anied by a corresponding fall in its concentration in the myocardial tissue. This must also have a beneficial effect on myocardial function, because an excess of ammonia can block several mitochondrial processes [2].

LITERATURE CITED

1. J. Bittl and K. L. Shine, Am. J. Physiol., 245, H406 (1983).
2. N. Katunuma, M. Okada, and Y. Nishi, Adv. Enzym. Reg., 4, 317 (1966).
3. H. L. Lazar, G. D. Buckberg, A. J. Mangarano, et al., J. Thorac. Cardiovasc. Surg., 80, 350 (1980).
4. G. H. Mudge, R. H. Mills, H. Taegtmeyer, et al., J. Clin. Invest., 58, 1185 (1976).
5. O. L. Pisarenko, E. S. Solomatina, I. M. Studneva, et al., J. Mol. Cell. Cardiol., 15, 53 (1983).
6. E. E. Rau, K. I. Shine, A. Gervais, et al., Am. J. Physiol., 236, 4873 (1979).
7. J. Rovetto, J. T. Whitmer, and J. R. Neely, Circ. Res., 32, 699 (1973).
8. T. Sanborn, W. Gavin, S. Bercovitz, et al., Am. J. Physiol., 237, 535 (1979).
9. H. G. Shertzer and J. Cascarano, J. Exp. Zool., 207, 337 (1979).
10. H. Taegtmeyer, M. B. Peterson, V. V. Ragavan, et al., J. Biol. Chem., 252, 5010 (1977).

HEMODYNAMIC CHANGES IN IMMOBILIZATION STRESS

L. S. Ul'yaninskii, O. S. Medvedev, A. M. Bunyatyan, D. D. Matsievskii, and N. I. Rozhanskaya

UDC 613.863-02:612.766.2]-07:616.1-008.1-092.9

KEY WORDS: hemodynamics; immobilization stress.

Hemodynamic disturbances in emotional stress may be due mainly to changes in cardiac output (CO) [7, 8] and in total peripheral resistance (TPR) [3, 10, 11]. Marked disturbances of regulation of blood pressure (BP), possibly leading to death of the animals, have been found [5, 9] in rats with immobilization stress (IS). However, the hemodynamic mechanisms of these disturbances have not yet been studied.

Changes in hemodynamic parameters of rats differing in resistance to IS and correlation between cardiac and vascular components of the hemodynamics during development of the terminal state in the course of immobilization were studied in the investigation described below.

EXPERIMENTAL METHOD

Experiments were carried out on 75 rats (Wistar, August, and noninbred, 25 of each). A model of IS was used (immobilization of the animals in a confined chamber for 30 h). BP was recorded in all experiments by means of a catheter introduced into the abdominal aorta through the caudal artery by the method in [4], and the ECG was recorded in standard lead II. As a first step, ultrasonic blood flow transducers were implanted on the ascending aorta of 20 of these animals (Wistar and August). By using an ultrasonic measuring technique it was possible to measure the linear velocity of the blood flow in the ascending aorta (VBA), and the stroke volume (SV) and CO could be determined by the use of electronic integrators [1, 2]. TPR also was calculated.

EXPERIMENTAL RESULTS

In unrestrained rats at rest, no differences in hemodynamic parameters could be found between the three different lines. The mean BP was 117.5 ± 3.5 mm Hg, the heart rate (HR)

Laboratory of Experimental Cardiology, P. K. Anokhin Research Institute of Normal Physiology, Academy of Medical Sciences of the USSR. Laboratory of Experimental Pharmacology, All-Union Cardiologic Scientific Center, Academy of Medical Sciences of the USSR. Bioengineering Laboratory, 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. V. Val'dman.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 100, No. 9, pp. 282-285, September, 1985. Original article submitted August 17, 1984.

0007-4888/85/0009-1176$09.50

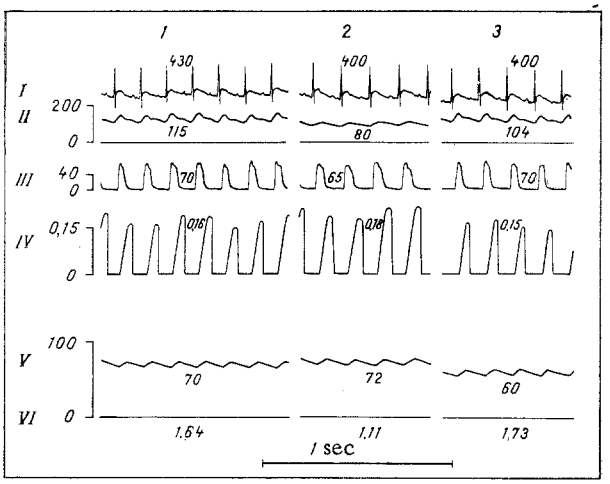

Fig. 1. Hemodynamic changes during adaptation to IS: 1) original hemodynamic parameters in a rat before immobilization; 2) 11th hour of immobilization: fall of BP and TPR, small increase in CO; 3) 28th hour of immobilization: stabilization of hemodynamic parameters at level different from original. I) HR (beats/min); II) mean BP in aorta (in mmHg); III) linear velocity of blood flow in ascending aorta (in cm/sec); IV) SV (in ml); V) CO (in ml/min); VI) TPR (in mm Hg/ml•min).

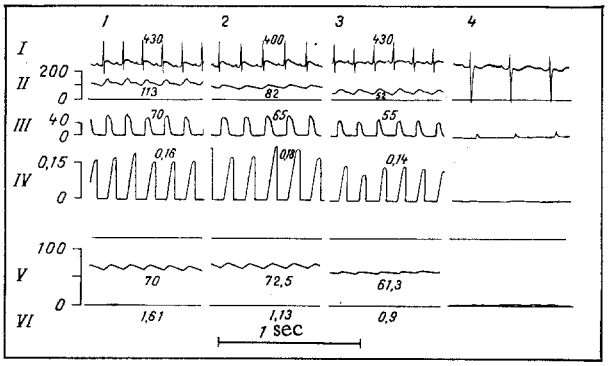

Fig. 2. Death of a rat during IS on account of a progressive fall of TPR. 1) Initial hemodynamic parameters of rat before immobilization; 2) 8th hour of immobilization: fall of BP and TPR, small rise of CO; 3) 11th hour of immobilization: further fall of BP and TPR, decrease of CO; 4) death at 12th hour of immobilization. Remainder of legend as to Fig. 1.

417 ± 10.3 beats/min, VBA 73.13 ± 2.8 cm/sec, SV 0.17 ± 0.01 ml, CO 63 ± 1.7 ml/min, and TPR 1.7 ± 0.1 mm Hg/ml•min.

Depending on the results of immobilization the animals were divided into the following groups: resistant, adapted, and predisposed to IS. All these groups were found among animals of each line, but in different relative percentages. Wistar rats were most resistant, August rats most predisposed.

The resistant group consisted of 15 rats in which, throughout the period of immobilization, no ECG disturbances were found, HR was stable and did not undergo any significant changes, and fluctuations of BP did not exceed 10-15 mm Hg. These fluctuations were the result of small changes in both CO and TPR; an increase in CO was accompanied by a decrease in TPR, and vice versa. The mean BP was thus maintained at a stable level.

The adapted groups consisted of 19 rats in which throughout immobilization marked fluctuations of BP (up to 30-40 mm Hg) and HR (up to 100-130 beats/min) were observed. Fluctuations of BP were usually accompanied by disturbances of the ECG. Toward the end of immobilization these parameters became stabilized at close to the original level. Fluctuations of BP were associated mainly with marked changes in TPR. For instance, a rise in BP was caused

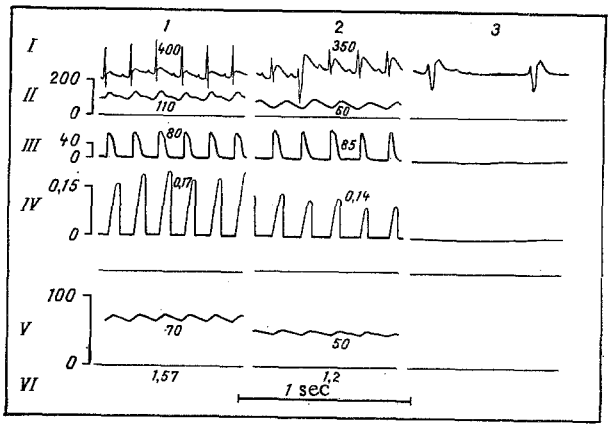

Fig. 3. Development of terminal state during IS with signs of cardiovascular failure. 1) Initial parameters of hemodynamics of rat before immobilization; 2) 25th hour of immobilization: sharp increase in T wave, extra systoles originating from main branch of bundle of His, fall of BP, CO, and TPR; 3) death of rats at 26th hour of immobilization. Remainder of legend as to Fig. 1.

by an increase in TPR, while CO remained unchanged, or actually was reduced slightly, whereas a fall of BP was caused by a decrease in TPR accompanied by a slightly raised CO. Stabilization of BP toward the end of immobilization at close to the original level took place when the ratio of CO to TPR differed from that observed at the beginning of immobilization (Fig. 1).

The predisposed group consisted of 41 rats. The mean BP in 20 of them toward the end of immobilization stabilized at 25-40 mm Hg above or below the original level, and 21 rats died at different times of immobilization. Analysis of the mechanisms of death of the animals yielded the following result: 14 rats died with a sharp fall of BP – to 30-40 mm Hg. During immobilization (before BP began to fall) CO and TPR remained close to the original level. A gradual fall of BP (to 60-75 mm Hg) was accompanied by a decrease in TPR, whereas CO was unchanged or actually increased a little. The subsequent fall of BP to 30-40 mm Hg was the result of an equally sharp decrease in TPR by 40-45% of its original value, and CO and HR did not begin to fall until this terminal stage (Fig. 2).

Four rats died with severe bradycardia. During the first 7-10 hours of immobilization their HR did not change significantly. Periodic fluctuations of BP were observed with a tendency toward some decrease, followed by a return to the original level, due as a rule to a decrease in CO and to some increase in TPR. Toward the 20th-22nd hour of immobilization HR fell to 240-260 beats/min. Under these circumstances BP could actually be a little higher than originally. CO fell to 60-70% of its original value on account of a fall in HR, whereas SV remained virtually unchanged. TPR under these circumstances increased, thereby compensating the reduced CO. The terminal stage developed with a further fall in HR and CO and an increase in TPR until immediately before the animal died, when all the parameters of the hemodynamics were close to zero.

Two rats died with signs of acute cardiovascular failure. The terminal stage began to develop when marked changes of ischemic character were already present in the ECG. Both hemodynamic parameters which reflect myocardial contractility (SV and CO) were reduced. Extrasystoles appeared. TPR also fell, and did not compensate the reduced CO (Fig. 3).

In most cases death during emotional stress is due to ventricular fibrillation [6, 12, 13]. An important role in the development of fibrillation has been shown to be played by increased functional and structural heterogeneity of the myocardium [6]. However, death during emotional stress may also arise as a result of acute cardiovascular failure [5, 9]. This model of IS in rats can help to shed light on the hemodynamic mechanisms of this type of death.

The results of the present experiments show that a leading role in disturbances of BP regulation in animals differing in resistance to IS is played by changes in TPR. The principal and commonest cause of death of animals with IS is a progressive fall of BP, due to a

sharp decrease in TPR. Meanwhile, the cardiac component of the hemodynamics may be the dominant factor in the mechanism of death: either rapidly progressive bradycardia or a combination of myocardial damage of ischemic character with a fall of TPR.

LITERATURE CITED

1. D. D. Matsievskii, Byull. Éksp. Biol. Med., No. 9, 119 (1970).
2. D. D. Matsievskii, Byull. Éksp. Biol. Med., No. 10, 123 (1965).
3. O. S. Medvedev, N. A. Stepochkina, and M. I. Dorokhova, in: Neuropharmacological Aspects of Emotional Stress and Drug Dependence [in Russian], Leningrad (1978), p. 109.
4. Yu. G. Skotselyas, L. I. Ivanova, and E. A. Yumatov, Fiziol. Zh. SSSR, No. 1, 154 (1977).
5. K. V. Sudakov, Systemic Mechanisms of Emotional Stress [in Russian], Moscow (1981).
6. L. S. Ul'yaninskii (L. S. Ulyaninsky), N. N. Beskrovnova, V. A. Kuznetsova, et al., in: Proceedings of 3rd USA–USSR Joint Symposium on Sudden Cardiac Death, Kaunas (1984), p. 361.
7. B. M. Fedorov, Emotions and Cardiac Activity [in Russian], Moscow (1977).
8. V. A. Tsybenko, Byull. Éksp. Biol. Med., No. 8, 3 (1983).
9. E. A. Yumatov, Fiziol. Cheloveka, 6, No. 5, 893 (1980).
10. J. Brod, M. Cachovan, J. Bahlmann, et al., Klin. Wschr., 57, 555 (1979).
11. A. Federici, L. Granata, O. Pinotti, et al., Atta Accad. Naz. Lincei Rend. Cl. Sci. Fis. Mat. Natur., 63, 458 (1977/1978).
12. B. Lown, in: Proceedings of 1st USA–USSR Joint Symposium on Sudden Death, Washington (1977), p. 387.
13. W. Raab, in: Advances in Cardiology [Russian translation], Moscow (1959), p. 67.

ACTIVATION OF LIPID PEROXIDATION IN CHRONIC ISCHEMIC HEART DISEASE

M. Khuzhamberdiev

UDC 616.127-005.4-036.12-07:616.008.939.15-039-092.9

KEY WORDS: lipid peroxidation products; blood plasma; vitamins E and C; ischemic heart disease.

In the modern view lipid peroxidation (LPO) is a continuous physiological process which, on intensification, participates in the development of a number of pathological conditions. It has been shown, in particular, that activation of LPO accompanies ischemic heart damage in experimental animals and is one of the key causes of disturbance of the functioning of heart muscle cells during ischemic injury [6]. It has also been shown that the level of primary products of LPO, namely lipid hydroperoxides, in the plasma rises significantly in chronic ischemic heart disease (CIHD) [3].

Experimental data also have been obtained to show that a combination of bioantioxidants (α-tocopherol + ascorbate + rutin + glutamate) significantly lowers the levels of LPO, cholesterol, and atherogenic lipoproteins in patients with CIHD [1]. Treatment with α-tocopherol reduced pain in the heart region, and positive changes in the ECG were observed in patients with ischemic heart disease (IHD) [2]. The investigations listed above indicate that it is possible to use the intensity of LPO in the clinical diagnosis of IHD and to assess the effectiveness of treatment. A direct investigation of the intensity of LPO processes in human heart muscle is naturally impossible.

The aim of this investigation was to study concentrations of LPO products in the blood plasma of patients with CIHD and the possibility of using vitamin E as a natural inhibitor of free radical processes in the treatment of ischemic heart disease.

M. I. Kalinin Andizhan Medical Institute.

(Presented by Academician of the Academy of Medical Sciences of the USSR T. T. Berezov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 100, No. 9, pp. 285-286, September, 1985. Original article submitted June 26, 1984.