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EFFECT OF ADENOSINE ON HEMODYNAMIC CHANGES DURING DEVELOPMENT OF NEUROGENIC MYOCARDIAL DAMAGE

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More and more importance is currently being attached to nervous factors in the development of cardiovascular pathology. External stimulation of the hypothalamic region or of the reflexogenic zone in the arch of the aorta under experimental conditions is accompanied by disturbance of energy metabolism of the heart muscle, by disorders of cardiac function and, finally, by the development of diffuse-focal necrosis of the myocardial tissue [4]. These processes are based on reactions that are common to all stress-induced damage [4, 5]. Massive release of catecholamines from the tissue depots and associated disturbances of the hemodynamics and metabolism [4] are particularly important.

Among the stress-limiting systems of the body an important role is ascribed to the system of adenosine and adenine nucleotides [5]. Besides its positive effect on energy metabolism [7], adenosine also inhibits sympathetic neurotransmission [8] and has an antiadrenergic action [1], which is accompanied by normalization of the hemodynamics [3]. The aim of this investigation was to study the action of adenosine on hemodynamic changes induced by electrical stimulation of the reflexogenic zone of the arch of the aorta.

EXPERIMENTAL METHOD

Experiments were carried out on male rabbits weighing 2.5-3 kg. The immobilized animals were anesthetized by intravenous injection of pentobarbital (50 mg/kg body weight). A nichrome electrode 120 μ in diameter, in polyethylene insulation, was introduced through the right common carotid artery into the arch of the aorta; the electrode tip, 0.3-0.5 mm long,

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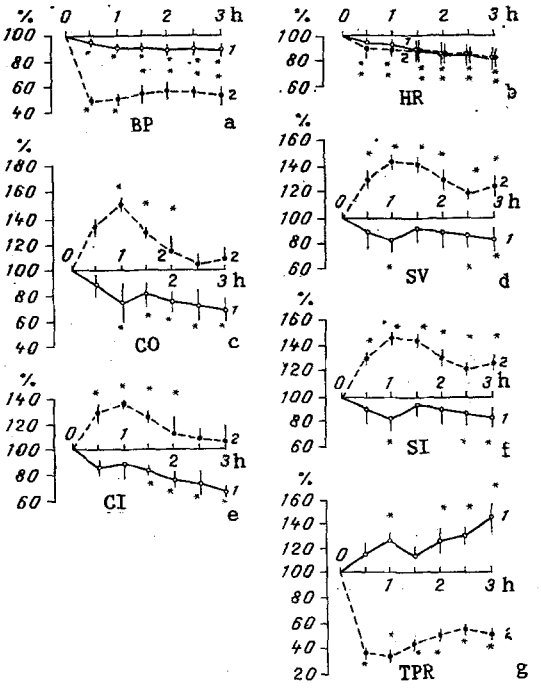

Fig. 1. Changes in hemodynamic parameters during electrical stimulation of arch of aorta. Infusion of: 1) physiological saline, 2) adenosine. *$p < 0.05$.

was not insulated. A second electrode, in the form of a needle, was inserted beneath the skin of the left forelimb. The arch of the aorta was stimulated for 3 h by a direct current (square pulses, 5-7 V, 1 msec, 50 Hz). Animals of the control group were given an injection of physiological saline (0.1 ml/min) into the femoral vein by means of a micropump throughout the period of electrical stimulation, whereas rabbits of the experimental group were similarly infused with adenosine (Reanal, Hungary) in a dose of 0.25 mg/(kg·min), in physiological saline. The hemodynamic parameters were determined by the method described previously [3]. The cardiac output (CO), mean blood pressure in the femoral artery (BP_m), and heart rate (HR) were estimated. The stroke volume (SV), stroke index (SI), cardiac index (CI), and total peripheral resistance (TPR) also were calculated. The results were subjected to statistical analysis by Student's test.

EXPERIMENTAL RESULTS

Electrical stimulation of the arch of the aorta in rabbits of the control group led to a disturbance of hydrodynamic type of the systemic hemodynamics (Fig. 1). Against the background of moderate bradycardia, BP_m fell and CO decreased progressively, accompanied by a marked increase in TPR. Values of SV, SI, and CI were correspondingly reduced.

Injection of adenosine caused an even greater fall of BP_m, for this dose of the compound has a marked hypotensive action [3] due to peripheral vasodilatation of arterioles and venules [2]. In fact, TPR of animals of the experimental group fell sharply, and there was a simultaneous increase in CO (after 1 h of the experiment by 50% compared with initially). After 3 h, TPR increased a little but CO decreased, so that both these parameters returned closer to their initial level. Changes in HR did not differ significantly from values in the control group.

Electrical stimulation of the arch of the aorta in rabbits thus caused definite changes in the hemodynamics, due primarily to an increase in the peripheral resistance to the blood blow superposed on depression of the pumping function of the heart. Spasm of the peripheral vessels was evidently caused by a flow of sympathetic impulses [4], inducing noradrenalin release from the tissue depots, and also by marked hypersecretion of the adrenal medulla and elevation of the blood adrenalin level. The increase in TPR could cause an increase in the

after-load on the heart and a reflex decrease in SV. Electrical stimulation of the arch of the aorta also leads to rapid exhaustion of the energy resources of the myocardium [4], and this also impairs the pumping function of the heart. Despite the increase in TPR, a considerable reduction of CO could lead to a decrease in BP_m.

Normalization of the hemodynamic parameters by the action of adenosine is due to several factors. First, adenosine is a peripheral vasodilator of arteriolo-venous type. Its use is accompanied by a considerable reduction of TYPR and lowering of the after-load on the heart. Second, adenosine has a marked antiadrenergic action and modulates noradrenalin release from nerve endings. These effects are connected with excitation of the purine receptors of the pre- and postsynaptic membranes, and also of the cytoplasmic membranes of smooth-muscle and endothelial cells and cardiomyocytes. Third, influsion of adenosine stimulates ATP resynthesis in the myocardium [6], for adenosine is easily transported inside the cardiomyocytes and activates adenosine- and adenylate-kinases, which convert it successively into AMP, ADP, and ATP.

Correction of energy metabolism by adenosine may bring about an improvement of the contractile function of the heart. The results are evidence that adenosine is involved in maintaining the optimal conditions for activity of the cardiovascular system in the presence of neurogenic myocardial damage, caused by extremal influences acting on the body.

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