CONTENT OF CATECHOLAMINES AND ADENOSINETRIPHOSPHATASE ACTIVITY IN THE MYOCARDIUM IN EXPERIMENTAL MYOCARDITIS

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The excess of catecholamines liberated in the heart from sympathetic nerve endings and reaching it from the blood stream plays an important role in the development of lesions of the heart muscle [10, 12, 21].

In experimental conditions lesions of the heart muscle from an excess of catecholamines are produced in the form of "adrenalin myocarditis" [4]. The metabolism in this state has been extensively investigated by workers in the laboratory directed by S. E. Severin, who have shown that in experimental myocarditis glycolytic [9] and oxidative [4] phosphorylation are disturbed in the myocardium, as a result of which the content of high-energy compounds is reduced [11]. A decrease in the content of contractile myofibrillary proteins of the myocardium per unit mass of heart muscle [2] and a decrease in the adenosinetriphosphatase (ATPase) activity of myosin [8] have also been demonstrated. However, no attempt has been made to investigate the effect of an excess of catecholamines in the body of metabolism of the catecholamines themselves in the heart muscle and the relationship between the lowering of the ATPase activity of the myocardium and the degree of injury to the myocardial tissue. Yet it is probable that the disturbance of catecholamine metabolism in the myocardium and the decrease in ATPase activity of the myosin arising under the influence of an acute increase in the content of catecholamines in the body may play an important role in the disturbances of the contractile function of the myocardium found previously by the authors [1].

In the present investigation the content of catecholamines and the ATPase activity of the heart muscle were studied in the presence of lesions caused by administration of theophylline and adrenalin.

EXPERIMENTAL METHOD

Lesions of the heart muscle by an excess of catecholamines were produced in rabbits weighing 2.0-2.5 kg by the intravenous injection of theophylline (1%; 2 ml/kg) and adrenalin hydrochloride (0.2 ml of a 1:1000 solution). Experiments were carried out on 27 animals. The test object was the myocardium of the left ventricle.

The content of catecholamines and of their biological precursors was determined in 6 experimental and 6 control (intact) rabbits. The content of catecholamines in the myocardial tissue of the experimental animals was determined on the 4th day after repeated injection of theophylline and adrenalin. The repeated injection was given 1 month after the first. Adrenalin, noradrenalin, and their precursors were determined in the myocardial tissue by the fluorometric method of É. Sh. Matlina and T. B. Rakhmanova, based on the method described by É. Sh. Matlina, Z. M. Kiseleva, and I. É. Sofieva [6].

The ATPase activity was investigated in three series of experiments on 15 animals (5 rabbits in each series). The animals of series I were intact and acted as controls, in those of series II the ATPase activity was determined on the 4th day after a single injection of theophylline and adrenalin, and in those of series III it was determined on the 4th day after the second injection of the same substances. Actomyosin was isolated by I. I. Ivanov's method [5]. The ATPase activity of the myocardium of the left ventricle was

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TABLE 1. Concentration of Catecholamines and Their Biological Precursors in Experimental Myocarditis (in μg/g Fresh Tissue)

Substance	Experiment	Control	Difference	P
Adrenalin	0,022±0,0051	0,065±0,0079	0,043±0,0095	<0,001
Noradrenalin	0,18±0,033	0,88±0,15	0,70±0,154	<0,001
Dopamine	2,7±0,83	7,2±1,02	4,5±1,31	<0,01
DOPA	0	0,35±0,016		

TABLE 2. ATPase Activity of Myocardial Tissue and Actomyosin in Experimental Myocarditis (in mg Phosphorus/g Fresh Tissue/ 10 min)

Experimental conditions	Tissue				Actomyosin			
	expt.	control	diff.	P	expt.	control	diff.	P
Single injection of theophylline and adrenalin	18,7±2,2	23,3±1,1	4,6	<0,1	1,2±0,07	1,6±0,1	0,4	<0,01
Repeated injection of theophylline and adrenalin	16,7±1,1	23,3±1,1	6,6	<0,01	1,0±0,1	1,6±0,1	0,6	<0,01

investigated by the method of P. M. Zubenko and co-workers [3], the inorganic phosphorus formed as a result of hydrolysis of ATP being determined by Lowry's method [17].

EXPERIMENTAL RESULTS AND DISCUSSION

The results of determination of the content of catecholamines and their precursors in the myocardium of the left ventricle in experimental myocarditis are given in Table 1. They show that the adrenalin content in the myocardium of the experimental animals fell by 67%, the noradrenalin content by 80%, and the dopamine content by 63% compared with the level of these compounds in the controls; practically no DOPA could be detected (0.016 μg/g was found in one case only). The results demonstrate that when lesions of the heart are caused by administration of massive doses of catecholamines and theophylline to animals, the content both of the adrenergic mediators and of their precursors is reduced.

A similar decrease in the content of catecholamines and their precursors is also observed after sympathetic denervation of the heart [13, 18, 19], and sympathetic denervation is known to depress adsorption of catecholamines by the tissues [15]. It may, therefore, be supposed that the decrease in the content of catecholamines and of their precursors in the myocardial tissue in these experimental conditions is the result of weakening of the influence of the sympathetic nervous system on the heart and of disturbance of the adsorption of catecholamines from the blood. The results also show that the largest fall occurred in the case of DOPA, of which absolutely none was found in the myocardial tissue. This suggests that another cause of the decrease in the content of catecholamines in the myocardium is a disturbance of synthesis at the tyrosine–DOPA stage. However, this hypothesis requires experimental verification and clarification of the extent to which the changes described are dependent on adrenalin and the extent to which they are dependent on theophylline.

Data in the literature show that a decrease in the catecholamine content, developing after sympathetic denervation [13, 18, 19] and administration of reserpine [20] is accompnaied by a disturbance of oxidative phosphorylation, glycogenolysis, and other energy-forming processes [16], and this, in turn, becomes one of the causes of the decrease in the contractile function of the myocardium, which we also have observed [1].

The results of determination of the ATPase activity of the myocardial tissue and of actomyosin are given in Table 2. They show that after a single injection of theophylline and adrenalin the ATPase activity of the myocardial tissue fell by 20%, compared with 28% for that of actomyosin, while after repeated injection of the same substances the ATPase activity of the myocardial tissue fell by 29% and that of actomyosin by 38% compared with the ATPase activity of the control animals.

The results obtained demonstrate that after repeated injection of theophylline and adrenalin the lowered ATPase activity of both the myocardial tissue and of actomyosin fell still further.

The fall in ATPase activity is perhaps dependent on the decrease in the concentration of actomyosin in the myocardium observed in experimental myocarditis [2]; the possibility that the ATPase activity of myosin itself is lowered likewise cannot be ruled out. In any case it is evident that the ATPase activity of the myocardium is lowered in experimental myocarditis by approximately the same degree as contractile function of the heart muscle in this state [1]. In fact, after a single injection of theophylline and adrenalin the contractile function of the myocardial tissue falls by 20% and the ATPase activity of actomyosin by 25%, whereas after the repeated injection of the same substances the contractile function of the heart muscle falls by 40% and the ATPase activity of actomyosin by 38%.

Accordingly it seems very probable that the fall in ATPase activity is one of the factors playing a role in the disturbance of the contractile function of the myocardium in experimental myocarditis.

The problem of the interdependence of the disturbance of catecholamine metabolism and the fall in the ATPase activity of actomyosin in the heart muscle in experimental myocarditis requires further investigation. Data obtained by F. Z. Meerson and co-workers [7], indicating that in the stage of gradual exhaustion and progressive cardiosclerosis associated with compensatory hyperfunction of the heart the fall in the content of catecholamines in the myocardium corresponds to the decrease of ATPase activity of myosin and of the contractile function of the heart muscle, make such an interrelationship highly probable.

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