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The Evaluation of The Oxidative Stres Parameters in Cases With Hypo -or Hyper- Thyroidism

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Abstract

We have investigated the oxidative stress and antioxidant capacity differences in cases with hyper- or hypo-thyroidism. We have evaluated Malonyldialdehyde (MDA) stages as an evidence of lipid peroxidation, protein carbonyl stages as a screen of protein oxidation and protein sulfydryl (SH) groups stages as a screen of antioxidant capacity in a group of 50 cases (clinically hyperthyroid, 12; subclinically hyperthyroid, 13; clinically hypothyroid, 10; and subclinically hypothyroid, 15).

In comparison to the control group, MDA levels of hypothyroid and subclinic hyperthyroid groups were found to be significantly higher, and protein carbonyl levels in subclinically hypothyroid patients were significantly higher and SH group levels in subclinically hypothyroid, clinically hyperthyroid and subclinically hyperthyroid groups were lower.

We have demonstrated that hyperthyroidism and hypothyroidism might lead to an increase in free radicals and might also cause a difference in the antioxidant defence system.

Key Words: Hyperthyroidism, hypothyroidism, oxidative stress

INTRODUCTION

Thyroid hormones accelarate the basal metabolic rate and the energy metabolism of tissues in several mammalian species [1]. Thyroid hormones ease this effect on energy metabolism by changes in the number and activity of mitochondrial respiratory chain components, and increase in the mitochondrial respiration, oxygen consumption, oxidative phosphorylation. Accelerated mitochondrial electron transport caused by the thyroid hormone-induced hypermetabolic state, results in the increased generation of superoxide at he site of ubiquinone. Super oxide radicals lead to the formation of many reactive species, including hydroxyl radicals, which quickly start the free radicals process of lipid peroxidation [1]. It has been suggested that increased oxygen radicals are responsible for the pathogenesis and complications of the disease via lipid peroxidation [1].

Free oxygen radicals caused oxidative damage of the molecules, have a role in the etiopathogenesis of several diseases including neurodegenerative disorders, diabetes mellitus, cardiovascular diseases and different cancer types. The reactive structure and intermediate products of oxygen have been thought to participate in autoimmune diseases of endocrine glands like some thyroid diseases. Among these, the most seen one is the Grave's disease characterized by excessive thyroid hormone synthesis due to continuous stimulation of thyroid stimulating hormone receptors by the thyroid stimulating antibodies. Oxidative stres has benn thought to have role in the pathogenesis of this disease [2]. The researches showed that by the normalization of increased thyroid hormones the lipid peroxitation levels decreased and the antioxidant vitamins accelerated this effect [3].

The effects of thyroid hormones in the metabolic pathways are well known, but the effects of the thyroid hormone excess and deficiency on the lipid peroxidation and antioxidant systems have not been brought out clearly till now.

On this background, we planned to investigate whether hyperthyroidism and hypothyroidism could induce an oxidative stress and antioxidant capacity difference or not.

MATERIAL AND METHODS

The patients who were enrolled in this study were selected among the patients who applied to Afyon Kocatepe University Medical Faculty Internal Medicine policlinics and not treated before. The patients did not have any systemic disease and were not using cigarette and alcohol. The diagnosis was made by determination of

serum thyroid stimulating hormone, free T3 and free T4 levels in addition to clinical manifestations and physical examination findings of the patients.

In this study, twelve overt hypothyroid, thirteen subclinically hyperthyroid, ten overt hypothyroid, and fifteen subclinically hypothyroid, totally fifty patients (40 women, 10 men) were evaluated. The mean age of the patients was 40+-20 years. Fifteen healthy individuals without any systemic disease and who were not using cigarette and alcohol were included in the control group. The serums of the patients were kept at -20 C. Thyroid hormones were analyzed by Hitachi E170 (Elecsys module) immunoassay analyzer using electrochemiluminence method. İn the analysis of Malonyldialdehyde (MDA) and carbonyl content, Shimadzu UV-1601 spectrophotometer was used. Sulfydryl (SH) groups measurements were made by Biotech Trinity device.

Statistical Analysis

The results were given as mean ± Standard deviation. Oneway – ANOVA test for comparisons within the groups, Tukey test for the groups of which the variants were homogenous, Tamhane test for the groups of which the variants were not homogenous were used. $P < 0,05$ was considered to be statistically significant.

RESULTS

In our study, MDA levels and carbonyl content and SH groups were compared in overt and subclinically hyperthyroid and hypothyroid patients with controls.

Serum MDA levels were found to be higher in overt hypothyroid and subclinical hyperthyroid patients than the control group and the difference was statistically significant (p<0,05). The levels of the other groups were higher than the controls also, but the differences were not significant (Figure 1).

The protein carbonyl levels of the patient groups were higher than control group (Figure 2), but the difference is significant only in the subclinical hypothyroid patient group (p<0,05). The serum SH levels were shown in figure 3. The serum SH levels of all the groups were lower than controls. The differences between the control group and overt hyperthyroid, subclinical hyperthyroid and overt hypothyroid groups were significant (p<0,05).

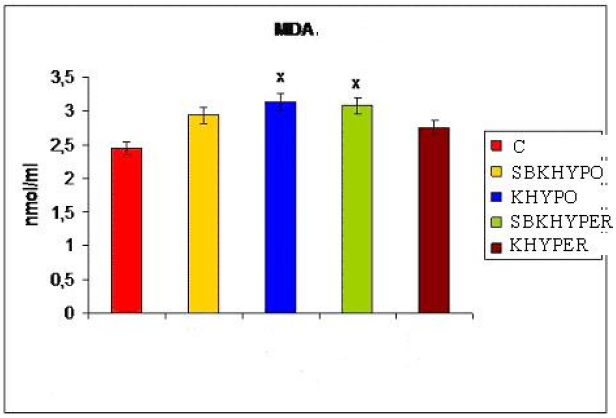

Fig 1. MDA levels, * p<0,05 C: control, SBKHYPO: subclinically hypothyroid, SBKHYPER:subclinically hyperthyroid, KHYPO: clinically hypothyroid, KHYPER: clinically hyperthyroid.

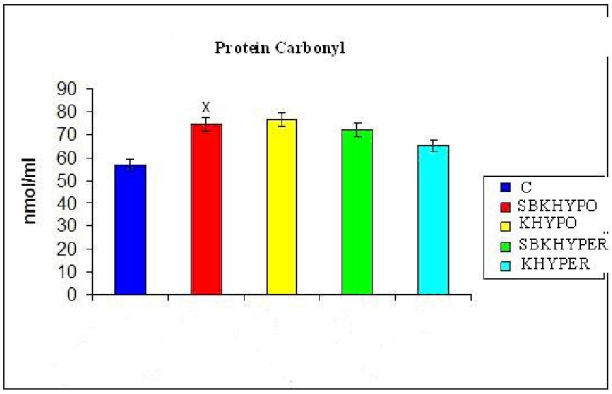

Fig 2. protein carbonyl levels, * p<0,05 C: control, SBKHYPO: subclinically hypothyroid, SBKHYPER:subclinically hyperthyroid, KHYPO: clinically hypothyroid, KHYPER: clinically hyperthyroid.

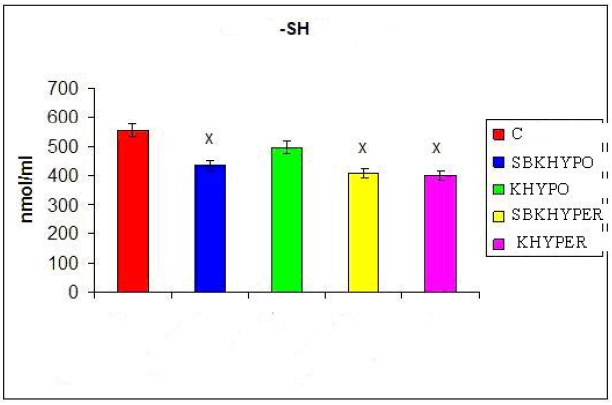

Fig 3. SH levels p<0,05 C: control, SBKHYPO: subclinically hypothyroid, SBKHYPER:subclinically hyperthyroid, KHYPO: clinically hypothyroid, KHYPER: clinically hyperthyroid.

DISCUSSION

Oxygen free radicals play a role in the pathogenesis of tissue damage in many pathological conditions via the peroxidation of membrane phospholipids [4]. Particularly it was stated that free oxygen radicals induced by thyroid hormones caused oxidative stress and eventually increased lipid peroxidation. Although the physiopathological consequences of this condition have not been explained exactly yet, this biochemical alteration was thought to be responsible from some of the complications hyperthyroidism [4]. One of major effects of thyroid hormone is to increase mitochondrial respiration by changes in the number and activity of mitochondrial respiratory chain components. In this condition, accelerated mitochondirial electron transport, results in the generation of many reactive oxygen species including hydroxyl radicals and of the superoxide radical at the site of ubiquinone [5].

Reactive oxygen species cause oxidative damage in protein, carbohydrate, and lipid molecules [6,7]. The reactive oxygen species induced by the effects of thyroid hormones have influences on lipids, proteins, nucleic acids, and carbohydrates. Lipid peroxidation and carbohydrate oxidation products make modifications in amino acid content of proteins and increase plasma protein carbonyl contents. The damage caused by ROS, is related to the imbalance between toxic molecules and antioxidant capacity [7]. The researchers suggested that increased thyroid hormone levels provoked hyperthyroidism symptoms and increase of free radical. Increase of free radical was also seen in the Grave's disease.

In our study, MDA levels and protein carbonyl contend and SH groups of the overt and subclinical hyperthyroid and hypothyroid patients were compared with the control group. Serum MDA levels were found to be higher in overt hypothyroid and subclinical hyperthyroid patients than the control group. Although the carbonyl and SH group levels were higher, the difference between the patients and controls was not significant. The increase in MDA levels in hyperthyroidism may be due to the increased metabolic rate.

Yılmaz et al [8] found that MDA levels in the muscle and liver tissues of experimental hypothyroid rats were higher than the controls groups. These findings were similar to our study. In another study, it was stated that plasma lipid peroxidation levels increased both in hyperthyroidism and hypothyroidism [9]. There were also studies which suggested that the lipid peroxidation levels decreased in both groups [10], and the increased MDA levels decreased [11] after the therapy in hyperthyroid patients [12].

Guerra et al [13] observed a positive correlation between the heart rates and urinary MDA levels of hyperthyroid patients. This correlation was supported after methimazole and antioxidant applications. There was also correlation between the thyroid hormone levels and urinary MDA levels. Increased plasma MDA levels in hyperthyroid patient were reported in other studies.

Serum protein carnonyl levels was the other parameter which we investigated in our study. The protein carbonyl levels of the patients groups were higher than control group, but the difference is significant only in the subclinical hypothyroid patient group. There was no statistically significant increase between the groups.

Çakatay et al [14] found that the plasma carbonyl levels of hyperthyroid patients increased.

Das K. et al [15] studied on the hypothyroidism induced rats and determined significant increases in the mitochondrial carbonyl contents of hypothyroid rats after PTU and T3 applications.

The free oxygen radicals induced by thyroid hormones cause oxidative protein damage and protein carbonyl levels may increase due to this damage.

Oxidative protein damage is characterized by increase in protein carbonyl levels and decrease in protein thiol levels. In our study serum SH levels of all the groups were lower than control. The differences between the control group and overt hyperthyroid, subclinical hyperthyroid and overt hypothyroid groups were significant. There was no significant difference between the patient groups.

Protein SH groups are important chain-break antioxidants. Protein SH groups are sensitive to the oxidative stress and decreased levels have been demonstrated in the diseases which oxidative stress exists like coronary artery diseases, diabetes mellitus, and rheumatoid arthritis [16].

Köse et al [17] investigated the plasma MDA and SH levels in hyperthyroid patients. Plasma MDA levels were found to be higher and SH levels were found to be lower than the controls. Our data are in agreement with these findings. The decrease in the SH levels may be attributed to the protein oxidation resulted from accumulation of lipid peroxide radicals and break down (degradation) products like MDA.

In conclusion, serum MDA and protein carbonyl levels increase and increase and SH levels decrease distinctively in hyperthyroid patients. The changes in thyroid hormone levels trigger free radical formation and increase the MDA and carbonyl levels. The decrease in the SH groups which are natural antioxidants protecting the organism from oxidative stress, is an important indicator of the oxidative damage.

These findings make us think that thyroid hormones can cause changes in antioxidant defence system and peroxidation and protein oxidation in tissues

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