LIPID METABOLISM AND CONCENTRATION OF ADENINE NUCLEOTIDES IN THE HEART MUSCLE IN EXPERIMENTAL AORTIC STENOSIS

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The intensity of oxidation of caprylic acid by homogenates of the left ventricle of the rabbit heart was studied on the fifth day after artificial stenosis of the aorta. Parallel determinations were made on the concentrations of nonesterified fatty acids (NEFA) and triglycerides in the heart tissue and blood and also of components of the adenyl system (ATP, ADP, AMP) in the myocardium. Under these conditions the NEFA concentration in the heart and blood falls significantly while the triglyceride content remains unchanged. Oxidation of endogenous substrates in heart homogenates of the animals with stenosis was indistinguishable from normal. However, the amount of oxygen absorbed during oxidation of added caprylate was 30% below the control. The ATP level in the myocardium was reduced by half.

Changes in metabolism of the hypertrophied heart have been shown to be based on relative hypoxia of the myocardium [3]. Under these conditions the oxidation of fatty acids in the heart, requiring a greater inflow of oxygen to the organ, can be expected to be inhibited.

The object of this investigation was to study lipid metabolism and the concentration of high-energy phosphates in the myocardium of rabbits in the early stages of development of compensatory hyperfunction of the heart.

EXPERIMENTAL METHOD

Aortic stenosis was produced in nine anesthetized rabbits by application of a metal ring to the initial part of the ascending aorta through a right-sided thoracotomy followed by aspiration of air from the pleural cavity. The myocardium of the left ventricle was taken for investigation on the fifth day after the operation, corresponding to the emergency stage of development of compensation [5].

Nonesterified fatty acids (NEFA) and triglycerides were isolated from the tissues of the myocardium on a thin layer of silica gel (KSK) in a solvent system of hexane–dietyl ether–acetic acid in the ratio

TABLE 1. Concentrations of NEFA and Triglycerides in Heart and Blood of Rabbits with Aortic Stenosis (M ± m)

Experimental conditions	Myocardium		Blood	
	NEFA (in moles/g)	triglycerides (in mg/g)	NEFA (in meq/liter)	triglycerides (in mg %)
Control (n = 10)	1,86±0,09	3,8±0,6	0,353±0,011	100±3
Aortic stenosis (n = 9)	1,02±0,01	3,6±0,2	0,273±0,011	95±3
P	<0,001	>0,5	<0,001	>0,2

Note. Weight of heart in control 3,300 ± 126 mg; in aortic stenosis 5140 ± 210 mg ($P < 0.001$).

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TABLE 2. Oxidation of Caprylate by Heart Homogenates under Normal Conditions and in Aortic Stenosis (M ± m)

Experimental conditions	O_2 consumption (in moles/h)		Quantity of O_2 used up in oxidation of caprylate (in moles/h)	Quantity of caprylate oxidized (in moles)
	without caprylate	with caprylate		
Control (n = 10)	7,8±0,3	14,2±1,2	6,3±0,4	0,57±0,02
Aortic stenosis (n = 9)	7,3±1,1	11,7±1,3	4,4±0,6	0,40±0,02
Change (in %)	−6	−18	−30	−30
P	>0,5	>0,1	<0,02	<0,02

TABLE 3. Concentration (in moles adenosine/g) of Components of Adenine Nucleotides in Heart with Aortic Stenosis (M ± m)

Experimental conditions	ATP	ADP	AMP
Control (n = 10)	1,85±0,08	1,38±0,01	1,30±0,04
Aortic stenosis (n = 9)	0,95±0,04	1,44±0,05	1,84±0,10
Change (in %)	−49	+4	+42
P	<0,001	>0,2	<0,001

80:20:1.5. The blood and tissue NEFA concentrations were determined colorimetrically [9]. The oxygen consumption of the myocardial homogenates during oxidation of caprylic acid also were determined by the method described earlier [1]. Components of the adenyl system were extracted from the heart muscle with 10% TCA and separated by paper chromatography in a solvent system of n-propanol–ammonia–water in the ratio of 60:30:10 [2]. The content of adenine nucleotides was determined on the SF-4 spectrophotometer at 260 nm and expressed in micromoles adenosine per gram fresh tissue.

EXPERIMENTAL RESULTS AND DISCUSSION

Under the conditions of aortic stenosis the NEFA concentration in the heart tissues was reduced almost to half the control level while the concentration of triglycerides was unchanged. Some decrease in the NEFA concentration (by 23%) was also observed in the blood (Table 1). This confirms the dependence of absorption of substrates by the heart on their blood concentration [8, 10]. The decrease in the NEFA level in the myocardium could also be associated with intensification of their oxidative conversions in that tissue.

The results in Table 2 show that oxidation of endogenous substrates was unchanged in the heart homogenates from animals with aortic stenosis. However, the quantity of oxygen absorbed during oxidation of the added caprylate was 30% smaller than in the control. Consequently, oxidation of fatty acids in the myocardium in the emergency stage of hyperfunction of the heart was slightly inhibited. It is not clear whether this was connected with a direct disturbance of oxidative metabolism in the heart, or whether it reflects adaptation of oxidative reactions in the heart to a lowered blood NEFA level [6].

Investigations by Vyalykh [4] showed that lactic acid and ketone bodies accumulate in the myocardial homogenates of rabbits five and 14 days stenosis of the aorta, indicating a relative decrease in the contribution of oxidative processes. This should have been accompanied by a decrease in the energy potential of the myocardial cell. In fact (Table 3), in this period the ATP concentration in the heart was reduced by half, and there was a corresponding increase in the AMP level. The ADP concentration showed no significant change. The lowering of the ATP level could be connected with a disturbance of its formation through inhibition of substrate phosphorylation [4, 7] or with its more intensive utilization by the hypertrophied and hyperfunctioning heart.

The emergency stage of compensatory hyperfunction of the heart in rabbits is thus accompanied by disturbance of the oxidation of fatty acids by the myocardium and by a decrease in the concentration of high-energy phosphates in the heart.

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