EFFECT OF PITUITARY SOMATOTROPIC HORMONE ON LIVER NITROGEN METABOLISM IN RABBITS WITH EXPERIMENTAL THYROTOXICOSIS

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Prolonged administration of pituitary somatotropic hormones to rabbits with experimental thyrotoxicosis, characterized by a decrease in the protein content of the liver and disturbance of its urea-forming function, restores the protein- and urea-forming function of the liver and increases the protein content in that organ.

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Pituitary somatotropic hormone (STH) is one of the principal anabolic hormones regulating nitrogen metabolism in the body. Its main action is to promote retention of nitrogen in the body as a result of stimulation of protein synthesis. This action of STH is confirmed by considerable experimental evidence, but few investigations have been made of the effect of STH on the regulation of nitrogen metabolism in pathological conditions, when the excretion of nitrogen from the body is increased as a result of predominance of catabolic processes. The study of the effect of STH on the protein-nitrogen indices in thyrotoxicosis is of special interest in this respect.

Previous investigations by the author [3, 4] revealed significant changes in the protain-nitrogen indices of the blood and, in particular, of the liver during the development of thyrotoxicosis in rabbits produced by administration of thyroid extract.

The object of the present investigation was to study the effect of STH on some protein-nitrogen indices of the liver in experimental thyrotoxicosis.

EXPERIMENTAL METHOD

Experimental thyrotoxicosis was produced in rabbits by administration of tablets of thyroid extract to the animals in accordance with a specified scheme (see [3] for details). The state of the liver metabolism of the experimental animals was assessed by the use of the following indices: the coefficient of proteolysis, calculated as the ratio between nonprotein and protein nitrogen in the liver, the coefficient of urea formation, calculated as the ratio between urea nitrogen and nonprotein nitrogen in the liver. Total and nonprotein nitrogen were determined by the Kjeldahl method, urea nitrogen by the phenol-hypochlorite reaction [2], and changes in the total content of amino acids in the liver tissue by the method of Pope and Stevens [8].

A Soviet preparation of STH obtained under laboratory conditions from bovine pituitaries by Wilhelmi's method [9] was used in the investigation. The biological activity of the STH was determined by the tibial test in hypophysectomized rats by Li's method [7] by comparing it with the international standard of activity of pituitary growth hormone. STH with an activity of 0.8-1.2 i.u./mg powder was used in the experiments. The STH was injected into rabbits with thyrotoxicosis daily for 30 days in a dose of 1 mg/kg body weight.

EXPERIMENTAL RESULTS

As the results given in Tables 1 and 2 show, during the development of thyrotoxicosis in the experimental rabbits the nonprotein nitrogen content and the coefficient of proteolysis in the liver both increased, indicating stimulation of catabolic processes of protein metabolism in the liver. These changes were

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TABLE 1. Changes in Coefficient of Proteolysis, Coefficient of Urea Formation, and Total Content of Protein in the Liver Produced by STH in Rabbits with Thyrotoxicosis (M±t)

Experimental conditions	Number of rabbits	Weight of rabbits (in kg)		Coefficient of proteolysis (in %)	Coefficient of urea formation (in %)	Protein content (in g%)
		Initially	Finally			
Control group	11	2.9	3.1	11.5±0.7	19.5±2.2	16.4±0.4
Thyrotoxicosis	8	3.0	2.1	15.9±0.5	11.1±0.5	15.0±0.5
P				< 0.001	< 0.001	< 0.01
Thyrotoxicosis + STH	11	2.2	2.7	9.2±0.5	21.9±2.4	17.0±0.4
P				< 0.001	< 0.001	< 0.01

TABLE 2. Changes in Principal Components of Nonprotein Nitrogen in the Liver Produced by STHin Rabbits with Thyrotoxicosis (M ± t)

Experimental conditions	Nonprotein nitrogen (in g%)	Main component of nonprotein nitrogen		
		Urea nitrogen (in mg%)	Amino-acid nitrogen (in mg%)	Residual nitrogen (in g%)
Control group	0.24±0.015	45.9±4.4	62.3±4.1	0.19±0.015
Thyrotoxicosis	0.39±0.02	46.7±4.8	86.9±6.6	0.34±0.02
P	< 0.001	–	< 0.01	< 0.001
Thyrotoxicosis + STH	0.25±0.15	54.8±4.5	90.7±5.5	0.19±0.05
P	< 0.001	< 0.5	< 0.5	< 0.001

accompanied by the accumulation of basic products of nitrogen metabolism in the liver tissue, as demonstrated by a marked increase in the residual nitrogen. However, as the previous investigations showed, in severe cases of thyrotoxicosis, in the so-called "thyrotoxic liver," the activity of enzyme systems responsible for urea synthesis was disturbed. Although the urea content in the liver tissue was not lowered in these cases, the process of urea formation was distinctly depressed. The coefficient of urea formation fell from 19.5 to 11.1% ($P < 0.001$).

Stimulation of catabolic processes in thyrotoxicosis led to a decrease in the total body weight of the animals. It will be noted that the protein content, when calculated per 100 g weight of liver, fell from 16.4 to 15.0 g% ($P < 0.01$).

Administration of STH in a dose of 1 mg/kg body weight for 30 days inhibited a further decrease in body weight and largely restored the normal protein-nitrogen indices in the liver. The protein- and urea-forming functions of the liver were completely restored. The protein content in the liver rose from 15 to 17 g% and the content of urea formation from 11.1 to 21.9% ($P < 0.001$).

Catabolic processes in the protein-nitrogen metabolism were depressed by STH as shown by the decrease in the coefficient of proteolysis and normalization of the principal nonprotein nitrogen indices. As the results given in Table 2 show, the total amino-acid nitrogen content in the liver tissue remained high, evidently because of disturbances of oxidative deamination of amino acids due to failure of the blood flow to satisfy the oxygen demand of the liver in thyrotoxicosis. Under the influence of STH and thyroid hormones the intensity of amino-acid synthesis in the liver is perhaps increased. According to some reports [1], under the influence of thyroid extract amino-acid synthesis from keto acids and ammonium salts is increased in the liver.

The disturbances of protein-nitrogen metabolism detected in the liver of rabbits with thyrotoxicosis are due both to the direct action of thyroid hormones on the liver and to their indirect action through the pituitary and adrenals, in which ACTH production is intensified and adrenal function is increased [5]. Meanwhile, in the liver in thyrotoxicosis inactivation of corticosteroids is increased, inhibiting the development of hypercorticism [6].

To sum up the results obtained, administration of STH has a definite normalizing action on certain aspects of protein-nitrogen metabolism of rabbits with thyrotoxicosis produced by administration of thyroid extracts.

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