IMPORTANCE OF MAGNESIUM IN PREVENTION OF METABOLIC DISORDERS IN THE MYOCARDIUM IN THYROTOXICOSIS

L. M. Gol'ber, K. A. Anan'eva, V. I. Kandror, I. V. Kryukova, and A. V. Negovskaya

UDC 615.31:546.46].035 4:616.127-008.9-02:616.441-008.61

Administration of magnesium together with thyroid prevents the decrease in the glycogen and creatine phosphate content and the decrease in the rate of protein renewal in the rabbit myocardium.

* * *

The magnesium concentration in various media of hyperthyroid animals and patients with thyrotoxicosis is reduced [5, 10] and the body requirement of this element is increased [12]. It has been suggested that the effect of thyroxin in dissociating oxidation and phosphorylation in the mitochondria is due to binding of magnesium ions maintaining the necessary spatial localization of the coupling factors [6]. Investigation of metabolism of the myocardium in experimental thyrotoxicosis [3] revealed a number of changes which are evidently based on the dissociating effect of an excess of thyroid hormones.

Considering that electrophoresis of magnesium in patients with thyrotoxicosis leads to an increase in weight, the diminution or total disappearance of the tachycardia, and a fall of the basal metabolism and arterial pressure [2], an attempt was made to correct the metabolic disturbances in the thyrotoxic heart by means of this cation.

EXPERIMENTAL METHOD

Experiments were carried out on male rabbits weighing 2.5-3.5 kg. Thyrotoxicosis was produced by administration of dry thyroid by mouth in accordance with a scheme [4] by which the dose of the preparation was progressively increased for one month. By the end of the experiment the body weight of the animals was reduced on the average by 30%, the heart rate had increased by 60%, and the concentration of protein-bound iodine in the serum had increased from 4 to 22 μg%. Throughout the experiment the animals were kept on a normal diet with water ad lib. Experiments were carried out on three series of rabbits: I—control, II—hyperthyroid, on which periods of galvanization without magnesium were given as a control of the effect of the actual procedure of magnesium administration, and III—hyperthyroid animals also receiving magnesium by electrophoresis. Magnesium was given daily (15% $MgSO_4$ solution) by means of a galvanization apparatus. Electrode pads (3 × 4 cm) were fixed to symmetrically opposite, shaved lateral surfaces of the animal's trunk. The procedure lasted 40 min, and the current density was 0.1-0.2 mA/cm^2. To test the effectiveness of the administration procedure, before and for a period of 1 h thereafter, the mangesium concentration in the plasma and erythrocytes of the experimental animals was determined. In the plasma this index showed a mean increase of 47%, and in the erythrocytes an increase of 62%. The magnesium concentration in the biological media was determined by the method of Orange and Rhein [9] as modified by Hänze [7]. At the end of the experiment the animals were sacrificed, the heart removed, and the concentrations of glycogen [11] and creatine phosphate [1] determined in the tissues of the left ventricle. The intensity of protein renewal in the myocardium was estimated from incorporation of methionine-S^{35} given 8 h before sacrifice in a dose of 10,000 pulses/min/g body weight.

Laboratory of Pathophysiology, Institute of Experimental Endocrinology and Hormone Chemistry, Academy of Medical Sciences of the USSR; Department of Physiotherapy, N. F. Vladimirskii Moscow Regional Research Institute. (Presented by Active Member of the Academy of Medical Sciences of the USSR, N. A. Yudaev.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 67, No. 3, pp. 23-26, March, 1969. Original article submitted July 25, 1968.

TABLE 1. Effect of Magnesium on Some Indices of Myocardial Metabolism of Rabbits with Experimental Thyrotoxicosis (M±m)

Index	Control	Thyrotoxicosis	Thyrotoxicosis + magnesium
Magnesium concentration in myocardium of left ventricle (in mg%)	17.4±1.8	12.0±0.96 P< 0.05	14.3±0.6 P> 0.1
Glycogen concentration in myocardium of left ventricle (in mg%)	0.29±0.03	0.05±0.02 P< 0.001	0.28±0.04 P=0.6
Creatine phosphate concentration in myocardium of left ventricle (in mg% creatine)	5.06±0.7	0.96±0.23 P< 0.001	2.14±0.27 P< 0.1
Radioactivity of myocardial protein of left ventricle 6 h after intravenous injection of methionine-S^{35} in Pulses/min/g protein × 100 / Pulses/min/g body weight	204.5±9.9	179.7±2.8 P< 0.05	206.9±8.9 P> 0.5

EXPERIMENTAL RESULTS AND DISCUSSION

Administration of thyroid by mouth to the rabbits in the manner described led to death of the least resistant animals. In this series of experiments 16 of the 26 rabbits receiving thyroid died. Meanwhile, of the 30 rabbits receiving thyroid together with magnesium, only 2 animals died ($P < 0.001$). This fact alone was sufficient to indicate the beneficial effect of magnesium ions on the hyperthyroid animals. In agreement with the results of our previous experiments [5], oral administration of thyroid led to a significant and very considerable decrease in the magnesium concentration in the myocardium (on the average by 31%; $P < 0.05$). This evidently took place on account of a decrease in the magnesium concentration in the intracellular fluid. Electrophoresis of magnesium during oral administration of thyroid prevented the appearance of this effect of excess of thyroid hormones, and the magnesium concentration in the myocardium of the animals of series III was indistinguishable from the control ($P > 0.1$; Table 1).

Administration of thyroid in excess to animals or thyrotoxicosis in man is known to be accompanied by severe depletion of the glycogen reserves in heart muscle [3, 8]. In this particular series of experiments oral administration of thyroid led to a decrease in the glycogen concentration in the myocardium of the left ventricle on the average by 80%. However, administration of magnesium simultaneously with thyroid completely prevented the changes in this index. In the animals of series III the glycogen concentration in the myocardium was the same as in the control ($P = 0.6$).

Administration of magnesium considerably reduced the decrease in creatine phosphate concentration in the myocardium of the hyperthyroid rabbits. Whereas in the animals of series II this index was 80% below the control level, in animals receiving magnesium together with thyroid it was reduced by only 57%, i.e., by a significantly smaller amount ($P < 0.05$). These results demonstrate an increase in the content of high-energy phosphorus compounds in the myocardium of the hyperthyroid animals under the influence of magnesium ions, i.e., presumptive evidence of the action of these ions in preventing the dissociating effect of thyroid hormones.

We showed previously [4] that marked thyrotoxicosis in rabbits is accompanied by inhibition of protein biosynthesis in the myocardium, thus preventing an adequate supply of structural materials for the intensively functioning myocardium. We interpreted these results as indicating competitive relationships between two endoergic processes: the physiological function of the organ and protein synthesis in it, under conditions of an inadequate formation of high-energy compounds. In the present series of experiments results were obtained confirming the previous investigations: under the influence of oral administration of thyroid for one month the intensity of renewal of myocardial protein was significantly reduced ($P < 0.05$). However, simultaneous administration of magnesium prevented the disturbance of the connection between physiological function of the organ and synthesis of its structural materials, while in the animals of series III this index was indistinguishable from the control ($P > 0.5$).

It can be concluded from these results that the series of metabolic disorders developing in the myocardium under the influence of an excess of thyroid hormones is related to magnesium deficiency. If these disorders were in fact due to a decrease in the energy-producing efficiency of tissue respiration, the normalizing effect of magnesium would indicate that competitive relationships in fact exist between the function

of the myocardium and synthesis of its structural materials in thyrotoxicosis resulting from a deficiency of biologically utilizable energy. The results indicate the desirability of including magnesium in the combination of therapeutic measures adopted in thyrotoxicosis.

LITERATURE CITED

1. A. M. Alekseeva, Biokhimiya, No. 2, 97 (1951).
2. K. A. Anan'eva, in: Endemic Goiter and Thyrotoxicosis in the Moscow Region [in Russian], Moscow (1961), p. 137.
3. L. M. Gol'ber and V. I. Kandror, Kardiologiya, No. 1, 53 (1967).
4. V. I. Kandror, Probl. Éndokrinol., No. 4, 88 (1965).
5. V. I. Kandror and I. V. Kryukova, Probl. Éndokrinol., No. 5, 102 (1966).
6. R. R. Rachev, Dissociation of Oxidative Phosphorylation in the Mitochondria and Its Reversibility, Candidate dissertation, Leningrad (1964).
7. S. Hänze, Der Magnesiumstoffwechsel, Physiologie und Klinik, Stuttgart (1962).
8. F. L. Hoch, Physiol. Rev., 42, 605 (1962).
9. M. Orange and H. C. Rhein, J. Biol. Chem., 189, 379 (1951).
10. I. E. Rizek, A. Dimich, and S. Wallach, J. Clin. Endocrinol., 25, 350 (1965).
11. S. Seifter, S. Dayton, B. Novic, et al., Arch. Biochem., 25, 191 (1950).
12. J. J. Vitale, D. M. Hegsted, M. Nakamura, et al., J. Biol. Chem., 226, 597 (1957).