EFFECT OF THYROXINE ON ASPARTATE AMINOTRANSFERASE AND MALATE DEHYDROGENASE ACTIVITY IN HEART MUSCLE OF GUINEA PIGS

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Small doses of thyroxine increase the content of soluble proteins and reduce activity of aspartate aminotransferase and malate dehydrogenase in the myocardium of guinea pigs.

If thyroxine is administered to certain species of animals it produces a series of metabolic and structural changes in the heart muscle, increases the oxygen consumption, modifies the activity of certain dehydrogenases [7], and so on. In thyrotoxicosis degenerative changes develop in the heart muscle as the result of disturbances of metabolism. However, comparatively few studies have been made of the effect of thyroid hormones on individual enzyme systems in heart muscle.

In the investigation described below the effect of prolonged administration of small doses of thyroxine on the activity of two enzymes, aspartate aminotransferase (AsAT; 2.6.1.1) and malate dehydrogenase (MDH; 1.1.1.37), in the heart muscle of guinea pigs was studied.

EXPERIMENTAL METHOD

Experiments were carried out on guinea pigs weighing 350-400 g. For 8 days the animals received daily subcutaneous injections of 50μg of the sodium salt of L-thyroxine (Reanal) per 100 g body weight [4, 10, 12]. On the ninth day the animals were decapitated, the heart was quickly removed, washed twice with ice-cold physiological saline, and then homogenized for 2 min. The homogenate was centrifuged for 25 min at 20,000 g. Enzyme activity and the protein content were determined in the supernatant.

Enzyme activity was determined by a spectrophotometric method based on the change in optical density at 340 nm, AsAT was determined by the method of Bergmeyer and Bernt [1], and MDH by Bochringer's ultraviolet test [3]. The content of soluble proteins was determined by Gornall's method [6].

Enzyme activity was expressed in Racker's units per gram fresh tissue and per gram protein, and the protein content in mg/g fresh tissue.

EXPERIMENTAL RESULTS AND DISCUSSION

Thyroxine increased the content of soluble proteins (Table 1). The same result under similar experimental conditions was obtained by Bressler and Wittels [4]. Activation of protein synthesis in the tissues is one of the important effects of physiological doses of thyroxine [4, 12, 13].

AsAT activity in the heart muscle of the experimental animals fell sharply (Tables 1 and 2). These observations do not agree with those of Rotzsch [10] and Canal and Maffei-Faccioli [5], who found an increase in the activity of this enzyme in the heart muscle of hyperthyroid rats. However, these workers used much higher doses of thyroxine, with a definite catabolic action. The decrease in enzyme activity

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TABLE 1. Content of Soluble Proteins and AsAT and MDH Activity in Heart Muscle of Guinea Pigs during Administration of Thyroxine (in Racker's units per gram fresh tissue)

Statistical index	Proteins		AsAT		MDH	
	control	exptl.	control	exptl.	control	exptl.
n	7	10	8	7	8	7
M	21,2	27,6	300,1	83,8	744,0	562,0
$\pm m$	0,9	2,0	51,6	4,0	5,8	80,9
P	<0,02		<0,01		<0,1	

TABLE 2. Relative Activity of AsAT and MDH in Heart Muscle of Guinea Pigs during Administration of Thyroxine (in Racker's units per mg protein)

Statistical index	AsAT		MDH	
	control	exptl.	control	exptl.
n	8	8	7	6
M	12,2	3,5	31,0	19,1
$\pm m$	2,4	0,3	3,1	1,8
P	<0,01		<0,01	

observed in the present experiments could be associated with the anabolic action of small doses of thyroxine, manifested in particular by an increase in the content of soluble proteins in heart muscle. Some workers [2,11] report an inverse relationship between protein content and amino transferase activity, i.e., that increased protein synthesis is accompanied by a decrease, and increased protein breakdown by an increase in aminotransferase activity. The observed decrease in enzyme activity can hardly be attributed to the inhibitory effect of thyroxine on pyridoxal phosphorylation, for this effect appears only if high doses of the hormone are used. In the present experiments, a tendency for the MDH activity to fall also was observed (Table 1); this tendency became statistically significant when the relative enzyme activity was calculated (Table 2). Data concerning the effect of thyroxine on MDH in the liver, where activation of this enzyme is observed, are given in the literature [7, 9]. The same effect has been found in the frog heart muscle, whereas in rat heart muscle (with a higher dose of thyroxine than in the present experiments, namely 300 g over a period of 4 days) inhibition of MDH activity was observed. In vitro thyroxine inhibits this enzyme in the heart muscle of both frogs and rats [14]. Inhibition of MDH with the consequent decrease in the oxaloacetate content have been held responsible by some workers for the increase in activity of the succinate oxidase system, which is inhibited by oxaloacetate [14]. Bearing in mind the high intensity of the tricarboxylic acid cycle in heart muscle [8], it can be postulated that the change in MDH activity plays an important role in the metabolic disturbances in the myocardium under the influence of thyroid hormones.

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