EFFECT OF ADAPTATION TO SHORT-TERM STRESS ON THE FIBRILLATION THRESHOLD AND ECTOPIC ACTIVITY OF THE HEART IN EXPERIMENTAL MYOCARDIAL INFARCTION

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UDC 616.127-005.8-092.9-092:612.17.014.49:613.863

KEY WORDS: adaptation to stress; antioxidant, fibrillation threshold

Adaptation to short-term stress prevents disturbances of myocardial metabolism and function in the presence of infarction [4]. However, the important question of whether disturbances of the electrical stability of the heart, regularly observed in infarction, can be prevented by preliminary adaptation to short-term stress, has not yet been studied.

The aim of this investigation was to assess the effect of preliminary adaptation to short-term stress on electrical stability of the heart in experimental myocardial infarction.

EXPERIMENTAL METHOD

Male Wistar rats weighing 250-350 g were used. To study the effect of an experimental infarct of two days' duration on electrical stability of the heart and the resistance of its pacemaker to the inhibitory influence of the vagus nerve the following series of experiments were undertaken: I) control, II) experimental infarction, III) adaptation to short-term stress, IV) adaptation to short-term stress plus infarction. The animals were adapted to short-term stress by temporary fixation in the supine position for 15 days: on the first day 15 min, on the second day for 30 min, on the third day for 45 min, and on the remaining days for 1 h. Myocardial infarction was induced by Selye's method [11] by ligating the descending branch of the left coronary artery. The animals were used in the experiments two days after infarction. The experiments were as follows. Under pentobarbital anesthesia (50 mg/kg) the reaction of the heart to stimulation of the distal end of the right vagus nerve (2 msec, 20 Hz) was evaluated. After determination of the threshold strength of the current (0.22-0.28 V), the response to stimulation with a strength of 1, 2, 3, and 4 thresholds was estimated at intervals of 5 min. The EKG and blood pressure (BP) in the coronary artery were recorded on a Mingograf-34 recorder (Siemens-Elema, West Germany). The negative chronotropic effect was assessed by the degree of reduction of the heart rate (ΔHR), whereas the inotropic effect was judged from BP. The next step was to determine the electrical threshold of ventricular fibrillation. For this purpose, after thoracotomy, the apex of the right ventricle was stimulated with premature single square pulses, 10 msec in duration, through a coaxial electrode by means of an SEN-3201 stimulator (Nihon Kohden, Japan). The ventricular fibrillation threshold was estimated as the minimal strength of the current (in mA) inducing fibrillation was recorded simultaneously with the EKG and BP.

EXPERIMENTAL RESULTS

Table 1 shows that 2 days after infarction, when the animals were first used in the experiments, HR did not differ from the control, the systolic BP in the postinfarction period was 37% lower than in the control, and the diastolic BP was 24% lower. The fibrillation threshold in animals with an infarct of 2 days' duration (Fig. 1) averaged 2.1 mA, i.e., the infarct lowered the fibrillation threshold by more than two-thirds compared with the control. This is in agreement with experimental and clinical data obtained by other investigators [9]. Adaptation to short-term stress itself had no effect on the fibrillation threshold, and at the same time it largely prevented the postinfarction fall of the fibrillation threshold. In accordance with existing ideas, lowering the fibrillation threshold reflects the increased

Kazakh Research Institute of Cardiology, Alma-Ata. (Presented by Academician of the Academy of Medical Sciences of the USSR A.D. Ado.) Translated from Byulletin' Éksperimental'noi Biologii i Meditsiny, Vol. 103, No. 3, pp. 271-273, March, 1987. Original article submitted April 16, 1986.

0007-4888/87/0003-0295$12.50

TABLE 1. Prevention of Postinfarction Lowering the Resistance of the Heart to Inhibitory Influence of Vagus Nerve and Increase in Ectopic Activity by Preliminary Adaptation to Short-Term Stress and by the Antioxidant Ionol (M ± m)

Series of experiments	Number of animals	Initial parameters			Δ HR		Ectopic activity during vagus nerve stimulation	
		HR, beats/min	BP, mm Hg		strength of vagus nerve stimulation, threshold			
			systolic	diastolic	2	3	number of animals with extrasystoles	total number of extrasystoles per series
Control	11	404±13	142±7	87±12	129±20	167±23	2	32
Infarction	10	394±17	90±7*	66±11	211±23*	264±19*	7	147
Adaptation to stress	11	401±11	124±8	76±5	80±14	108±15	0	0
Adaptation + infarction	11	384±13	94±6*	68±4	116±19	167±19	2	15
Ionol	10	409±12	126±5	72±4	92±23	136±30	2	3
Ionol + infarction	10	386±16	88±6*	60±8	95±24	201±25	4	35

Legend. *p < 0.05. Ionol is 2,6-di-(tert-butyl-4-methylphenol).

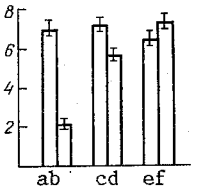

Fig. 1. Prevention of postinfarction lowering the fibrillation threshold by preliminary adaptation to short-term stress and the antioxidant ionol. Ordinate, strength of current (in mA). a) Control; b) infarct of 2 days' duration; c) adaptation to short-term stress; d) infarct + adaptation to stress; e) ionol; f) infarction + ionol.

"readiness" of the heart to develop arrhythmias [8]. Thus adaptation to short-term stress substantially reduces the probability of onset of ventricular fibrillation in the late period of acute myocardial infarction. It will also be clear from Table 1 that, besides lowering of the fibrillation threshold, a decrease in resistance of the sinus node pacemaker to the inhibitory action of the vagus nerve also was observed in the postinfarction period. This effect was particularly marked in the case of stimulation by a current with a strength of 2-3 thresholds. Adaptation itself reduces the negative chronotropic effect of the vagus nerve compared with the control, but the effect of adaptation was even more marked in the presence of an infarct. In fact, during stimulation of the vagus nerve with a strength of 2 thresholds HR of the control animals was reduced by about 130 beats/min, compared with 80 beats/min in adapted animals. For animals with infarcts this negative chronotropic effect was 211 beats/min, whereas for animals adapted before infarction it was 116 beats/min. The same pattern also was observed in relation to the negative inotropic effect.

It is important to note that during vagus nerve stimulation 70% of animals with an infarct developed extrasystoles, whereas in the control they were found much less frequently — 18% of cases.

This phenomenon was evidently due both to deeper inhibition of the sinus node pacemaker in the presence of an infarct and to the appearance of ectopic foci of excitation, revealed on depression of the normal pacemaker [6, 7, 10, 12].

These experiments showed that preliminary adaptation to short-term stress lowers the level of ectopic activity in animals with myocardial infarction. Extrasystoles were observed during vagus nerve stimulation in 70% of unadapted animals but only in 18% of adapted animals with infarction. The total number of extrasystoles in animals with myocardial infarction was

low, even compared with animals without infarction. It is important to note that ectopic activity not only leads to the appearance of extrasystoles, but it is also an essential component of the re-entry mechanism in spontaneous fibrillation [6]. Depression of ectopic automatism by adaptation thus means lower probability of the development of the arrhythmias and ventricular fibrillation in the postinfarction period.

When these data are assessed it must be recalled that adaptation to short-term stress is accompanied by activation and increased effeciency of the stress-limiting system, i.e., the opioidergic [3], GABA-ergic [1], and other central inhibitory systems of the brain, and also the prostaglandin system [13] and the antioxidant system [5] in target organs.

It has been postulated in this connection that metabolites of stress-limiting systems or their synthetic analogs can induce the same protective effect as adaptation to short-term stress [4]. To test this hypothesis, the antioxidant ional (dibunol) was used; this substance has a powerful cardioprotective action [2].

Daily injection of ional into the animals for 3 days in a dose of 50 mg/kg before production of the experimental infarct was found to have a protective effect similar to that of adaptation to short-term stress, namely, it prevented the lowering of the fibrillation threshold and the increase in ectopic activity of the heart.

On the whole these results are evidence that adaptation to stress may help to prevent or limit disturbances of electrical stability of the heart associated with experimental infarction. Besides other stress-limiting systems, it is very probably that the antioxidant system may play a role in the mechanism of this effect.

LITERATURE CITED

1. F. Z. Meerson, Adaptation, Stress, and Prophylaxis [in Russian], Moscow (1981).
2. F. Z. Meerson, Pathogenesis and Prevention of Stress-Induced and Ischemic Heart Lesions [in Russian], Moscow (1984).
3. F. Z. Meerson, A. D. Dmitriev, and V. I. Zayats, Kardiologiya, No. 9, 81 (1984).
4. F. Z. Meerson, Byull. Vses. Kardiol. Nauch. Tsent. Akad. Med. Nauk SSSR, No. 1, 34 (1985).
5. N. El-Sherif, R. Mehra, W. Gough, et al., Circulat. Res., 51, 152 (1982).
6. E. Kaplinsky, S. Ogawa, E. Michelson, et al., Circulation, 63, 333 (1981).
7. P. Kowey, S. Khuri, M. Josa, et al., Am. Heart J., 108, No. 4, 884 (1984).
8. B. McGovern, J. Dimarco, H. Garan, et al., Curr. Probl. Surg., 7, 1 (1983).
9. P. Penkoske, B. Sobel, and P. Corr, Circulation, 58, 1023 (1978).
10. H. Selye, E. Bajusz, S. Grasso, et al., Angiology, 11, 398 (1980).
11. B. Scherlag, N. El-Sherif, R. Hope, et al., Circulat. Res., 35, 372 (1974).
12. G. L. Wallace et al., Am. J. Physiol., 247, No. 2, G127 (1984).