

Effect of Thyroid State on Magnesium Concentration of Rat Tissues

Jack W. Oliver, DVM, PhD

SUMMARY

The effect of alteration of thyroid status by thiouracil (0.1% concentration in drinking water for 60 days) or exogenous thyroxine (25 mg/dg of body weight administered SC from days 30 to 60) on magnesium content of rat tissues following exogenous magnesium was evaluated.

Treatment of rats with magnesium solution (25 mg of magnesium sulfate/dg of body weight) resulted in increased magnesium concentration in most tissues of hypothyroid and hyperthyroid rats, with the mesenchymal-derived tissues (aorta, trachea, and ear cartilage) exhibiting the greatest increases (respectively, 154, 130, and 133% of control group values for hypothyroid rats, and 115, 108, and 107% of control group values for the hyperthyroid group). Magnesium concentration in skeletal and cardiac muscle was similar for hyperthyroid and control rats, but magnesium concentration in these same tissues of hypothyroid rats was decreased.

Magnesium distribution and retention in rat tissues is altered considerably, depending on the functional status of the thyroid gland.

The role of the thyroid gland in metabolic activities has been exten-

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From the Department of Veterinary Physiology and Pharmacology, College of Veterinary Medicine, The Ohio State University, Columbus, OH 43210. Dr. Oliver's present address is Department of Environmental Practice, College of Veterinary Medicine, University of Tennessee, Box 1071, Knoxville, TN 37901.

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sively studied, as has its effect on growth and differentiation.¹⁹ Although considerable research has been directed toward thyroid effects on connective tissues,³ the influence of hypothyroid and hyperthyroid states on the chemical and molecular makeup of these tissues is still ill defined. Thyroid hormones are known to markedly influence the amount of polyanionic hyaluronate in animal tissues^{12,16} which undoubtedly affects the dynamics of cellular nutrition. For a discussion of the chemical, physicochemical, and mechanical properties of connective tissue, the reader is referred to Langgard.⁸

The purpose of this study was to investigate the effects of hypothyroid, as well as hyperthyroid states, on the ability of various body tissues to retain an administered quantity of magnesium. Also, the intent was to demonstrate that changes which occur in tissues during hypothyroid states, notably accumulation of polyanionic hyaluronate, interfere with diffusion of cationic substances in the intercellular milieu.

Materials and Methods

Experimental Design—Male Sprague-Dawley rats ($n = 18$), initially weighing between 260 and 280 g, were used in a 60-day study involving the effects of hyperthyroid and hypothyroid states on ionic composition of tissues. Rats were castrated to remove androgenic influence and were housed in a controlled temperature and humidity environment, with 12 hours of constant lighting. Diet consisted of regular pelleted rat feed^a ad libitum.

Hypothyroidism was induced²¹ in 6 rats by administration of thiouracil in the drinking water at a concentration of 0.1% from day 0 to day 60 of the experiment. Hyperthyroidism was induced in another group of 6 rats by daily (from days 30 to 60 of the experiment) SC injections of 1-

^a Purina Rat Chow, Ralston Purina Co, St Louis, Mo.

thyroxine^b (25 µg/dg of body weight). Thyroxine was solubilized with 2.5 N sodium hydroxide and placed in a solution containing 0.45% sodium chloride and 2.5% dextrose. Six euthyroid rats served as controls.

Body weights of the rats were recorded weekly and plasma samples were collected (retroorbitally) at days 0, 20, 40, and 60 for determination of thyroxine concentration by the radioimmunoassay method (modified) of Werner et al.²⁰ Thyroxine was freed from thyroxine-binding globulin by 8-anilino-1-naphthalenesulfonic acid instead of ethanol extraction. At the end of the 60-day experimental period, rats were administered magnesium sulfate^c intraperitoneally at a dose of 25 mg/dg of body weight. Rats were necropsied exactly 6 hours later and tissues taken for determination of magnesium content by atomic absorption spectrophotometry^d were the liver, kidney, cardiac muscle, skeletal muscle, aorta, trachea, ear cartilage, and small intestine (free of intraluminal content).

Analytical Methods—Tissues from individual rats were dried at 105°C for 65 hours and stored in a desiccator jar. Dried tissues were ground to a coarse powder with a glass rod in a disposable polystyrene weigh tray.^e Magnesium was extracted from the dry tissue by constant agitation in 0.5 N nitric acid (1 ml added per each 40 mg of dried tissue) for 24 hours at 25°C, followed by another 24 hours without agitation at 4°C. The supernatant fluid was decanted into polypropylene test tubes and centrifuged to remove any tissue residue. Aliquots of the supernatant fluid were then taken for analysis of magnesium content.

Statistics—Tissue samples from each of the 6 rats in each group were analyzed for magnesium content. Duplicate analyses for magnesium were performed on each tissue extract and a mean value was

^b 1-thyroxine, acid-free, Sigma Chemical Co, St Louis, Mo.

^c Magnesium sulfate-chloral hydrate ("Mag-Chloral") solution, Haver-Lockhart Laboratories, Shawnee, Kan.

^d Analytical methods for atomic absorption spectrophotometry, Perkin-Elmer Corp, Norwalk, Conn.

^e Polystyrene ("Van Lab") weigh tray, VWR Scientific Division, Univar, Atlanta, Ga.

obtained. Data were evaluated statistically by comparison of control group values and treated values, using the Student's *t* test.

Results

Weight gain of rats was similar except for thyroxine-treated rats (hyperthyroid), which had marked reduction of body weight following exogenous administration of the hormone (Table 1). Thyroxine concentration in plasma of thiouracil-treated (hypothyroid) rats was 2.6, 2.0, and 2.3 µg/dl at days 20, 40, and 60, respectively, varying from 47 to 62% of normal concentration (4.3, 4.2, and 3.7 µg/dl, respectively, for the same time periods). Thyroxine treatment of rats increased plasma thyroxine concentration to 6.6 and 8.3 µg/dl at days 40 and 60, respectively, compared with control group values of 4.2 and 3.7 µg/dl. The respective concentrations were 157 and 224% of control group values. Although insufficient sample numbers were available for valid statistical analysis, values represent mean thyroxine concentration in pooled plasma samples (3 rats/sample) run in duplicate and also establish that hypo- or hyperthyroid states existed.

Magnesium concentration in tissues of hypothyroid rats 6 hours post-treatment with magnesium solution was decreased in muscle (skeletal and cardiac) and intestinal tissues but increased in other tissues examined—the increase being marked in tracheal tissue (6.9 vs 5.3 mg/dg of body weight for hypothyroid and control animals, respectively (Table 2). The greatest increase in magnesium content occurred in mesenchymal tissues (aorta, trachea, and ear cartilage).

Magnesium concentration was increased in all tissues of hyperthyroid rats except cardiac muscle and the small intestine, with the concentration of the aorta being markedly higher than that of control animals (1.5 vs 1.3 mg/dg of body weight).

Discussion

Thiouracil treatment of rats (hypothyroid) resulted in reduction of plasma thyroxine concentrations (47 to 62% of normal), attributable to the known effect of thiouracil on the iodination of tyrosine by the thyroid gland.¹⁹ Plasma thyroxine concentrations for rats (hyperthyroid) treated

TABLE 1—Mean Body Weight of Euthyroid, Hypothyroid, and Hyperthyroid Rats*

Days of experiment	Experimental group		
	Nontreated control (n = 6)	Hypothyroid, thiouracil-induced (n = 6)	Hyperthyroid, thyroxine-induced (n = 6)
0	280.7 ± 10.4	261.7 ± 9.8	274.3 ± 8.9
20	317.2 ± 10.1	306.3 ± 11.9	315.7 ± 8.0
40	340.7 ± 10.2	323.5 ± 14.3	308.2 ± 6.9**
60	367.7 ± 12.3	348.0 ± 13.8	301.0 ± 4.6**

* Data are expressed as mean body weight in grams ± SEM. **P = < 0.05.

TABLE 2—Mean Concentration of Magnesium (mg/dg of Body Weight ± SEM) in Tissues of Euthyroid, Hypothyroid, and Hyperthyroid Rats*

Tissue	Experimental group		
	Euthyroid control (n = 6)	Hypothyroid, thiouracil-induced (n = 6)	Hyperthyroid, thyroxine-induced (n = 6)
Liver	3.6 ± 0.1	3.7 ± 0.1	3.9 ± 0.2
Kidney	3.3 ± 0.1	3.6 ± 0.3	3.3 ± 0.1
Cardiac muscle	3.7 ± 0.1	3.5 ± 0.1	3.7 ± 0.2
Skeletal muscle	4.6 ± 0.3	3.9 ± 0.1**	4.7 ± 0.3
Aorta	1.3 ± 0.0	2.0 ± 0.3	1.5 ± 0.0†
Trachea	5.3 ± 0.5	6.9 ± 0.3**	5.7 ± 0.3
Ear cartilage	1.5 ± 0.0	2.0 ± 0.3	1.6 ± 0.1
Small intestine	3.9 ± 0.2	3.8 ± 0.1	3.6 ± 0.1

* From tissues posttreatment (6 hours) with magnesium solution. **P = < 0.05. †P = < 0.01.

with thyroxine were greater than control group concentrations, as would be expected.

The concentration of magnesium in most tissues of hyper- and hypothyroid rats was increased over that of control rats. However, magnesium concentration of skeletal and cardiac muscle was found to be reduced in hypothyroidism, similar to results of a study by Szelenyi et al,¹⁸ although concentration in these same tissues in hyperthyroid rats was similar. Rizek et al¹⁵ suggested that skeletal muscle analyses in thyroid dysfunction might not adequately reflect body magnesium stores because magnesium in skeletal muscle exchanges slowly. The present study did not attempt to differentiate extracellular from intracellular magnesium stores. However, based on the study of Madsen et al,⁹ it seems likely that the increases over control group concentrations were largely due to extracellular accumulation in hypothyroid rats and intracellular accumulation in hyperthyroid rats. The increase of magnesium in tissues of hypothyroid rats was most noticeable in mesenchymal-derived tissues rich in glycosaminoglycans, such as aorta, trachea, and ear cartilage. Presumably, the major reason for the increase in magnesium content of these tissues would be increased complexation with the greater amount of polyanionic hyaluronic acid which occurs in tissues of hypothyroid rats.¹⁶ The reason for the increased concentrations of magnesium in tissues of

hyperthyroid rats is most likely due to increased cardiovascular function, which occurs in hyperthyroidism,^{5,6} and thus greater absorption of the element from the abdominal cavity as well as the gastrointestinal tract. In addition, the fact that tissue concentrations of hyaluronate are reduced in hyperthyroidism^{2,4} may lead to increased distribution and intracellular concentration of magnesium, and thus augmented values of tissue magnesium concentration. Hyaluronate has been shown to have effects on solute distribution in tissues.^{11,13,17}

Recent studies^{1,10} have documented the fact that trace mineral concentrations of similar feeds vary considerably between different geographic areas of the United States and even within a specific geographic location. Also, the important interrelationships which exist for mineral elements have recently been reemphasized,⁷ with concern expressed that proper mineral concentrations are frequently not fed to animals. Diseases associated with high production have become more prevalent,¹⁴ and these will continue to increase in importance as productivity of individual animals is increased by various means, placing new stresses on the physiologic, immunologic, and metabolic systems. Nutritional problems caused by interrelationships between minerals, nutrients, and nonnutritive materials (eg, hormones) constitute important constraints to production¹⁴ which undoubtedly will increase as

feed sources and animal productivity change. Thus, because mineral content of feed varies naturally, as well as in formulated rations, and because altered hormonal states of animals (thyroid) affect the way minerals (in this case, magnesium) are utilized, it follows that greater awareness of the hormonal status of animals is needed, along with frequent surveillance of mineral concentrations of feeds, if maximal animal production is to be realized.

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