CARDIAC TROPONIN I IS NOT INCREASED IN SEVERE ACUTE HYPOTHYROIDISM IN PATIENTS WITH DIFFERENTIATED THYROID CARCINOMA

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ABSTRACT

Objective: *Of all malignant cancers, differentiated thyroid carcinoma (DTC) has the most rapidly increasing incidence rate in both women and men. Cardiac complications can occur due to the hypothyroidism occurred before radioactive iodine^{131} whole-body scan (I^{131}-WBS). Fifteen days after thyroid hormone treatment withdrawal, TSH levels were measured and the cases over 50 mU/L are accepted as severe acute hypothyroidism. The purpose of this study was to investigate, whether severe acute hypothyroidism before treatment with the I^{131}-WBS caused any myocardial damage in patients with DTC during postablative follow-up period.*

Material and Method: *Forty-eight patients with DTC were recruited to the study. Twenty-four patients were assigned to the subclinical hyperthyroidism (SH) and euthyroid subgroups each. Blood samples were collected from patients under levothyroxine (LT4) treatment 15 days after cessation of thyroid hormone therapy, after the occurrence of acute severe hypothyroidism before I^{131}-WBS blood samples were collected second time. Serum cardiac troponin I (cTnI) were measured by automated electrochemiluminescence immunoassay.*

Results: *No significant difference was detected ($p>0.05$) between cTnI values measured under LT4 treatment SH and euthyroid subgroups. Within each subgroup, cTnI values under LT4 treatment and in the hypothyroid condition showed no significant either ($p>0.05$).*

Conclusion: *We concluded that severe acute hypothyroidism observed before I^{131}-WBS in patients with DTC may not cause myocardial damage. Therefore, cTnI may still be a reliable marker in differential diagnosis in patients with severe acute hypothyroidism mimicking acute coronary syndrome.*

Keywords: *Hypothyroidism, acute hypothyroidism, troponin I, differentiated thyroid carcinoma.* ***Nobel Med 2016; 12(3): 47-50***

DİFERANSİYE TİROİD KARSİNOMLU HASTALARDA CİDDİ AKUT HİPOTİROİDİDE KARDİYAK TROPONİN I ARTMAZ

ÖZET

Amaç: Tüm malign kanserler arasında, diferansiye tiroid karsinom (DTK) insidansı hem kadın hem de erkeklerde en hızlı artan karsinomdur. Radyoaktif İyot^{131} tüm vücut taraması (I^{131}-TVT) öncesi oluşturulan hipotiroidi nedeniyle kardiyak komplikasyonlar oluşabilir. Tiroid hormone tedavisi kesildikten 15 gün sonra TSH seviyeleri ölçüldü ve 50mU/L'nin üzerinde olan vakalar ciddi akut hipotiroidi olarak tanımlandı. Bu çalışmanın amacı; DTK'li hastalarda postablatif dönemde I^{131}-TVT öncesi oluşturulan ciddi akut hipotiroidinin herhangi bir miyokard hasarına sebep olup olmadığını araştırmaktı.

Materyal ve Metot: Bu çalışmaya DTK'li 48 hasta dahil edildi. Herbiri 24 hasta içeren subklinik hipertiroidi (SH) ve ötiroid iki subgruba ayrıldı. Hastalardan levotiroksin (LT4) tedavisi altında ve tiroid hormone tedavisi kesildikten 15 gün sonra I^{131}-TVT öncesi akut ciddi hipotiroidi oluştuğunda kan örnekleri alındı. Automated electrochemiluminescence immunoassay ile serum kardiyak troponin I (cTnI) ölçüldü.

Bulgular: LT4 tedavisi altında ve hipotiroidi durumunda SH ve ötiroid subgrupların cTnI değerleri arasında anlamlı fark saptanmadı (p>0,05). Alt grupların kendi içinde LT4 tedavisi altında ve hipotiroidi durumunda ölçülen cTnI değerleri arasında da anlamlı fark saptanmadı (p>0,05).

Sonuç: DTK'lu hastalarda I^{131}-TVT öncesi görülen ciddi akut hipotiroidinin myokard hasarına sebep olmadığı sonucuna vardık. Akut koroner sendromu taklit eden ciddi akut hipotiroidili hastalarda ayırıcı tanıda cTnI güvenilir bir marker olabilir.

Anahtar kelimeler: Hipotiroidi, akut hipotiroidi, troponin I, diferansiye tiroid karsinomu. **Nobel Med 2016; 12(3): 47-50**

INTRODUCTION

Among endocrine cancers, differentiated thyroid carcinoma (DTC) is the most frequent and has the most rapidly increasing incidence rate in women and men.[1,2] In these patients, cardiac complications may occur postoperatively and before radioactive iodine^{131} whole body screening (I^{131}-WBS).

Serum cardiac troponin I (cTnI) is a very sensitive and specific indicator of myocardial damage.[3-6] Because of its cardiac complications, the acute hypothyroidism might elevate cTnI levels and complicate the diagnosis of acute coronary syndrome. Fifteen days after thyroid hormone treatment withdrawal, TSH levels were measured and the cases over 50 mU/L are accepted as severe acute hypothyroidism. The purpose of this study was to evaluate, on postablative follow-up, whether severe acute hypothyroidism before treatment with I^{131}-WBS caused any myocardial damage in patients with DTC. To our knowledge, this is the first prospective study to be published about cTnI in patients with severe acute hypothyroidism.

MATERIAL AND METHOD

Patients and Study Design

Forty-eight patients with DTC who received treatment and follow-up in Karadeniz Technical University Medical Faculty Endocrinology and Metabolism Diseases Clinic were recruited to the study. Twenty-four patients were assigned to the subclinical hyperthyroidism (SH) (21 women and 3 men; median age 49±11 years) or euthyroid (20 women and 4 men; median age 48±13 years). Diagnosis of DTC was made by pathologic examination after thyroidectomy. All patients received radioactive iodine (I^{131}) ablation therapy for DTC treatment. Patients with diseases that could increase cTnI levels, such as coronary heart disease, diabetes mellitus, and individuals with smoking history were excluded from the study. Blood samples were taken from patients under levothyroxine (LT4) treatment. Subsequently, LT4 treatment was discontinued and triiodothyronine (T3) 3 x 25 mg/day was given for 15 days. Blood samples were taken 15 days after cessation of T3 treatment, after the occurrence of acute severe hypothyroidism before I^{131}-WBS. Informed consent was obtained from all enrolled patients, and the study was approved by the local ethics committee of Karadeniz Technical University (No: 2013/88).

Laboratory Analysis

Blood samples were taken in the morning between 08:00 and 09:00 following 8 hours of fasting. Serum levels of thyroid stimulating hormone (TSH), free thyroxin (FT4) and cTnI were measured by automated electrochemiluminescence immunoassay (Beckman Coulter, USA). Normal range for adults are 0.27-4.2 µIU/mL for TSH, 0.9-1.7 ng/dL for FT4, and 0-0.04 ng/mL for cTnI.

Statistical Analysis

Data normality was assessed by the Kolmogorov-Smirnov test. All data were analyzed as normally

distributed. Statistical analyses were performed by Student's t test for normally distribution data and by Mann-Whitney U test for data not normally distributed. Data are presented as mean ± standard deviation (SD), $p<0.05$ was accepted as statistically significant.

RESULTS

No significant difference was detected ($p>0.05$) between values measured under LT4 treatment in the SH and euthyroid subgroubs (Table). cTnI values under LT4 treatment and in a hypothyroid condition were compared in the subgroups, and no significant difference was found ($p>0.05$). Levels of TSH, FT4 and cTnI measured under LT4 treatment and in a hypothyroid condition were compared in all patients. cTnI values were not significantly different ($p>0.05$).

Tablo. Biological parameters of patients with differentiated thyroid carcinoma

Parameter	Under LT4 treatment (mean± SD)	Hypothyroidism state (mean± SD)	*p*
TSH	0.90±1.05	76.97±23.56	<0.001
FT4	1.51±0.15	0.37±0.19	<0.001
cTnI	0.0047±0.0094	0.0060±0.0168	NS

NS: Non significant (p>0.05), **FT4:** free thyroxine, **SD:** standart deviation, **TSH:** thyroid stimulating hormone, **cTnI:** cardiac troponin I,

DISCUSSION

Diagnosis with DTC is made at an average age of 49 years and three times more frequent in women than in men.[2] Age is the most important risk factor for mortality in patients with DTC and the risk prominently increases after the age of 45.[7] Differential diagnosis of acute and severe hypothyroidism is difficult because of symptoms mimicking coronary artery diseases, which is observed at similar ages.

Thyroid hormones directly affect the cardiovascular system. T3 hormone has several regulatory roles on the cardiovascular system. T3, through its nuclear receptors, induces peptide mediator production that increases the number and the sensitivity of adrenergic receptors.[8,9] In hypothyroidism, cardiac output, heart rate, stroke volume and myocardial contractility decreases while systemic vascular resistance, cardiomyocyte atrophy, and endothelial dysfunction increases.[8-10] Mild hypothyroidism may affect several cardiac functions even in the very early stages.[9,11] Coronary atherosclerosis frequency is doubled in long-term hypothyroidism due to endothelial dysfunction, increased blood pressure, and hypercholesterolemia.[9,11-13] Because cTnI is related only to myocardium, it is a valuable indicator of myocardial damage.[6,12,14] As confirmed by invasive diagnostic methods, even mildly elevated cardiac troponin levels have a prognostic importance in patients diagnosed with or without acute coronary syndrome.[8,15] The high cTnI in patients with acute coronary syndrome has been shown to be an independent risk factor for mortality.[1,16,17] In published studies, cTnI has been reported to increase without acute coronary syndrome, even in the conditions of supraventricular tachycardia, rotational atherectomy, acute pulmonary embolism, thalassemia major, norma pregnancy, preeclampsia and myocarditis.[5,6,18-23] In such diseases, it is thought that without a structural damage in myocardium, cardiac troponin can be released from free cytosolic pool owing to the changes in membrane permeability of myocytes.[24, 25]

To our knowledge, no studies of cTnI in patients with severe acute hypothyroidism has been published. Only one prospective study on patients with chronic hypothyroidism was found in the literature. In that study, Cohen et al. reported that cTnI did not increase in hypothyroidism.[12] Similarly, we found that cTnI also did not increase in severe acute hypothyroidism. Case reports have reported conflicting results that cTnI either increased or did not.[8,24,25]

The presence of hypothyroidism in patients with chest pain and slightly elevated cardiac troponin levels in the emergency clinics can create confusion upon diagnosing acute coronary syndrome.[8] From this study, we conclude that severe acute hypothyroidism was not a likely cause of myocardial damage. We believe that in patients with severe acute hypothyroidism mimicking acute coronary syndrome, cTnI may be a reliable marker for the differential diagnosis of these two diseases. In patients with apparent hypothyroidism and a slight increase in cTnI, acute coronary syndrome must be considered. Further and more comprehensive studies are needed to evaluate the relationship between severe acute hypothyroidism and cTnI.

*The authors declare that there are no conflicts of interest.

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