HYPOXEMIA, ACID–BASE BALANCE SHIFTS, AND BLOOD SYSTEM REACTIONS IN THE MECHANISMS OF ADAPTATION

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The sympathoadrenal system is responsible for mobilizing the vital functions of the body during physiological stress and also during the development of various pathological processes. A method simulating moderate stress of the sympathetic nervous system, by injecting noradrenalin (NA) into the blood stream in a dose of 1 μ/kg every 6/min for 25 min, has recently been developed, and can be used to assess reactivity of the main homeostatic systems to adrenalin [5]. It was decided to study metabolic reactions, reflected in parameters of the acid–base balance (ABB) and gas levels of the blood to NA loading in normal dogs and after various procedures affecting homeostasis.

EXPERIMENTAL METHOD

Three series of experiments were carried out on 34 dogs of both sexes weighing 16-24 kg. The first series was carried out on unanesthetized dogs on the 3rd-4th days after catherization of the veins of the neck. Blood samples were taken through an arterial catheter. In the remaining series, thoracotomy was performed under thiopental sodium anesthesia, with controlled ventilation and catherization of the aorta and superior vena cava for the function tests and to obtain blood samples. Artificial ventilation was provided by an RO-5 apparatus, working on normocapnic mode. Responses to NA were studied during 25 min of its administration and 25 min after its withdrawal. Experiments of series 2 were carried out on intact animals, and those of series 3 24 h after the end of a 6-day course of NA infusions, in a dose of 2.3 μg/kg/min for 2 h (the dose was chosen experimentally as that causing minimal damage [10]), Parameters of ABB were studied on the AME-1 apparatus ("Radiometer," Denmark), and the partial pressure of oxygen in the blood by means of a Clark's electrode on the same apparatus. At all stages of the experiment the hemoglobin concentration, erythrocytes, hematocrit, and erythrocyte sedimentation rate of the blood were determined. The results were subjected to statistical analysis by computer, using Wilcoxon's two-sample test.

EXPERIMENTAL RESULTS

The time course of the ABB and blood gas parameters in unanesthetized dogs is shown in Fig. 1. The H^+ concentration is unchanged at all stages. Concentration of buffer bases fell from the 15th minute of NA infusion until the end of the observations. The standard bicarbonate reaction was similar. During the same period a significant shift of the BE index toward negative values was recorded. The partial pressure of oxygen fell from the 15th minute of NA infusion and until the end of the experiment (to a minimum of 87.2 ± 2.6 mm Hg). At the same times a decrease of pCO_2 is observed, reflecting the tendency toward moderate hyperventilation. These changes indicated a shift toward metabolic acidosis, but none of the parameters studied went beyond normal physiological limits.

More profound changes affecting the ABB parameters in the animals of this series may perhaps be due to the fact that, as was shown previously in our laboratory, after drip infusions of NA for 6 days in dose 2.3 μg/kg/min increased synthesis and secretion of catecholamines (CA) [8], alteration of metabolism with activation of the glycolytic pathway [7], the appearance of focal lesions of the cardiovascular system [10], and an increase in the myoglobin

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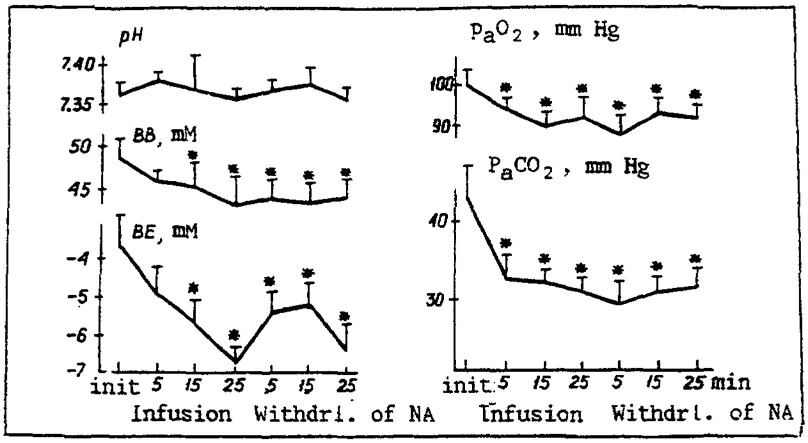

Fig. 1. Reactions of ABB and arterial blood gases to noradrenalin loading test on unanesthetized dogs. Here and in Figs. 2 and 3: init) initial values in control, *) values for which $p < 0.05$ compared with control.

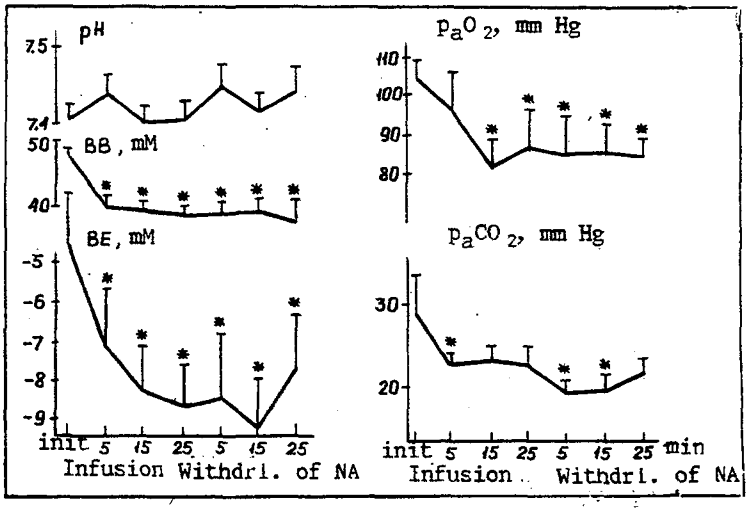

Fig. 2. Reactions of ABB and arterial blood gases to noradrenalin loading test on intact, anesthetized dogs with open chest.

concentration in the myocardium were observed [2]. Parameters of ABB shifted to the level of compensated metabolic acidosis without any significant changes in pO_2 and pCO_2 [3].

A study of the hematologic parameters in all three series reveals an increase in hemoglobin concentration, erythrocyte count, and hematocrit during NA infusions, accompanied by slowing of the ESR (Table 1). After the ending of NA infusions, these parameters returned to their initial levels. Thus in all three series of experiments the character of the changes in ABB parameters, partial pressure of oxygen in the arterial blood, and hematologic parameters was similar, differing only in degree.

Any extremal situation is accompanied by the development of activation of the stress-realizing systems, leading to increased entry of Ca and corticosteroids into the blood stream, an essential component of stress [9]. Meanwhile, some idea of the possible mechanisms of adrenergic activation of lipid peroxidation (LPO) have been formed. The formation of CA from phenylalanine and their decomposition to autooxidation have been shown to be accompanied by generation of the superoxide anion-radical and, consequently, they can activate LPO [11]. The action of large doses of CA leads to an increase in the content of LPO products in mitochondrial membranes by 90% [12]. Activation of LPO plays an essential role in the response of the body to extremal factors, and it can therefore be regarded as a nonspecific component of the stress reaction [4]. The oxidative and antioxidant stages are important

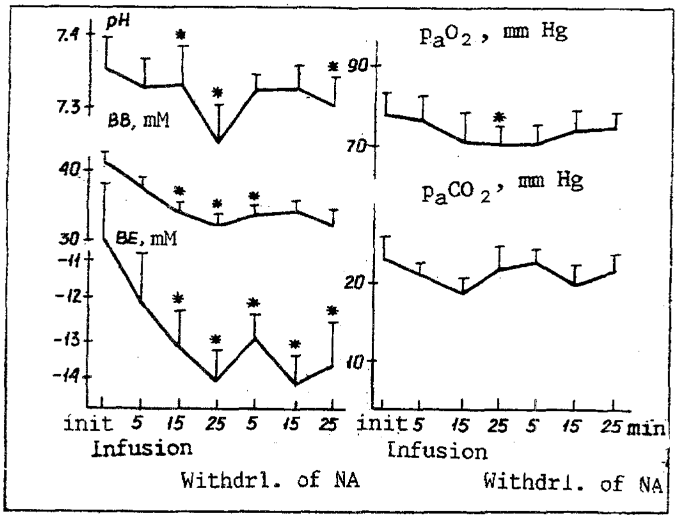

Fig. 3. Reactions of ABB and arterial blood gases to noradrenalin loading tests on anesthetized dogs with an open chest and with focal lesions of the cardiovascular system.

TABLE 1. Changes in Blood Parameters of Dogs during Drip Infusion of Noradrenalin (M ± m)

Parameter studied	Series No.	Before NA infusion	NA infusion, min			Time after withdrawal of NA, min		
			5	15	25	5	15	25
Hemoglobin, g/liter	1	12,2±0,4	12,9±0,4*	13,2±0,3*	12,7±0,3	12,3±0,3	12,2±0,5	12,8±0,4
	2	12,7±0,5	13,5±0,7	13,6±0,6	12,9±1,1	13,4±0,3	12,9±1,0	12,9±0,8
	3	13,8±1,0	14,6±0,8	13,9±0,9	13,9±0,8	13,2±0,9	12,2±1,0	13,1±0,9
Erythrocytes, × 10^{12}	1	4,23±0,18	5,36±0,36*	4,89±0,18*	4,76±0,2*	4,86±0,26	4,56±0,2	4,51±0,2
	2	4,13±0,43	5,0±0,3	5,16±0,32	4,81±0,27	4,68±0,19	4,78±0,24	4,16±0,3
	3	4,95±0,3	5,3±0,4	5,1±0,4	4,86±0,3	4,45±0,4	4,58±0,2	4,58±0,3
Hemotacrit, %	1	42,3±2,0	46,5±1,3*	47,2±2,2*	45,1±1,7*	43,2±1,5	40,0±1,5*	40,4±2,0*
	2	42,0±1,7	46,2±2,1*	45,8±2,1	46,6±1,7*	43,7±1,9	43,5±1,9	42,8±2,4
	3	38,5±2,2	43,5±1,9*	40,9±2,3	40,7±1,9	37,7±2,2	36,4±2,5	36,4±2,2
	1	14,3±3,0	6,8±2,9*	0,75±0,2*	2,67±0,8*	14,2±3,0	14,8±2,4	14,0±1,8
	2	5,4±2,4	4,6±0,2	2,1±1,3	1,4±0,4	3,9±0,4	4,4±0,3	4,8±2,3
	3	35,6±5,3	18,4±3,1*	17,9±2,8*	16,9±3,2*	19,5±5,0*	36,7±6,2	36,7±6,1

Legend. Asterisk indicates values for which $p < 0.05$ compared with control.

components of homeostasis. Reactions observed during the first minutes of action of the stressor are a manifestation of "emergency" adaptation, taking place through ready-made physiological mechanisms. It has been shown [6] that, in response to the action of stimuli of different strength (number) qualitatively different adaptive reactions develop. In response to the action of weak stimuli (small doses) physiological adaptive reactions develop, whereas to average doses, the reaction is one of activation. These reactions, encountered during the normal life of the organism, are the nonspecific basis of physiological processes. This is how we can regard the reactions observed to NA in small doses. Lowering of the partial pressure of oxygen in the blood, which develops under these circumstances, can be interpreted as a reaction in the antioxidant direction. As the investigation shows, a moderate decrease of pO_2 and, consequently, some decrease in the supply of dissolved oxygen to the tissues took place under the influence of small doses of NA. The presence of molecular oxygen, dissolved in the biological fluids, and its constant contact with readily oxidized compounds creates conditions favorable for the development of nonenzymic chain reactions of autoperoxidation, especially in the presence of active forms of oxygen, which play the role of autocatalysts [4]. If there is a relative deficit of molecular oxygen, generation of its active forms and intensification of LPO are limited [9].

In our view, the fall of the partial pressure of oxygen in the arterial blood at a time of moderate strain on the sympathetic nervous system can be regarded as a unique kind of antioxidant reaction. Our investigations showed that the metabolic shift and the fall of pO_2 observed during NA infusions are accompanied by a moderate increase in erythrocyte count, hematocrit, and hemoglobin concentration, which increases the oxygen capacity of the blood. The shift of pH toward the acid side reduces the affinity of hemoglobin for oxygen and facilitates its release at the tissue level. Slowing of the erythrocyte sedimentation rate observed during NA infusion is due to an increase in stability of the erythrocyte suspension. This reaction may play a role in the mass transfer of oxygen in the microcirculatory system on account of an increase in the duration of membrane erythrocyte-endothelial interactions, whose activity is increased in hypoxia [1]. Meanwhile the responses of pH and pO_2 to injection of microdoses of NA facilitate metabolic autoregulation of the peripheral circulatory system, the functional role of which is to adapt the local blood flow to the functional needs of an organ.

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