INFLUENCE OF HYPERTHYROIDISM ON ZINC DISTRIBUTION IN RATS

Ratlarda çinko dağılımı üzerine hipertiroidinin etkisi

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Özet: *Tiroid hormonlarının rat dokularında bakır ve çinko dağılımını etkilediği ileri sürülmektedir. Çalışmamızda, T4 yükleyerek oluşturulan hipertiroidide eritrosit, plasma, beyin, kalp, kas, karaciğer, böbrek, dalak, timus ve kemik dokusundaki çinko dağılımı incelenmiştir. Hipertiroidi eritrosit çinko konsantrasyonunu önemli derecede değiştirmiştir. Eritrositteki ortalama çinko miktarı kontrolde 7.482±0.117 mg/l iken hipertiroidili grupta 4.089±0.371 mg/l olarak bulunmuştur. Hipertiroidizmin rat doku çinko konsantrasyonları üzerine etkisi de önemlidir.Kasta %33, karaciğerde %14 çinko artışı olurken, böbrekte %10 azalma meydana gelmiştir. Bu çalışmanın sonuçları, hipertiroidinin çinko metabolizmasını etkilediğini göstermektedir.*

Anahtar Kelimeler: *Çinko, Tiroksin, Triiyodotironin, Hipertiroidi*

Summary: *The zinc distribution was determined in rats 15 days after beginning of the treatment. The zinc was investigated in RBC, plasma, brain, heart, muscle, liver,kidney, spleen,thymus and bone. The results confirm that T4 modified zinc in RBC and tissues. Zinc was significantly decreased in RBC(45%)but no statistically significant difference was found in plasma zinc between experimental and control groups. Zinc was decreased 33% in muscle and 14% in liver, but was increased 10% in kidney. Brain,heart,spleen,thymus were the least affected tissues. Bon's zinc was decreased but no statistically significant difference was found between two groups.The results of this study suggest that the zinc metabolism is abnormal in hyperthyroid rats.*

Key Words: *Zinc, Thyroxine, Triiodothyronine, Hyperthyroidism*

Heavy metals have been shown to have some effects on thyroid hormones at several levels (7, 11), and thyroid hormones have been shown to affect heavy metal metabolism (1). A few studies have been reported on zinc metabolism in several tissues in hyperthyroidism. But, no previous reports are available to discuss the effect on zinc concentration whole tissues in patients or experimental animals with hyperthyroid.

The aim of this study was to investigate Zn concentration in plasma, red blood cell (RBC), and many tissues such as brain, heart, muscle, liver, kidney, spleen, thymus and bone in hyperthyroid rats.

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METHODS

In the experiments, 30 male Swiss-albino rats, weighing about 180-220 g, were used. They were divided into two groups of 15 rats each (hyperthyroid group and control group) and maintained in stainless-steel and plastic platformed cages on a commercial diet and provided with top water. Rats were made hyperthyroid by the subcutaneous injection of T4 dissolved in 10 mM-NaOH/0.03% bovine serum albumin (100 µg/100 g body weight per day) for 3 cosecutive days, being starved during the initial 2 days of treatment and re-fed on day 3. Control rats were injected with an equivalent amount of solvent. Animals were slightly anesthetized to take whole blood from their carotid-arteries 15 days after the beginning of the treatment. Their organs were quickly excised, washed in deionized water, dried, weighed, and stored at -20 °C until analysis.

Blood samples were centrifuged at 3000 rpm for 10 minutes, and plasma was seperated carefully because of avoiding hemolysis. The sedimented blood cells were washed in isotonic saline and centrifuged at 3000 rpm for 5 minutes. The supernatant and buffy coat were removed. This procedure was repeated three times to yield packed erythroctes. These samples were stored at - 20 ^{0}C until analysis.

Analytical determinations: Zn metal determinations were performed with a Hitachi Z800 Model Polarize Zeeman Atomic Absorption spectrophotometer. After thawing, whole organs were dried at 110 ^{0}C for 48 hours. Concentrated nitric acid (0.5 ml), hidrocloric acid (0.5 ml) and tridistilated deionized water (1 ml) were added to these tissues of 100 mg. Aliquots of homogenate were used to measure Zn concentration directly. Plasma and erythrocytes were prepared by dilution with deionized distilled water, plasma in a dilution of 1/100, erythyrocytes in dilution of 1/100. Zinc concentrations were calculated by linear regression lines.

Total plasma concentrations of T4 and T3 were measured by radioimmunoassay (RIA). Plasma thyroid stimulating hormone (TSH) was determined by highly sensitive radioimmunometric assay. The experimental data were analyzed by student t-test and the values were given means±SD.

RESULTS

Table 1 shows the effects of T4 on body weight and on the food intake of the rats fed a commercial diet ad libitum.Hypertyroid rats suffered from a significant decrease in weight gain and ther was an increase the food intake ($p<0.001$).

Table 2 shows the results of thyroid function testing in hyperthyroid rats. T3, T4 and TSH in plasma were greatly influenced by T4 administration ($p\leq0.001$).

Hyperthyroid altered concentration of zinc in red blood cell.Zn was significantly decreased in red blood cell (45%). However, we did not observe a significant change of zinc in plasma. The effect of hyperthyroidism on zinc concentrations in rats are shown in Table 3. Zinc was decreased by 33% in muscle and 14% in liver, but was increased by 10% in kidney. Whereas zinc concentration was greatly influenced in muscle, liver and kidney, it was not changed in heart, brain, spleen, thymus and bone.

Table 1. Weight and food consumption in rats with hyperthyroid (means+SD from 15 rats).

Groups	Body wt gain (g/d)	Food consumed g/100g body wt/d
Control	8.1+0.4	6.9+0.1
Hyperthyroid	5.3+0.3b	10.3+0.4
p	<0.001	<0.001

Table 2. T3,T4 and TSH concentrations in hyperthyroid rats (means+SD from 15 rats).

Groups	Plasma T3 (ng/ml)	Plasma T4 (µg/100ml)	Plasma TSH (µU/ml)
Controls	1.2+0.2	7.3+1.3	1.0+0.3
Hyperthyroidism	3.9+1.3	18.7+3.4	0.03+0.007
Significance level (p)	<0.001	<0.001	<0.001

Table 3. Effect of hyperthyroidism on zinc concentrations in plasma(mg/l), RBC(mg/l) and in tissues(Mg/g dw) of rats (means+SD from 15 rats).

	Groups		
	Control	Hyperthyroidism	p
Plasma	1.025+0.044	1.037+0.028	>0.05
RBC	7.482+0.117	4.089+0.371	<0.001
Brain	38.01+2.56	39.47+3.44	>0.05
Heart	51.73+3.01	48.04+0.34	>0.05
Muscle	30.51+2.15	20.42+3.02	<0.001
Liver	90.32+4.76	76.88+3.53	<0.001
Kidney	66.53+2.75	73.20+2.37	<0.01
Spleen	60.10+2.53	58.06+4.90	>0.05
Thymus	52.96+6.30	50.44+2.48	>0.05
Bone	376.54+22.4	350.02+12.55	>0.05

DISCUSSION

There have been a few studies on plasma and erythrocyte zinc concentration in patients with thyroid diseases (3, 4, 9). High serum zinc values have been reported in hyperthroidism (9), and serum zinc concentrations have been noted to correlate well with T3 and T4 (4). However, in agreement with our study, Morley et al (5) found no correlation between serum zinc levels and T4 levels in alcoholic cirrhotic patients. Hambridge (3) suggested that plasma zinc concentration does not always reflect the total body zinc status, and that even in zinc-deficient patients the plasma zinc concentration may be normal. The measurement of the erythrocyte zinc content appears to be another useful indicator of zinc status (8). Erythrocyte zinc concentration in hyperthyroidism was significantly lower than in control rats ($p \leq 0.001$). The present study confirms that the red blood cell zinc concentration is decreased in hyperthroidism. Changes in body metabolic rate have been shown to be reflected in altered zinc metabolism. Yadav et al (10) suggested that thyroxine administration to rats significantly enchanced the rate of Zn-65 turnover and altered its distribution in various organs leading to an almost 50% depletion in soft tissue zinc. Our study is also in agreement with their results. In our study zinc concentration is decreased in various tissues such as heart, muscle, liver, spleen, thymus and bone except brain and kidney. The zinc concentration in kidney is increased in hyperthroid rats, compared to the control rats. We did not find any significant modifications in brain, probably because of the particularity of the blood brain barrier. In liver (14%), muscle (33%) and kidney (10%), the variations represent major changes. Although urinary zinc concentration was not measured in our study, the zinc depletion in various tissues may result in higher urinary zinc excretion in hyperthyroid rats than in control rats. But, a few studies showed a significantly higher urinary zinc excretion in hyperthyroid patients than in other thyroid patients or control subjects and a significant correlation between zinc levels in urine and erythrocytes, and serum T4 or T3 levels (2, 6). Despite the increased urinary zinc loss, the plasma zinc level remained normal in hyperthyroid patients and there was no correlation between plasma and urine zinc levels in these studies.The present study also did not find any significant changes in plasma zinc concentration in hyperthyroid rats, despite the increased kidney zinc level. This may reflect the mobilization to plasma of the zinc from tissues such as erythrocytes, bone, muscle, liver, spleen, thymus and heart.

The effect mechanism of thyroid hormones on zinc distribution in certain organs have not been known. Further studies are needed to establish the mechanism of changes in zinc levels after hyperthyroidism and hypothyroidism and clinical significance of these changes.

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