidants.

The aim of this investigation was to study the response of the adrenals in control rats and rats receiving α-tocopherol (AT) kept under exposure to cold.

EXPERIMENTAL METHOD

Experiments were carried out in winter on Wistar rats divided into eight groups (12-14 animals in each group). Control animals and animals receiving AT for 7 days (5% AT acetate in oil, 4 mg daily per rat with the food) were exposed to cold (5°C for 2, 5, and 20 h). The intensity of LPO in the body was judged from the AT concentration in the liver [6] and the content of diene conjugates (DC) in the hepatic lipids. The rate of ascorbate-dependent lipid peroxidation (ADLP) in a 5% liver homogenate was estimated from the accumulation of malonic dialdehyde (MDA) [5]. Meanwhile corticosteroid production by the adrenals of the experimental animals was studied in vitro. Slices of adrenals from four rats were pooled into two parallel samples and incubated for 2 h at 37°C in 4 ml of Krebs–Ringer bicarbonate buffer with 200 mg % glucose, saturated with a mixture of 95% O_2 and 5% CO_2. ACTH was added to one of the parallel samples in a dose of 6 U/g tissue.

Corticosteroids were separated by thin-layer chromatography and determined quantitatively [4].

EXPERIMENTAL RESULTS

As was expected, keeping the rats for 5-20 h in the cold induced stress. Biosynthesis of deoxycorticosterone (DOC) and corticosterone at these times was higher than in the control (Table 1). Elevation of the MDA level and an increase in the rate of ADLP in liver homogenates from these animals could be regarded as a manifestation of this stress. The DC concentration fell (Table 2).

Prolonged administration of AT did not change the character of hormone synthesis. The DC and MDA levels in the liver likewise were unchanged. Meanwhile accumulation of AT was observed in the liver, and this probably was the reason for the steep decline in the rate of ADLP in the liver homogenates (Tables 1 and 2).

Institute of Clinical and Experimental Medicine, Siberian Branch, Academy of Medical Sciences of the USSR, Novosibirsk. (Presented by Academician of the Academy of Medical Sciences of the USSR V. P. Kaznacheev.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 99, No. 6, pp. 669-671, June, 1985.

 0007-4888/85/9906-0714$9.50