Turkish Journal of Endocrinology and Metabolism, (2005) 3 : 85-88 **ORIGINAL ARTICLE**

The Level of Serum High Sensitive C-Reactive Protein in Women with Hyperthyroidism

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High-sensitive C-reactive protein (hs-CRP) levels, a marker of subclinical inflammation, have been identified as an independent predictor of atherosclerosis. Although it is well known that thyroid hormones play an important role in cardiovascular hemodynamics, the association between elevated thyroid hormones and low grade inflammation is still unclear. We aimed to investigate the serum hs-CRP in women patients with hyperthyroidism.

Twenty-five women with hyperthyroidism and 25 healthy-control subjects who were age (31.3±12.3 years, 29.6±7.7 years respectively, p> 0.05) and body mass index-matched (24.0±3.6 kg/m^2, 24.3±4.5 kg/m^2, p> 0.05) were included into this study. Patients were evaluated at the time of diagnosis. Serum concentrations of free T4 (fT4), fT3, TSH, and lipid parameters (total cholesterol, triglyceride, high density lipoprotein-cholesterol (HDL-C), low density lipoprotein-cholesterol (LDL-C) were measured in all subjects. Serum hs-CRP levels were assessed by ELISA method.

Mean total cholesterol and LDL-C levels of hyperthyroid group were lower than control group (p= 0.001, p< 0.01). There were no statistically significant differences in hs-CRP levels between hyperthyroid and control groups (0.05±0.032 mg/l, 0.04±0.038 mg/l, p> 0.05; 2.3±1.5, 1.4±0.5, p> 0.05, respectively) and also had not been found any correlation between levels of hs-CRP and thyroid hormones.

In this study, these results shown that the elevated thyroid hormones have no effect on the serum hs-CRP level. We conclude that hyperthyroidism do not induce low grade inflammation of atherosclerosis in women.

Keywords: Hyperthyroidism, hs-CRP, subclinical inflammation

Introduction

C-reactive protein (CRP), a classic acute-phase reactant, is an important sensitive marker of low grade inflammation; increased concentrations of high sensitive-CRP (hs-CRP) have been shown in several studies to be associated atherosclerosis and coronary artery disease (1). It is well established that overt hyperthyroidism induces a hyper-dynamic cardiovascular state (high cardiac output with low systemic vascular resistance), which is associated with a faster heart rate, enhanced left ventricular systolic and diastolic function, and increased prevalence of supraventricular tachyar-rhythmias (2). Although thyroid hormones play an important role in cardiovascular hemodynamics, the association between elevated thyroid hormones and low grade inflammation is still unclear. Thus, the aim of the study was to investigate changes in serum hs-CRP levels in women hyperthyroid patients.

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Materials and Methods

Twenty-five women with hyperthyroidism and 25 healthy premenapousal women were enrolled in the study. Among the 25 hyperthyroid patients, 22 had diffuse toxic goitre, 3 had a toxic adenoma. Hyperthyroid patients had undetectable level of thyrotropin (TSH), high thyroid hormone levels (free triiodothyronine [fT3], free thyroxine [fT4]). All patients gave informed consent to participate in

the study. Acute and subacute thyroiditis were excluded. None of the participants had clinical antecedents of stroke, coronary heart disease, or peripheral vascular disease and diabetes mellitus, hepatic and renal dysfunction, chronic inflammatory conditions. Subjects with treatment known to affect haemostatic variable (lipid lowering agents, antiinflammatory agents, menopausal hormone replacement therapy…) were excluded. All participants were not current smokers.

Height, weight, waist circumference and hip circumference were recorded by a standardized protocol. Body mass index (BMI, kg/m2) and waist-hip ratio (WHR) were calculated.

Blood samples were collected from an antecubital vein after an overnight fast. Fasting serum glucose was measured using the glucose oxidase technique (Beckman Coulter LX20). Spectrophotometric method (Beckman Coulter LX20) was used to measure triglyceride, total cholesterol and high density lipoprotein-cholesterol (HDL-C). Low density lipoprotein-cholesterol (LDL-C) level was calculated according to Friedewald formula. TSH (third generation, normal range 0.4–4 μIU/mL), free thyroxine (fT4, normal range 0.8–1.9 ng/dL), free triiodothyronine (fT3, normal range 1.8–4.2 pg/mL) levels were measured by immunometric assay method, chemiluminescent immunoassay method, competitive immunoassay method, respectively (Immulite DPC 2000, CA). Serum hs-CRP levels (Biocheck, Inc, CA) were assessed by ELISA method.

Statistical Analyses

Statistical analyses were performed with the SPSS for Windows. Student-t test was applied to evaluate differences in continuous variables between patients and control subjects. Correlations between variables were assessed using Pearson correlation analysis. $p < 0.05$ was considered as statistically significant.

Results

The main characteristics of the patients and controls are shown in Table 1. No significant differences in the means of age, BMI and WHR were found between hyperthyroid and control groups. Mean glucose levels of hyperthyroid group were higher and the total cholesterol, LDL-C levels of hyperthyroid group were lower than control group ($p < 0.05$, $p = 0.001$, $p < 0.01$, respectively). There was no statistically significant difference in hs-CRP level between hyperthyroid and control groups ($p > 0.05$) (Figure 1). Serum fT4 levels were negatively correlated with cholesterol ($r = -0.449$, $p < 0.05$) and LDL-C ($r = -0.457$, $p < 0.05$) levels. No significant correlation was observed between hs-CRP and FT3, FT4, and TSH ($r = 0.113$, $p > 0.05$, $r = 0.05$, $p > 0.05$, $r = -0.27$ $p > 0.05$, respectively) in hyperthyroid group.

Table 1. Laboratory and clinic characteristics of groups.

	Hyperthyroid Group n= 25	Control Group n= 25	p
Age (years)	31.2 ± 12.3	29.6 ± 4.5	*
BMI (kg/m^2)	24.0 ± 3.6	24.3 ± 4.5	*
WHR	0.78 ± 0.05	0.76 ± 0.60	*
Cholesterol (mg/dl)	134.9 ± 33.6	167.0 ± 25.3	0.001
Triglyceride (mg/dl)	72.2 ± 38.1	57.1 ± 32.3	*
HDL-C (mg/dl)	53.3 ± 7.2	53.1 ± 6.8	*
LDL-C (mg/dl)	75.4 ± 30.6	101.7 ± 19.0	< 0.01
Fasting glucose (mg/dl)	95.6 ± 9.5	87.5 ± 8.0	< 0.05
fT3 (pg/mL)	11.5 ± 9.9	3.8 ± 0.2	< 0.001
fT4 (ng/dL)	4.3 ± 1.3	1.3 ± 0.2	< 0.001
TSH (μIU/mL)	0.04 ± 0.02	1.25 ± 0.86	<0.001
hs-CRP (mg/dl)	0.05 ± 0.03	0.046 ± 0.038	*

* not significant.

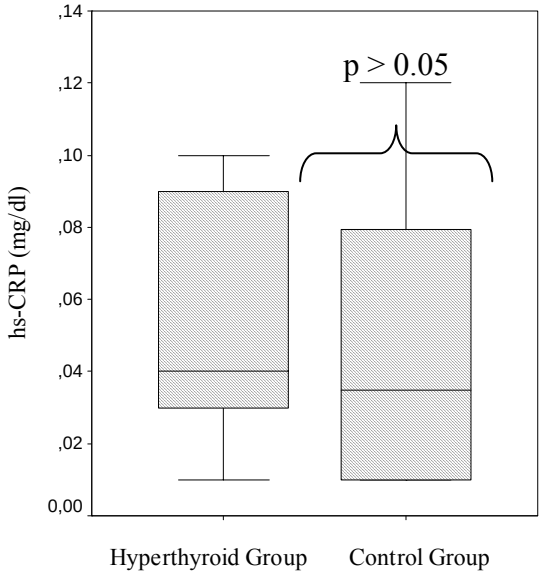

Figure 1. Serum hs-CRP levels in hyperthyroid and control groups.

Conclusion

In this study, we found that the increased levels of thyroid hormones did not show a significant relationship to the levels of hs-CRP. This finding suggests that hyperthyroidism could not promote the subclinical inflammation state.

Atherosclerosis is a complex process; lipid oxidation and inflammation play a central role in the development of atherosclerosis. Oxidation of LDL particles directly trigger several alterations in the endothelium and vascular zone such as the synthesis and expression of chemotactic and adhesion molecules, the proliferation of smooth muscle cells. The results of these alterations cause macrophages migration into the subendothelial space, where they are converted to foam cells rich in oxide-LDL particles (4, 5). These foam cells interact with T lymphocytes and consecutively initiate immune response and cause secreting proinflammatory cytokines and acute phase reactant (6). Into the this cascade, it has been showed that paraoxonase activity is an antioxidant defense system which protects against the action of free radicals and accordingly causes the decreased oxidation of LDL particles. In addition, paraoxonase activity has been shown to inhibit the pro-inflammatory responses of macrophages and endothelial cells (7). Furthermore, it has been reported that higher levels of hs-CRP were associated with low levels of paraoxonase activity (8). In other words, paranoxonase activity is essential for preventing the atherosclerotic process. Hyperthyroidism accelerates production of free radicals and lipid peroxidation, and consequently atherosclerosis (9). Recent studies showed that serum paraoxonase activity was decreased in hyperthyroid patients (10, 11). Moreover, hyperthyroidism exhibits an enhanced excretion of cholesterol and an increased turnover of LDL resulting in a decrease of total and LDL cholesterol, whereas HDL are decreased. Paraoxanase is an important antioxidant enzyme found in HDL and decreased paraoxanase levels may be due to secondary to HDL changes in hyperthyroidism (10, 12). These studies suggest that low paraoxonase activity may occur as part of an inflammatory response in hyperthyroidism. In this context, we speculated that hs-CRP, the most important marker of subclinical inflammation, might be increased in hyperthyroid patients. However, our findings did not support our estimation and hs-CRP levels were not found to be increased in hyperthyroid patients. Nowadays, the studies, which are investigated the association between hyperthyroidism and subclinical inflammation, are not enough. When Lee et al (13) examined the relationship between thyroid diseases and cardiovascular risk factors by dividing thyroid diseases according to their degree into four groups; they did not find a correlation between thyroid function and hs-CRP levels. They reported that hs-CRP level was not a sensitive marker of metabolic change induced by thyroid hormones. It has been demonstrated in the another study that hs-CRP levels were negatively correlated with fT4 levels in euthyroid hyperlipidemic patients, suggesting that low fT4 levels constitute a new marker of cardiovascular disease (14). They did not report any data about the association between the increased thyroid hormones and hs-CRP levels. In a study on endothelial function in hyperthyroid patients, Bergdorf et al (15) did not determine any association between excess thyroid hormones and inflamemation markers such as interleukin-6, tumor necrosis factor-α, CRP.

This study has several limitations. First, the numbers of groups were small. Second, the duration of hyperthyroidism was not evaluated. These factors could be effective on hs-CRP levels.

In conclusion, we suggest that hyperthyroidism is not thought to be risk factor the development subclinical inflammation in atherosclerosis. Further, detailed studies are needed to clarify the mechanism of atherosclerosis in the hyperthyroidism.

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