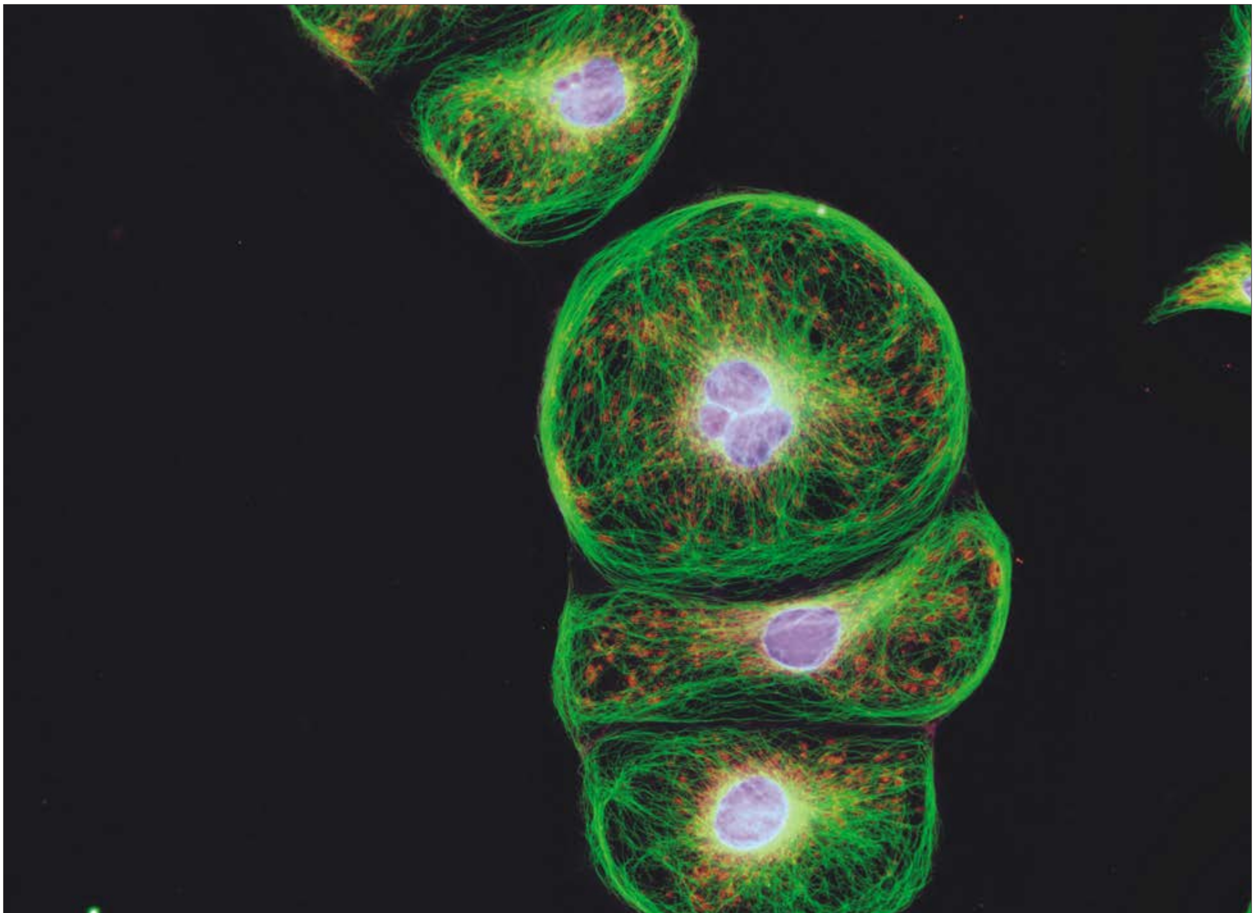

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Lipid Peroxidation in the Serum of Hypothyroid Patients (In Gorgan-South East of Caspian Sea)

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Abstract: This study was designed to determine if lipid peroxidation can be modified by hypothyroidism. Twenty eight subjects with hypothyroidism and 33 euthyroid subjects participated in this study (2007). Blood samples were collected and serum malondialdehyde, T3, T4 and TSH were measured. An increase in lipid peroxidation (expressed as Malondialdehyde, MDA) and TSH levels and also a decrease in T4 level were observed in the hypothyroid patients when compared with control groups ($p<0.001$). The level of T3 was not changed when compared with control groups. The results shows that hypothyroidism may not modulate the free-radical-induced oxidative damage and that hypothyroidism may not present some protection against lipid peroxidation. Thus, the enhancedlipid peroxidation may play a role in the free-radical-induced oxidative damage of some tissues in hypothyroidism. These may show that there is an important relation between hypothyroidism and lipid peroxidation.

Key words: Hypothyroid patients-lipid peroxidation

INTRODUCTION

Thyroid hormones play an important role in the control of human metabolism. Acceleration of the basal metabolic rate and the energy metabolism of tissues in several mammalian species represent one of the major functions of thyroid hormones (Schawrtz and Oppenheimer, 1978). Thyroid hormones include the iodinated amino acid derivatives T3 (3, 3, 5-triiodo-L-thyronine) T4 (3, 3, 5-tetraiodo-L-thyronine) the only iodinated hormones produced endogenously. T3 is the biologically active hormone and is mostly produced from T4 in extra thyroidal tissues. T4 lacks significant bioactivity and is a hormone precursor. With the possible exception of the adult brain, anterior pituitary, spleen and testes, thyroid hormone exerts a thermogenic (calorigenic) effect and increases oxygen consumption and energy expenditure through its effect on ATP formation and breakdown (Bhagavan, 1992). Hypothyroidism (underactivity of the thyroid gland) is a disease in which the thyroid gland produces less than the normal amount of thyroid hormones (T3 and T4). The result is a slowing down of many bodily functions. While decreased thyroid function is commonly associated with weight gain, fatigue, cold intolerance and depression, suboptimal thyroid function has also been associated with increased frequency of heart failure, coronary heart disease (Chokrabarti *et al*., 2006;

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Schmidt-Oft and Ascheim, 2006). Free radicals are highly reactive molecules generated by biochemical redox reactions that occur as a part of normal cell metabolism and in the course of free radical mediated diseases such as cancer, diabetes mellitus, cardiovascular and renal diseases (Kohen *et al*., 1996). Free radicals may cause lipid peroxidation (the level of lipid peroxidation expressed as malondialdehyde) and damage macromolecules and cellular structure of the organism, endothelium and erythrocytes. Oxygen free radicals have important effects on the pathogenesis of tissue damage of several pathologic conditions (Halliwel, 1994). Serum Malondialdehyde (MDA) is the breakdown product of the major chain reactions leading to definite oxidation of polyunsaturated fatty acids such as linoleic and linolenic acid and thus serves as a reliable marker of lipid peroxidation (Boaz *et al*., 1999; Fiorillo *et al*., 1998). Free radicals are eliminated from the body by their interaction with non-enzymic and enzymic antioxidants such as uric acid, albumin, bilirubin, vitamins E, C, A, glutathione, glutathione peroxidase, super oxide dismutase and catalase (Kohen *et al*., 1996). Previous clinical and experimental studies showed a changed free radical level (with different results) in hypothyroidism. Some of the studies showed an increase (Dumitriu *et al*., 1988; Chattopadhyay *et al*., 2003; Sawant *et al*., 2003) while some other showed a decrease (Brzezińska, 2003; Yilmaz *et al*., 2003) or no significant differences (Mano *et al*., 1995; Venditti *et al*., 1997; Gredilla *et al*., 2003; Dariyerli *et al*., 2004). For this reason the present study was designed to evaluate the effect of hypothyroidism on lipid peroxidation and compare to euthyroid subjects in Gorgan (South East of Caspian Sea).

MATERIALS AND METHODS

Twenty eight hypothyroid patients (mean age 37.25±12.16 years) and 33 euthyroid subjects (mean age 38.06±11.40 years) participated in this study. Subjects were selected randomly from the population referred to the Danesh Medical Laboratory in Gorgan (2007). Groups were matched for age and sex. This study was carried out during 2007. A blood sample was collected from each subject and serum Malondialdehyde (MDA), T3, T4 and TSH (thyroid stimulating hormone) levels were measured for each of these groups. Lipid peroxidation (the level of lipid peroxidation expressed as Malondialdehyde [MDA]) was determined using previously described method (Satoh, 1978) and spectrophotometry techniques (Model JENWAY 6105 UV/VIS) in the Laboratory of Biochemistry (Faculty of Medicine). T3, T4 and TSH were determined with Radio Immune Assay method and Gamma Counter techniques (Model DL 100 Operation Manual) in Danesh Medical Laboratory. Results were evaluated by student t-test and expressed as mean±standard deviation. $p<0.05$ was considered significant.

Malondialdehyde Measurement

About 2.5 mL of trichloroacetic acid is added to 0.5 mL plasma and the tube was left to stand for 10 min at room temperature. After centrifugation at 3500 rpm for 10 min, the supernatant was decanted and the precipitate was washed once with sulfuric acid. Then 2.5 mL sulfuric acid and 3 mL Thiobarbituric Acid (TBA) in sodium sulfate were added to this precipitate and the coupling of lipid peroxide with TBA was carried out by heating in a boiling water bath for 30 min. After cooling in cold water, the resulting chromogen was extracted with 4 mL of n-butyl alcohol by vigorous shaking. Separation of the organic phase was facilitated by centrifugation at 3000 rpm for 10 min and its absorbance was determined at the wavelength of 530 nm.

RESULTS AND DISCUSSION

When the results of the two groups were compared, serum MDA and TSH levels were significantly higher in the patient group than in the euthyroid group ($p<0.001$). Serum levels of T4 was

Table 1: Serum lipid peroxidation, T3, T4 and TSH in hypothyroid patients and euthyroid subjects

Parameters	Hypothyroid	Euthyroid	p-value
No. of subjects	28.00	33.00	--
Age (year)	37.25±12.16	38.06±11.4	0.596
MDA (nmol mL^{-1})	1.92±0.41	1.11±0.36	<0.001
TSH (mU L^{-1})	9.56±6.01	2.13±1.08	<0.001
T3 (ng dL^{-1})	1.38±0.45	1.53±0.42	0.184
T4 (mg dL^{-1})	63.75±16.94	91.51±19.0	<0.001

All values shown are expressed as the mean±SEM. $p<0.05$ was considered significant

significantly lower in the patient group than the euthyroid group ($p<0.001$). Serum level of T3 was not changed when compared with euthyroid group (Table 1).

The data presented in this study show that hypothyroid patients may not be resistant to oxidative stress than euthyroid subjects and this maybe can not protect the hypothyroid patients against oxidative stress and tissue damage. Present study confirms that lipid peroxidation is markedly higher in hypothyroidism than euthyroid subjects. In previous studies, different interpretations were given. Venditti *et al*. (1997) showed that in all tissues of hypothyroid rats, the Malondialdehyde (MDA) levels did not differ significantly from euthyroid values. Mano *et al*. (1995) found that the concentration of lipid peroxides, determined indirectly by the measurement of thiobarbituric acid reactants, did not change in hypothyroid rats when compared with euthyroid animals. Gredilla *et al*. (2003) demonsterated that *in vivo* and *in vitro* lipid peroxidation did not change in the hypothyroid state. Dariyerli *et al*. (2004) showed that there is no statistically significant difference found between hypothyroid and control groups. Brzeziñska-Slebodziñska (2003) investigated that the induced hypothyroidism resulted in a significant decrease in the serum concentration of the lipid peroxidation end-product malondialdehyde, as measured by the thiobarbituric-acid assay (another marker for measuring of lipid peroxidation). Dumitriu *et al*. (1988) showed that the mean malondialdehyde level was significantly higher in both hyperthyroid and hypothyroid patients by comparison to the control group. Chattopadhyay *et al*. (2003) observed that lipid peroxidation, an index of oxidative stress, was elevated in the heart tissue in hypothyroid state. Yilmaz *et al*. (2003) showed that malondialdehyde level of hypothyroid rats was increased in liver, but they were decreased in the tissues of the heart and thyroid.

Sawant *et al*. (2003) demonsterated that the tissue lipid peroxidation level significantly increased in hypothyroid rats. We determined that the level of lipid peroxidation products was higher in the hypothyroidism group than control levels. The results of this study are in agreement with the results of studies showing that the level of MDA is significantly increased (Dumitriu *et al*., 1988; Chattopadhyay *et al*., 2003; Sawant *et al*., 2003). But present results are not in agreement with the other studies (Mano *et al*., 1995; Venditti *et al*., 1997; Gredilla *et al*., 2003; Dariyerli *et al*., 2004; Brzeziñska, 2003; Yilmaz *et al*., 2003). The increase in reactive oxygen species induced by thyroid hormone may cause an oxidative stress condition in some tissues with a consequent lipid peroxidative response. Possible sources of elevated free radicals in hypothyroid patients include increased production of radical oxygen species, especially from lipid peroxidation processes and probably decreased antioxidant defense systems. The cause of our observed increase of MDA in hypothyroid patients is not known. It is possible that hypothyroid-related changes in fatty acid composition of cells may provide sufficient substrate for lipid peroxidation.

In conclusion, the results show that hypothyroidism may not modulate the free-radical-induced oxidative damage and that hypothyroidism may not present some protection against lipid peroxidation. Thus, the enhanced lipid peroxidation may play a role in the free-radical-induced oxidative damage of some tissues in hypothyroidism. These may show that there is an important relation between hypothyroidism and lipid peroxidation. In summary; hypothyroidism is associated with increased susceptibility to lipid peroxidation compared to that in the euthyroid state.

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