4. R. N. Glebov and G. N. Kryzhanovskii, Usp. Fiziol. Nauk, 15, No. 3, 83 (1984).
5. G. N. Kryzhanovskii, Determinant Structures in Pathology of the Nervous System [in Russian], Moscow (1980).
6. G. N. Kryzhanovskii and R. N. Glebov, Zh. Nevropatol. Psikhiat., No. 930 (1984).
7. L. Lashas and D. Lashene, Human Somatotropin [in Russian], Vilnius (1981).
8. V. V. Shkolovoi and R. N. Glebov, Byull. Éksp. Biol. Med., No. 12, 1434 (1976).
9. E. Elomaa, R. Lehtovaora, D. Johansson, et al., Epilepsy: Clinical and Experimental Research, Vol. 5, Basel (1980), pp. 30-31.
10. Handbook of Neurochemistry, Vol. 8, London (1984).
11. H. C. Ho and W. V. Kover, Mol. Cell. Endocrinol., 39, No. 3, 184 (1985).

EFFECT OF ADAPTATION TO PERIODIC AND CONTINUOUS ANOXIA ON DISTURBANCE OF THE ELECTRICAL STABILITY OF THE HEART IN POSTINFARCTION CARDIOSCLEROSIS

E. E. Ustinova, V. A. Saltykova, V. V. Didenko, P. V. Beloshitskii, and F. Z. Meerson

UDC 612-127-005.8-092.9-092: 612.273.2.014.49

KEY WORDS: adaptation to anoxia; electrical stability of the heart; cardoisclerosis

Research published previously yielded evidence that marked disturbances of electrical stability of the heart, usually developing during postinfarction cardiosclerosis, and including lowering of the electrical threshold of fibrillation and enhancement of ectopic activity of the heart, can be abolished by adaptation of animals to periodic anoxia under pressure chamber conditions [4, 5]. However, the question whether this result can be achieved by adaptation of animals at average altitudes in the mountains has not hitherto been studied.

The aim of this investigation was to compare the effect of adaptation to periodic anoxia under pressure chamber conditions and adaptation to anoxia at average altitudes in the mountains on disturbances of electrical stability of the heart during postinfarction cardiosclerosis.

EXPERIMENTAL METHOD

Experiments were carried out on male Wistar rats weighing 180-200 g. Under ether anesthesia the descending branch of the left coronary artery was ligated by the method in [10], after which the animals gradually developed postinfarction cardiosclerosis in the form of a massive scar in the wall of the left ventricle. In the first stage of the experiment, adaptation to anoxia in the pressure chamber began in the case of animals 2 weeks after ligation of the coronary artery: the 1st and 2nd days at an altitude of 1000 m above sea level for 2 h, then every 2 days later the altitude was increased by 1000 m up to 5000 m. The duration of stay in the pressure chamber was then increased daily by 1 h up to 6 h. Altogether the rats were exposed to anoxia 45 times. The experiments were done in March and April.

At the second stage of the experiment, done in July and August, 2 weeks after ligation of the coronary artery the animals were taken up to the base laboratory of high-altitude physiology, A. A. Bogomolets Institute of Physiology, Academy of Sciences of the Ukrainian SSR, in the village of Terskol at an altitude of 2100 m above sea level, where they remained for 30 days in the animal house, under conditions identical with those in Moscow, after which they were returned to Moscow, where experiments to study parameters of the electrical stability of the heart were carried out during the first 3 days.

The electrical threshold of fibrillation of the heart was determined in acute experiments under pentobarbital anesthesia after thoracotomy. By means of the SFN-3201 stimulator (Nihon Kohden, Japan), triggered by the R wave of the ECG, the heart was stimulated by

Research Institute of General Pathology and Pathological Physiology, Academy of Medical Sciences of the USSR, Moscow. A. A. Bogomolets Institute of Physiology, Academy of Sciences of the Ukrainian SSR, Kiev. (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. 5, pp. 533-535, May, 1988. Original article submitted April 13, 1987.

 0007-4888/88/0005-0636$12.50

TABLE 1. Effect of Adaptation to Continuous Anoxia at Average Altitudes in the Mountains on Parameters of Electrical Stability of the Heart during Postinfarction Cardiosclerosis (M ± m; n = 10)

Experimental conditions	Heart rate, beats/min	Fibrillation threshold, mA	Total number of extrasystoles (for 10 animals) during vagal stimulation
Control	388±11	5,6±0,8	23
Postinfarction cardiosclerosis	369±15	2,7±0,5*	185
Adaptation to average altitudes in the mountains	376±15	5,7±0,4	34
Postinfarction cardiosclerosis + adaptation to average altitudes	390±10	5,6±0,3**	119

Legend. Here and in Table 2: *p < 0.05 compared with control, **p < 0.05 compared with postinfarction cardiosclerosis.

premature single square pulses with a duration of 10 msec, through a coaxial electrode, inserted into the myocardium at the apex of the right ventricle. The threshold of ventricular fibrillation was taken to be the minimal strength of current at which fibrillation occurred.

Ectopic activity of the heart was estimated against a background of vagal bradycardia, induced by stimulation of the peripheral end of the divided vagus nerve (square pulses, duration 2 msec, delay 5 msec, frequency 20 Hz), by a current with a strength of 1, 2, 3, and 4 thresholds. The number of extrasystoles in 30 sec of stimulation was counted in a total of four periods of stimulation, and calculated for a group of 10 animals.

After the end of the experiment the heart was removed, the absolute weight of the left and right ventricles calculated, and the weight of the scar determined.

EXPERIMENTAL RESULTS

The data in Table 1 indicate that 2 months after creation of the infarct (during postinfarction cardiosclerosis) the electrical threshold of ventricular fibrillation in the rats was depressed by half, and ectopic activity (the number of extrasystoles against the background of vagal bradycardia) was increased eightfold. These disturbances of electrical stability are evidence of the readiness of the heart to develop arrhythmias, and they agree with data published previously [8]. It follows from Table 1 that under the influence of adaptation to average altitudes in the mountains the threshold of fibrillation returned to the control level, and ectopic activity of the heart was reduced by more than one-third, although it still remained significantly higher than in the control.

Table 2 gives analogous data on the effect of adaptation to periodic anoxia under pressure chamber conditions on the parameters of electrical stability of the heart studied. In the control animals used to study adaptation to the periodic action of anoxia under pressure chamber conditions the threshold of ventricular fibrillation was rather high, and ectopic activity was somewhat less marked than in the animals used in the second stage of the experiment. Just as in the experiments described previously, postinfarction cardiosclerosis caused the fibrillation threshold to fall from 6.4 to 2.7 mA, and ectopic activity was enhanced even more: in the group of 10 animals, 285 extrasystoles were observed during vagal bradycardia. Adaptation to periodic anoxia under pressure chamber conditions led to restoration of the fibrillation threshold virtually to the control level, and reduced ectopic activity of the heart by 19 times. Thus both versions of adaptation to anoxia which were used were able to limit or abolish disturbances of electrical stability of the heart arising during postinfarction cardiosclerosis.

When the mechanism of this important phenomenon is assessed it will be recalled that adaptation to anoxia involves extensive changes in neurohumoral regulation of the heart and, in particular, activation of the opioid peptide system [5] and it also increases the effec-

TABLE 2. Effect of Adaptation to Periodic Anoxia under Pressure Chamber Conditions on Parameters of Electrical Stability of the Heart during Postinfarction Cardiosclerosis (M ± m; n = 10)

Experimental conditions	Heart rate, beats/min	Fibrillation threshold, mA	Total number of extrasystoles (for 10 animals) during vagal stimulation
Control	338±11	6,4±0,3	5
Postinfarction cardiosclerosis	349±14	2,7±0,2*	293
Adaptation in pressure chamber	339±12	5,9±0,4	4
Postinfarction cardiosclerosis + adaptation in pressure chamber	350±15	5,4±0,4**	16

tiveness of vascularization of the heart [7] and the energy supply to the heart muscle [9]. Ultimately this adaptation, taking place against a background of postinfarction cardiosclerosis, as has recently been shown, results in a reduction in the weight of the post-infarction scar by about 30% [4]. In the present experiments the weight of the scar in animals subjected to adaptation by both versions, also was reduced compared with that of unadapted animals by 27-31%. Besides changes in neurohumoral regulation, this change could also play a role in the anti-arrhythmic effect of adaptation.

In the context of the present description, the important fact is that the effect of adaptation to periodic anoxia under pressure chamber conditions was more radical: this adaptation led not only to restoration of the electrical threshold of ventricular fibrillation, but also to the almost total disappearance of the extrasystoles observed during postinfarction cardiosclerosis against the background of vagal bradycardia. Two explanations of this greater effect of periodic adaptation may be suggested. First, the dose of anoxia, namely the product of the degree of anoxia and its duration [6], corresponded during the last month of adaptation when a pressure chamber was used to a continuous all-day stay in an altitude of 1300 m above sea level, i.e., it was more than 1.5 times less than when the animals were kept at average altitudes in the mountains. Moderate anoxia of this kind may perhaps be optimal as regards the antiarrhythmic effect of adaptation. Second, adaptation to the periodic action of anoxia does not simply mean adaptation to oxygen deficiency, but also the influence of gradual ascents to an altitude followed by reoxygenation. In this connection it has been shown [1, 2] that during adaptation to periodic anoxia increased activity of antioxidative enzymes is regularly observed, whereas during adaptation to continuous anoxia this activation is absent. The antioxidative protection of the body, as several investigations have shown [3], plays an important role in the increased resistance of the heart to arrhythmias.

The results are evidence that rationally graded adaptation to periodic anoxia may be promising for use as an anti-arrhythmic factor.

LITERATURE CITED

1. A. M. Gerasimov, E. A. Kovalenko, N. V. Kasatkina, et al., Dokl. Akad. Nauk SSSR, 244, No. 2, 492 (1979).
2. A. M. Gerasimov and N. V. Delenyan, Stress, Adaptation, and Functional Disturbances [in Russian], Kishinev (1984), pp. 57-58.
3. F. Z. Meerson, V. A. Saltykova, and V. V. Didenko, Kardiologiya, No. 5, 61 (1984).
4. F. Z. Meerson and E. E. Ustinova, Metabolism, Structure, and Function of the Heart Cell [in Russian], Baku (1986), p. 122.
5. F. Z. Meerson, E. E. Ustinova, and E. V. Shabunina, Dokl. Akad. Nauk SSSR, 293, No. 2, 489 (1987).
6. M. G. Pshennikova, Fiziol. Zh. SSSR, 59, No. 3, 421 (1973).
7. A. Kerr, R. B. Diasio, and W. J. Bommer, Am. Heart, J., 69, 841 (1965).
8. F. Lombarde, R. L. Verrier, and B. Lown, Am. Heart J., 105, 958 (1983).
9. L. C. Ou and S. M. Tenney, Resp. Physiol., 8, 151 (1970).
10. H. Selye, E. Bajusz, S. Grasso, and P. Mendell, Angiology, 11, 398 (1960).