CONVERSION OF BIOGENIC MONOAMINES AND METABOLISM OF NONESTERIFIED FATTY ACIDS IN THE MYOCARDIUM

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Adrenalin, adrenoxyl, iproniazid, reserpine, and pyrogallol increase lipase activity and raise the level of nonesterified fatty acids (NEFA) in the blood and mobilize them from the fat depots. These substances have different actions on the NEFA content in the heart, evidently because of differences in their level of consumption and utilization of NEFA depending on changes in the metabolic pathway of the catecholamines.

The energy metabolism of the heart is closely bound up with the catecholamines (CA) and metabolism of the biogenic monoamines. Monoamine metabolism can be acted upon by modifying the activity of enzymes which catalyze their individual conversion reactions or by influencing the biosynthesis of the monoamines or their storage in depots. If individual enzymes of monoamine metabolism are inhibited, not only may these substances accumulate, but the direction of their metabolism may be altered.

The object of the present investigation was to study one link connecting the conversion of the biogenic monoamines and the content of nonesterified fatty acids (NEFA) in the heart. For this purpose the effect of adrenalin and of its stabilized oxidation product adrenoxyl, of the monoamine-oxidase inhibitor iproniazid, of the catechol-O-methyltransferase inhibitor pyrogallol, and of reserpine on the blood lipase activity and the NEFA concentration in the blood and heart was investigated.

EXPERIMENTAL METHOD

Experiments were carried out on 120 male albino rats weighing 180-230 g. Adrenalin and adrenoxyl were injected subcutaneously in a dose of 0.5 mg/kg, reserpine was injected in a dose of 2.5 mg/kg, iproniazid in a dose of 100 mg/kg, and pyrogallol in a dose of 50 mg/kg. The animals were sacrificed after 40 min, 24 h, 18 h, and 30 min respectively. Intact rats were used as controls. The heart was thoroughly minced in the cold and its catecholamine (CA) concentration was investigated by Osinskaya's trihydroxyindole fluorescence method [1]. The NEFA content in the blood serum and heart was determined [3] after extraction by Folch's method, and the lipase activity was estimated [4] in the blood.

EXPERIMENTAL RESULTS AND DISCUSSION

After injection of adrenalin and adrenoxyl the noradrenalin (NA) concentration in the heart was increased by 63 and 13% respectively (Table 1). Adrenalin lowered the NEFA level by 34%, while adrenoxyl raised it by 17%. Injection of iproniazid considerably increased the NA concentration, and the NEFA concentration also had a tendency to increase. Reserpine led to marked exhaustion of the NA reserves (68%), while the NEFA remained unchanged. Pyrogallol had the opposite effect on the NA and NEFA concentrations in the heart: its administration led to a decrease in the NA and an increase in the NEFA concentrations.

Adrenalin, adrenoxyl, iproniazid, reserpine, and pyrogallol all increased the lipase activity and the NEFA concentration in the blood, while in the case of adrenalin and pyrogallol, these levels were actually doubled.

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TABLE 1. Effect of Certain Pharmacological Agents on Dynamics of CA and NEFA in the Heart and Lipase Activity and the NEFA Level in the Blood (M ± m)

Material tested		Experimental conditions					
		intact animals	adrenalin	adrenoxyl	reserpine	iproniazid	pyrogallol
Heart	A	—	29,5±1,3	20,6±0,4 $P<0,001$	—	—	—
	NA	75,2±0,5	123±1,0 $P<0,001$	85,5±0,6 $P<0,01$	24,1±0,2 $P<0,001$	124,4±0,3 $P<0,001$	63,2±3,6 $P<0,01$
	NEFA (in mg %)	85,9±1,4	56,9±2,4 $P<0,001$	100,4±3,3 $P<0,001$	85,9±4,7	92±4,7 $P>0,05$	103,2±4,4 $P<0,01$
Blood	Lipase activity (in ml NaOH)	0,41±0,02	0,80±0,018 $P<0,001$	0,73±0,01 $P<0,001$	0,74±0,01 $P<0,001$	0,79±0,01 $P<0,001$	0,89±0,005 $P<0,001$
	NEFA (in μeq/ml)	0,841±0,04	1,58±0,01 $P<0,001$	1,35±0,003 $P<0,001$	1,18±0,007 $P<0,01$	1,5 ±0,06 $P<0,001$	1,4±0,08 $P<0,001$

The increase in the concentration of endogenous CA after administration of adrenalin and iproniazid was not accompanied by any increase in the NEFA concentration in the heart but, on the contrary, led to its decrease. This can be explained on the grounds that adrenalin stimulates oxidative processes in skeletal muscle, liver, and in particular, in the heart [5]: the energy requirements under these conditions are completely satisfied by NEFA.

Iproniazid, which changes the activity of the enzyme monoamine oxidase, promotes the accumulation of NA and allows the energy-producing and functional work of the heart to be controlled [2]. Adrenoxyl, the stabilized product of quinoid oxidation of adrenalin, does not change the CA concentration in the heart, and mobilizes NEFA from the fat depots without any marked utilization of these acids in the heart. The mechanism of action of adrenoxyl on the fat depot is possibly through an increase in the sensitivity of the depot receptors to the action of endogenous CA. Injection of reserpine increases the concentration of free functionally active forms of the monoamines [6], thus leading to excitation of the sympathico-adrenal system and subsequent mobilization of NEFA from the fat depot.

The absence of any increase in the NA concentration in the heart after inhibition of catechol-O-methyltransferase by pyrogallol occurs because the enzyme plays no part in the conversion of intracellular catecholamines, but mainly inactivates only the catecholamines brought by the blood stream or administered from outside. The lipid-mobilizing action of pyrogallol is evidently due to an increase in the concentration of active monoamines in the other organs (blood, liver, adrenals).

The increase in lipase activity and in the NEFA level in the blood suggests that all the pharmacological factors mentioned above mobilize NEFA from the fat depot.

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