THE USE OF Na-1-C^{14} ACETATE FOR BIOSYNTHESIS OF LIPID COMPONENTS OF ORGANS AND THE BLOOD SERUM AT DIFFERENT STAGES OF EXPERIMENTAL MYOCARDIAL ISCHEMIA

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Biosynthesis of total lipids and its fractions (cholesterol, phospholipids, triglycerides, and nonesterified fatty acids) was studied during utilization of Na-1-C^{14} acetate in the heart, liver, adrenals, adipose tissue, and blood serum on the fifth and 30th days after the beginning of experimental myocardial infarction. Disturbances of lipid metabolism were shown not always to precede the myocardial infarct, and acute myocardial ischemia can initiate changes in lipid metabolism.

KEY WORDS: lipid metabolism; myocardial ischemia; blood serum.

Previous investigations [1, 5, 6] showed that acute myocardial ischemia leads to changes in lipid biosynthesis in the myocardium and liver.

Hence the need for the study of the pathochemistry of lipid metabolism in myocardial infarction.

EXPERIMENTAL METHOD

Experiments were carried out on 12 rabbits, in 8 of which experimental myocardial infarction was induced by ligation of the descending branch of the coronary artery in the usual way. The animals were divided into three groups: 1) 4 healthy animals, 2) 4 animals with experimental myocardial ischemia in the acute period (fifth day), 3) 4 animals with experimental myocardial ischemia 30 days after the operation.

To study lipid biosynthesis in healthy rabbits and also 5 and 30 days after ligation of the coronary artery, Na-1-C^{14} acetate was injected intravenously in a dose of 100 μCi/kg body weight. After exposure for 60 min to the isotope, the necessary volume of blood was taken from the rabbits, and they were then decapitated. Lipids were extracted by the usual (Folch's) method from the blood serum and tissues of the heart, liver, and adrenals and adipose tissue. The lipid components were fractionated by thin-layer chromatography on silica-gel KSK. Petroleum ether, diethyl ether, and acetic acid in the ratio of 90:10:1 were used as the solvent. Cholesterol was precipitated with digitonin [3] and fatty acids were investigated after saponification and hydrolysis followed by extraction with petroleum ether.

Radioactivity was expressed in counts/min/10 mg of each of the lipid components after their removal from the silica-gel. The DP-100 radiometer was used for the measurements. Specific radioactivity was calculated, allowing for the coefficient of self-absorption.

EXPERIMENTAL RESULTS AND DISCUSSION

In the healthy animals, synthesis of lipid components took place with highest intensity in the adrenals,

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TABLE 1. Incorporation of C^{14} from Na Acetate-1-C^{14} into Lipid Components of Blood Serum and Different Organs in Experimental Myocardial Ischemia (in counts/min/10 mg lipid component) (M ± m)

Test object	Total lipids			Cholesterol (free)			Phospholipids
	group of animals						
	1st	2nd	3rd	1st	2nd	3rd	1st
Blood serum	390±5	700*±40	—	350±40	1050*±65	360±45	30±5
Myocardium (perinecrotic zone)	65±6	45*±3	25*±2,6	250±30	220±35	200±20	45±2,8
Liver	60±4	180*±6	70±8	300±30	1000*±75	350±25	50±5
Adrenal	100±6	105±8	145*±12	900±70	600*±35	125*±30	40±4
Adipose tissue	27±3	70*±5	37*±2,5	210±12,0	400*±8	235±23	50±5

Test object	Phospholipids		Triglycerides			NEFA		
	group of animals							
	2nd	3rd	1st	2nd	3rd	1st	2nd	3rd
Blood serum	80*±7	72*±4,8	57±7	40±7	—	70±4	470*±45	150*±20
Myocardium (perinecrotic zone)	80*±7	80*±10	20±2	460*±5	40*±5	32±4	120*±7	40±5
Liver	160*±7	42±4	97±6	370*±7	90±5,5	60±6	550*±28	130*±10
Adrenal	90*±7	90*±10	—	—	—	90±10	25*±5	170*±17
Adipose tissue	10*±1,6	15*±2,8	12±2,5	25*±2,6	15±2,5	16±2	60*±7	13±2,5

*$P \leq 0.05$ relative to group 1

followed in order by the liver, myocardium, and adipose tissue (Table 1). With the development of necrosis in the left ventricle, a decrease in the biosynthesis of total lipids by up to 70% of the normal level was observed. Meanwhile, fractionation of the lipids into triglycerides, phospholipids, and nonesterified fatty acids (NEFA) showed that the biosynthesis of these components was intensified, especially on the fifth day after development of the myocardial infarct. The results differ in direction from the character of metabolic activity of lipids when acetate-2-C^{14} was used [16]. The reason is probably differences in the metabolic fate of the radioactive carbon of the acetic acid, the metabolism of which is modified in the ischemic myocardium [1, 5].

The results of investigation of the other tissues showed a sharp change in the intensity of lipid biosynthesis in the intact organs. For instance, the most intensive lipogenesis took place in the liver, where an increase in the incorporation of labeled precursor was observed into practically all the components studied, especially on the fifth day after the beginning of the experiment.

Similar stimulation of lipid biosynthesis also was observed when acetate-2-C^{14} was used as the indicator [6], evidence of the intensive utilization of acetate as a whole in the processes of lipogenesis. A reflection of the lipogenetic function of the liver was the high radioactivity of most of the lipid components of the blood serum, and this was especially marked for cholesterol and NEFA.

The low specific radioactivity of lipids of adipose tissue after myocardial infarction was evidently connected not only with inhibition of lipogenesis, but also with activation of lipolysis, which is known to be intensified during stress.

The state of the lipid metabolism in the adrenals is of considerable interest. For instance, the specific activity of free cholesterol was considerably reduced, but this evidently did not correspond with the level of its synthesis from low-molecular-weight precursors. In stress states cholesterol is actively utilized for corticosteroid formation, and this evidently takes place also in acute myocardial ischemia. This view was confirmed by clinical data showing an increase in the urinary excretion of metabolic products of corticosteroids in myocardial infarction. Increased synthesis of other lipid components is evidence of activation of the lipogenetic activity of the adrenals in myocardial ischemia.

The most marked metabolic changes affecting lipid metabolism in acute myocardial ischemia are thus observed on the fifth day. On the 30th day the processes of lipogenesis are reduced in intensity, pointing to the role of the acute ischemic state in determining the changes in lipid metabolism. These investigations, it will be noted, were carried out on animals with no evidence of atherosclerosis. Evidently disturbances of lipid metabolism do not always precede myocardial infarction, and acute myocardial ischemia can initiate

changes in lipid metabolism such as are often observed in atherosclerosis. This view has recently obtained clinical confirmation [2, 4].

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