Serum creatin kinase and its isoenzymes in thyroid diseases

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Objective To investigate the relationships between serum creatinine kinase isoenzymes and thyroid hormone concentrations.

Methods 50 hypothyroid and 25 hyperthyroid patients and 30 healthy subjects as controls were included the study. Serum CK isoenzymes were studied by enzymatic colorimetric method after obtaining isoenzyme eluants by colon chromatography. Serum T4, T3 and TSH levels were determined by radioimmuno-assay methods.

Results Serum CK levels, particularly CK-MM fraction, were found to be significantly high in hypothyroid and low in hyperthyroid patients compared to controls. Serum CK levels were correlated to TSH ($r=0.70$, $p<0.001$) and thyroid hormone concentrations ($r= -0.32$, $p<0.01$ for T4 and $r= -0.28$, $p<0.01$ for T3).

Conclusions We agree that routine use of CK isoenzyme measurements to monitor thyroid status may be useful.

Key words Hypothyroidism, Hyperthyroidism, CK, CK-MM.

Introduction

Thyroid hormones regulate the total activity of creatine kinase and its isoenzyme distribution (1-5). In comparison with normal thyroid state (euthyroidism), hypothyroidism is characterized by decreased total creatine kinase activity owing to diminished fraction of creatine kinase (3,6-8).

Subclinical hypothyroidism is found in about 7.5 % of females and in about 3 % of males. It appears to be a risk factor for atherosclerosis and for coronary heart disease.It is very difficult to diagnose subclinical hypothyroidism, especially if the symptoms are not clear. Since cardiovascular symptoms are common in hypothyroidism, these patients may present increased serum CK activities and symptoms that suggest a cardivascular disease This presentation may focus the initial attention on the cardivascular disease rather than the thyroid disease as the cause of the enzyme elevation (2,3)

In this study, we aimed to investigate the relation between levels of the thyroid hormones and serum CK, particularly its isoenzymes.

Materials and Methods

This study was done in 50 patients with primary hypothyroidism (20 males, 30 females), 25 patients with hyperthyroidism (11 males, 14 females) and in 30 similarly age-matched healthy volunteers. Diagnosis were confirmed with clinical and laboratory findings.

Serum T3, T4, TSH, total CK and its isoenzymes(CK-MM, CK-MB, CK-BB) were measured in the patient and the control groups. T3, T4, and TSH levels were measured by commercially available radioimmuno assay kits(D.P.C.Lot.No:TT3 0129, TT4 0151 and TSH-2 0054, respectively, USA)

The eluants contained CK isoenzymes were obtained by colon chromotography (CK Profile Centrifi Chem,USA). Then total CK and its isoenzymes were measured by enzymatic colorimetric methods with commercial test kits (Sclavo, Cat.No:81343, Italy) by autoanalyzer.

The relationship of thyroid hormones to CK and its isoenzymes was examined by linear regression analysis, calculating the Pearson's productmoment correlation coefficient (R) and the significance of correlation (α) Results were statistically analysed using unpaired student's tets and one-way analysis of variance. All statistical analyses were performed with the SPSS statistical package for Windows (SPSS, Chicago, IL).

Results

Ages and weights of the patients and of the controls are given in Table 1. No significance was found between the groups in terms of age ($p>0.05$). Body weights were higher in the hypothyroidism group ($t=2.03$, $p<0.05$) and lower in the hyperthyroidism group ($t=2.47$, $p<0.05$) when compared with the controls.

Some statistical comparisons for CK and its isoenzymes between the groups are shown in Table 3. CK and its isoenzymes were found to be significantly higher in the hypothyroid patients ($p<0.05$) and lower in the hyperthyroid patients ($p<0.05$) than those in the controls. The correlation analysis results between thyroid function tests and CK, and its isoenzymes are given in Table 4.

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Table 1. Ages and weights of the patients and controls

Hyperthyroid Group n=25		Control Group n=30	Hypothyroid Group n=50
52 ± 16	AGE (Year)	50 ± 13	48 ± 15
58 ±10	WEIGHT (Kg)	64 ± 8	69 ±12

Table 2. Laboratory findings of the patients and controls (Mean ± SD)

PARAMETERS	Hypothyroid Group n=50	Hyperthyroid Group n=25	Control Group n=30
T3 (ng/ml)	45.6 ± 22	316 ± 92	140.4 ± 22.8
T4 (µg/ml)	2.5 ± 1.8	13.9 ± 3.5	8.3 ± 1.4
TSH (µu/ml)	8.7 ± 4.8	0.17 ± 0.09	1.6 ± 0.51
CK (U/L)	350 ± 160	36.2 ± 16	106.6 ± 26
CK-MM (U/L)	336 ± 145	29.2 ± 12	97 ± 24
CK-MB (U/L)	13.4 ± 9.8	6.5 ± 1.2	8.4 ± 4
CK-BB (U/L)	2.5 ± 2.3	1.4 ± 0.5	1.8 ± 0.7

Table 3. Statistical Comparisons Between The Groups.

	CK		CK-MM		CK-MB		CK-BB	
Groups	t	p	t	p	t	p	t	p
Hypo - Hyper	13.7	<0.001	13.6	<0.001	2.50	<0.05	2.16	<0.05
Hypo - Control	10.4	<0.001	10.3	<0.001	2.24	<0.05	1.98	<0.05
Hyper - Control	11.4	<0.001	11.2	<0.001	2.74	<0.01	2.70	<0.01

Table 4. Correlation coefficient values between thyroid function tests and CK , CK isoenzymes in Hypothyroid and Hyperthyroid Groups.

	Hypothyroid Group		Hyperthyroid Group	
Parameters	r	p	r	p
T3 - CK	-0.28	<0.01	-0.44	<0.001
T4 - CK	-0.32	<0.01	-0.24	<0.050
TSH - CK	0.70	<0.001	0.75	<0.001
T3 - CK MM	-0.37	<0.001	-0.40	<0.001
T4 - CK MM	-0.30	<0.001	-0.45	<0.001
TSH - CK MM	0.56	<0.001	0.49	<0.001

In Table 2, some laboratory results (mean ± SD) in the patients and the controls are given

In hypothyroid group, a negative correlation between CK and T3, T4 levels ($p < 0.01$), and a strong positive correlation between CK and TSH ($p < 0.001$) were found.

The correlation between CK-MM and thyroid function tests (T3,T4,TSH) was very significant ($p < 0.001$)

In hyperthyroid group, a weak negative correlation between CK and T4 ($p < 0.05$) and a strong negative correlation between CK and T3 ($p < 0.001$) were detected. The correlation between CK (especially CK-MM) and TSH levels was positive and very significant ($p < 0.001$)

Discussion

There are many studies in the literature on thyroid disfunction that is one of the most important endocrine diseases, and on its metabolic effects. These studies investigated the effects of thyroid hormones on liver function tests, electrolytes, some hormones, enzymes and isoenzymes (1,2,11)

In hypothyroidism, particularly primary hypothyroidism, abnormally high levels of serum CK are common and may also be found in up to 90% of cases; therefore hypothyroidism must be taken into account in diagnosis when high CK levels was detected (3,7,12).

Graig et al (1963) firstly described elevated CK levels in hypothyroidism and this finding confirmed by numerous reports. In hypothyroid patients, isoenzyme analysis has revealed only CK-MM isoenzyme to be present in the majority of cases (3,5,6,13).

Jenkins (1978) determined CK levels in 671 patients and found significant negative was correlation between low plasma protein bound iodine level and increased CK activity and, the patients with low plasma bound iodine levels showed increased CK-MM that was the main form present in isoenzyme analysis (1). Further studies have been done on this

subject in the literature and negative correlation between CK and thyroid hormones was confirmed by investigators (2,3,7,14).

Docherty et al reported that high total CK activities in 15 hypothyroid patients exceeded the upper limit of normal by 1,4-4 fold; and in 15 hyperthyroid patients that have low total CK levels increased after treatment (11).

Lemar et al and other authoes found that high levels of serum CK, especially CK-MM, and CK-MB were not as increased as patients with sustained myocardial infarction (3,16,17). It was also reported that CK levels decreased to normal levels with thyroxin treatment. The time course for its normalization correlated better with the decline in TSH than with the rise of serum thyroxine levels (3,9-11).

In our study, we found a strong positive correlation between total CK and TSH, and a negative correlation between total CK, particularly CK-MM and T3, T4 in both of hypothyroidism and hyperthyroidism. Our findings were consistent with the data mentioned above.

Even though several theories have been proposed for the mechanism of CK and its isoenzymes, differences in thyroid disfunction were not well understood. Some authors suggested that the increase in CK activity in hypothyroid patients resulted from leakage of the enzyme from muscle cells, perhaps related to the subnormal body temperature accompanying primary hypothyroidism (11, 17). Karlsberg et al. reported decreased rate of CK clearance in hypothyroid dogs and it has been suggested that thyroid hormones stimulate the fractional removal of CK (15). Other possibilities for mechanism of CK elevation in hypothyroidism are the presence of CK activating factor in hypothyroid myopathy (17), increased muscle membrane permeability (18-20).

As a result, these findings show that the absence of substantial amounts of CK-MB isoenzyme can help in differential diagnosis of myocardial injury and hypothyroidim thus, the absence of significant CK-MB fraction and the persistence of an elevated CK value beyond the usual time course of myocardial infarction should prompt the consideration of hypothyroidism.

References

1. Jenkins DJ. An investigation into creatine kinase and other plasma enzymes in thyroid disorders.Clinica Chimica Acta. 85: 197-204,1978.
2. Staub JJ, Althaus BU, Engler H, Ryff AS, Trabucco P, Marquardt K, et al. Spectrum of subclinical and overt hypothyroidism: effect on thyrotropin, prolactin, and thyroid reserve, and metabolic impact on peripheral target tissues. The Am. Journal of Medicine. 92: 631-642,1992.
3. Lemar HJ, West SG, Garret CR,Hofeldt FD. Covert hypothyroidism presenting as a cardiovascular event. The American Journal of Medicine. 91:549-552,1991.
4. Chertow BS, Motto GS, Shah JH. A biochemical profile of abnormalities in hypothyroidism. American Journal of Clinical Pathology. 61: 785-787,1974.
5. Goldman J, Matz R, Mortimer R, Freeman R. High elevations of creatine phosphokinase in hypothyroidism. JAMA. 238: 325-326,1977.
6. Jacobs DS, Kasten BL, Demott WR, Wolfson WL. Laboratory Test Handbook.Lexi-Comp Inc. Ohio 1990, pp:166-167.
7. Page SR, Nussey SS. Myositis in association with carbimazole therapy. The Lancet. 29:964,1989.
8. Morley JE, Slag MF, Elson MK. The interpretation of thyroid function tests in hospitalised patients. JAMA. 249: 2377-2379,1983.
9. Baker JR, Endocrine Diseases, Basic And Clinical Immunology (Ed Terr AI)Appleton and Large Medical Publication.Lebenon 1991, pp:470-471.
10. Berkow R: The Merck Manual of Diagnosis and Therapy. Merck and Co. USA 1987,pp:1038-1043.
11. Docherty J, Harrop JS, Hine KR, Hopton MR, Mathews HL, Taylor CJ. Myoglobin concentration, creatin kinase activity, and creatine kinase b subunit,t concentrations in serum during thyroid disease. Clin. Chem, 30: 42-45,1984.
12. Lott JA, Stang JM: Differantial diagnosis of patients with abnormal serum creatine kinase isoenzymes, Clinics in Laboratory Medicine. (Ed. Pappas NJ) WB Saunders Co. Philadelphia 1989 pp: 627-642.
13. Graig FA, Ross G. Serum creatine phosphokinase in thyroid disease. Metabolism. 12: 57-59,1963.
14. Goto I. Serum creatine phosphokinase isozymes in hypothyroidism, convulsion, myokardial infarction and other diseases. Clinica Chimica Acta. 52: 27-30,1974.
15. Karlsberg RP, Roberts R. Effect of altered thyroid function on plasma creatine kinase clearance in the dog. Am. J. Physiol. 235: 614-618,1978.
16. Minutiello L: The enzymatic and electrocardiographic changes falsely indicative of an acute myocardial infarct during hypothyroidism. Minerva Cardiangiol. 41: 579-602,1993.
17. Miyamoto T, Nagasaka A, Kato K, Masunaga R. Immunoreactive creatine kinase-MB and creatine kinase isozyme concentrations during treatment of hypothyroid patients. Eur J Clin Chem. Clin. Biochem. 32: 589-593,1994.
18. Godet J, Fardeau M. A clinical, histological and ultrastructural study of a case of hypothyroid myopathy, in international congres, on muscle disease. International Congress Series. Excerpta Med. 1983;186:57.
19. Burnett JR, Crooke MJ, Delahunt JW, Feek M. Serum enzymmes in hypothyroidism. NZ Med J. 14: 355-356,1994.
20. Comtois R, Lemay C, Laliberte A. Coexistence of hypothyroidism and myocardial infarction. Can. J. Cardiol. 11: 37-42, 1995

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