OXIDATION OF CAPRYLATE AND CONCENTRATION OF KETONE BODIES IN THE HEART MUSCLE OF RABBITS WITH THYROTOXICOSIS

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The concentration of ketone bodies is increased in the blood serum and heart tissue of rabbits receiving thyroid extract for two weeks. Meanwhile the intensity of oxidation of succinate and caprylate by heart homogenates increases. It is postulated that the accumulation of ketone bodies in the myocardium is connected with the relative insufficiency of the throughput of the tricarboxylic acid cycle of the heart.

No firm decision has been reached whether the lipid components of the heart muscle can be used as an energy substrate during an excessive intake of thyroid hormones. According to Crisolia [6], stimulation of the oxidative conversion of lipids in the heart during thyrotoxicosis takes place through the unavailability of other sources of oxidation and not as a result of the true activation of fatty acid dehydrogenases by thyroxine. However, on the basis of an analysis of the respiratory quotient and the absorption of palmitate-C^{14} by the myocardium in hyperthyroidism, some investigators conclude that in this case substances of noncarbohydrate origin, and mainly lipids, are utilized as sources of energy.

In this investigation the oxidation of succinate and caprylate by homogenates of the "thyrotoxic" heart was studied and a parallel determination made of the concentration of ketone bodies in the heart tissue and blood.

EXPERIMENTAL METHOD

Adult male rabbits weighing 2.5-3 kg, kept on a standard diet, were used. Thyrotoxicosis was induced by feeding the animals with thyroid extract in doses calculated to produce the pathological state within two weeks [2]. Oxidation of succinate and caprylate was investigated in homogenates of the left ventricle by the method described previously [1]. The incubation mixture contained 2×10^{-3} M ATP, 1×10^{-2} M succinate, and 1.6×10^{-6} M caprylate; the pH of the Krebs-Ringer-phosphate buffer was 7.4. The level of oxidation was estimated from the quantity of oxygen consumed per hour in the Warburg apparatus at 37°C.

TABLE 1. Concentration of Ketone Bodies (in mg% acetone) in Blood and Heart Muscle (M ± m).

Animals	Total ketone bodies		Acetoacetate in myocardium
	in serum	in myocardium	
Control (n = 10)	9±0,6	23±1,1	7,5±0,4
With thyrotoxicosis (n = 10)	12±0,7	27,6±0,8	7,8±0,2
P	<0,01	<0,01	>0,5

The total ketone bodies and acetoacetate in the serum and heart tissue were determined by a colorimetric method [4] using alkaline salicyl-aldehyde.

EXPERIMENTAL RESULTS

The results given in Table 1 show that an increase in the total concentration of ketone bodies by 33 and 20%, respectively, over normal was observed in the blood serum and heart tissue

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TABLE 2. Oxidation of Caprylate by Heart Homogenates from Normal and Thyrotoxic Animals (in moles O_2/h; M ± m)

Animals	O_2 consumption (moles)		Quantity of O_2 util. for oxid. of caprylate (in μmoles)	Quantity of caprylate oxidized (in μmoles)
	succinate	succinate + caprylate		
Control (n = 10)	7,8±0,3	14,2±1,2	6,3±0,4	0,57±0,04
With thyrotoxicosis (n = 10)	10,5±0,7	20,3±0,6	10,7±1,1	0,97±0,10
P	<0,01	<0,001	<0,001	<0,001

of the thyrotoxic animals. The concentration of acetoacetate, determined in the heart tissue only, remained substantially unchanged. Since ketones are oxidation substrates for heart muscle [9] and usually do not accumulate in it [5], the changes observed could indicate a disturbance of the intensity of oxidation in the heart tissue in thyrotoxicosis. However, the results in Table 2 show that intensive oxidation of substrates took place in the heart homogenates from thyrotoxic animals.

During oxidation of succinate the absorption of oxygen by homogenate of the ventricle of the thyrotoxic animals was 35% higher than the control. The addition of caprylate to the insulation medium led to a further increase in the oxygen consumption in both the control and the experimental series. The quantity of oxygen used up for the oxidation of caprylate in the heart homogenates from rabbits with thyrotoxicosis was 70% higher than the control. Consequently, in thyrotoxicosis the conditions in the heart muscle are favorable for intensive oxidation and the final stages of oxidation of fatty acids are undisturbed. The accumulation of ketone bodies in the myocardium under these conditions is probably explained by the inadequacy of the C_2 fragments formed in excess as a result of the increased ketogenesis in the liver [8].

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