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Research Article

Blood Glucose, some Electrolytes Levels and Stress Oxidative Status of Female Hyperthyroid Patients under Treatment

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Abstract

The present study was designed to investigate the hyperthyroidism effects on stress oxidative state, blood glucose, hemoglobinand serum electrolytes levels in female patients under treatment. In this work 24 cases of overt hyperthyroidism were chosen, 24 age matched controls were chosen. Blood samples were collected from them and T3, T4 and TSH levels were measured. Also, glucose, hemoglobin, MDA, GSH, Sodium, Potassium and Chloride levels in blood was measured. Results obtained show that Lipid peroxidation ($p < 0.01$), blood glucose ($p<0.05$) and hemoglobin ($p<0.001$) level were significantly elevated simultaneously with a significant decrease ($p < 0.05$) in the levels of GSH in all patients with thyroid dysfunction as compared to control. The levels of serum sodium was significantly increased ($p < 0.05$)in these cases than controls and on the other hand serum potassium and chloride concentrationswere significantly and non-significantly decreased successively in hyperthyroid patients when compared to the control subjects. In hyperthyroidismpatients, there was a significant negative correlation ($r= - 0.998$; $P<0.05$) between the levels of reduced glutathione (GSH) with concomitant increase in MDA levels butthere was a no significant correlation ($P>0.05$) between serum MDA values and serum electrolytes and TSH levels.The results of this study reveal the importance of monitoring the levels of thosestress oxidative levels and biochemicalparameters in thyroid dysfunction patients before therapy, especially when the disease ismore severe.

Keywords: Hyperthyroidism, Stress oxidative, Electrolytes, Sodium

Introduction

Thyroid hormones influence the growth andmaturation of tissue, energy metabolism, and turnover of both cells and nutrients.Thyroid hormones perform a wide array of metabolicfunctions including regulation of lipid, carbohydrate, protein and electrolyte and mineral metabolisms [1]. Hyperthyroidism is a condition caused by unregulated production of thyroid hormones. Thyrotoxicosis is a serious sequel of hyperthyroidism that corresponds to an overt tissue exposure to excess circulating thyroid hormones. It is well known that oxidative stress (OS), defined as an imbalance between radicals and antioxidant defense, isimplicated as a pathophysiological mechanism of different diseases and is a topic of growing interest[2]. There is much evidence that show both hyperthyroidism and hypothyroidism are related to oxidative stress and cellular damage[3].Variations in the levels of thyroid hormones can be one of the main physiological modulators of in vivo cellular oxidative stress due to their known effects on mitochondrial respiration[4]. In particular, it has been suggested that the increases in reactive oxygen species induced by a deficiency of thyroid hormones can lead to an oxidative stress conditions in the liver and in the heart and some skeletal muscles with a consequent lipid peroxidative response [5]. The primary role of electrolytes lies in the maintenance

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of body ionic and water balance. Thus the requirements for strong ions that have characteristic effects on body fluids homeostasis cannot be considered individually because it is the overall balance that is important. It is well known that nutrition and environment influenced the bird's acid-base balance[6]. Electrolyte disorders are common in hospitalised patients with dysnatraemia being the most common ones [7]. In recent years research has focused on outcomes of patients with electrolyte disorders, mainly hypo- and hypernatraemia, which were found to be associated with increased mortality[8]. Sodium and potassium are important components of the enzyme Na^+-K^+ ATPase, which is an enzyme present on the cell membrane that helps in the transport of water and nutrients across the cell membrane[9]. Thyroid hormones regulate the activity of sodium potassium pumps in most of the tissues[10].On the other hand, hypocalcaemia were mentioned in patients with thyrotoxicosis[11]. The higher prevalence of thyroid disease in women suggests that estrogen might be involved in the pathophysiology of thyroid dysfunction. Estradiol has an antagonistic effect on the hormones T3 and T4. The reason being, estradiol competes with T3 and T4 for binding sites on the receptor proteins [12].With this background the present study was undertaken to assess the stress oxidative and the alterations in the levels of serum electrolytes in, hyperthyroid patients and euthyroid subjects. Hence the present study was done only in female thyroid patients and controls.

Materials and methods

Subjects

Ethical approval (Appendix) was sought and approved by the Ethical Committee of the Department of Cell and Molecular Biology, Faculty of natural science and life, University of ElOued. We studied patients with newly diagnosed and treated hyperthyroidism (24 females), mean aged 43.83 ± 4.86 years. A total of 24females' healthy volunteers (mean aged 38.83 ± 5.45 years) served as controls with normal serum TSH. To eliminate the factors which might affect free radical antioxidant activity, we excluded all diabetics and other chronic diseases subjects from patient groups and healthy controls.

Analysis of samples

3ml of fasting venous blood sample was drawn from the patients and controls. blood samples were collected and placed into containing tubes. After centrifugation at 3000 ×zzzz g for 5 min the serum were removed and retained for assay of the level of glucose, MDA, GSH and all the electrolytes, respectively. Serum samples were stored at -20°C until analysis. Serum concentration of total tri iodothyronine (T3), total thyroxin (T4) and TSH were measured by mini-VIDIS assay using kit supplied by Biomerieux Marcy-l´Etoile/ France. Serum Electrolyte levels (Na+, k+ &Cl-) were determined by Electrolyte Analyzer (Easylyte PLUS Na/K/Cl de Medica) . The thiobarbituric acid method of Buege and Aust (1978) [13] was used to measure MDA, which reacts with thiobarbituric acid to yield a pink color. Absorbances were determined at 532 nm.The reduced glutathione (GSH) was measured spectrophotometrically in serum, by the method of Akerboom and Sies (1981)[14], using 5, 5dithiobis(2-nitrobenzoic acid). Absorbances were determined at 412 nm.

Statistical analysis

The reported data are the means of measurements and their standard error of mean (SEM) values. The results of cases and controls were compared by student't' test using minitab software (version 13.31). $P < 0.05$ was considered the limit for the statistical significance.

Results

The results show a highly significant ($p < 0.001$) increase in the levels of T3 inwomen hyperthyroidism patients compared to control. A similar trend of significance ($p < 0.01$)was noticed in the serum level of T4 in women hyperthyroidism patients. On the other hand there was ahighlysignificant ($p < 0.001$) decrease in TSH value of hyperthyroidismpatients when compared to control group (Table 1).

Table 1.Clinical characteristics of females hyperthyroid patients and controls

Group description	Control subjects (n=24)	Hyperthyroid patients (n=24)
Mean age	38.83±5.45	43.83±4.86
T3 (µmol/L)	5.01±0.27	10.06±3.29***
T4 (µmol/L)	13.53±1.24	19.03±2.98**
TSH (mUI/l)	3.68±0.51	0.096±0.026***

Values are mean ± SE.

Significant difference with control group: ** $p < 0.01$ *** $p < 0.001$

Resultsobtained shown that, hyperthyroid caused a significant increases in blood glucoselevel ($p<0.05$) and in hemoglobin concentration ($p<0.001$) compared to the control subject(Table 2).as shown in table2, serum MDA shows a highly significant ($p < 0.01$) increase in hyperthyroid patients groups compared with that of control group. A significant ($p < 0.05$) decrease in serum glutathione reduced GSH occurs in hyperthyroid patients group as compared with control group.

Table 2.Blood glucose level, hemoglobin concentration and oxidative stress parameters in patient and control subject

Group description	Control subjects (n=24)	Hyperthyroid patients (n=24)
Blood glucose (g/l)	0.83±0.02	1.07 ± 0.01*
Hb (g/l)	119.38±2.16	138.88±3.78***
MDA (µmol/l)	1.219 ±0.206	1.786± 0.140**
GSH (nmol/l)	0.169± 0.026	0.157 ± 0.019*

Values are mean ± SE.

Significant difference with control group: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Also, results shows a significant ($p < 0.05$) increase in the levels of serum sodium and a significant decrease in the levels of serum potassium occur in hyperthyroid patients as compared with control subjects. Serum chloride shows a no significantly difference in hyperthyroid patients compared with that of control subjects as shown in figure 1

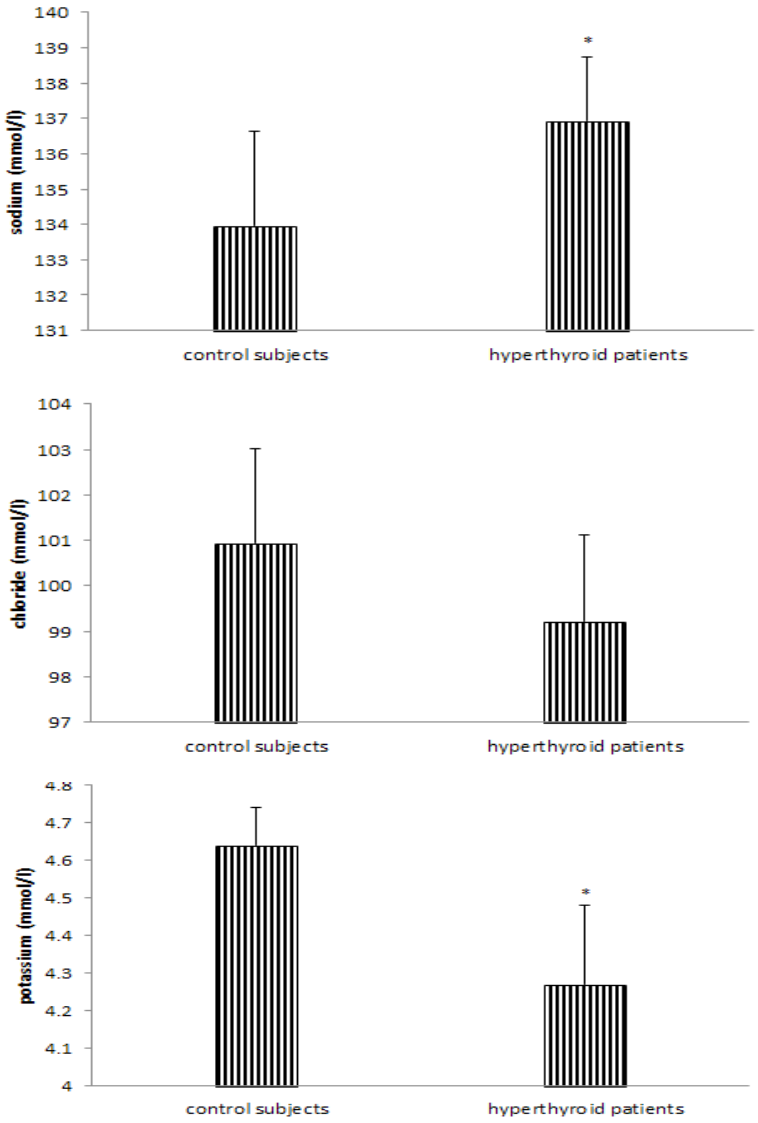

Figure 1.Serum Sodium, Potassium and Chloride level in women hyperthyroid patients and controls. Values are mean ± SE. Significant difference with control group: * $p < 0.05$.

Table 2 shows the results of correlation between oxidative stress index (represented by MDA level) and concentration of GSH, TSH and electrolytes in hyperthyroid patients, a significant correlation was noticed between MDA and GSH (r=0.998; P<0.05) in hyperthyroidism patients. Also, a non-significant correlation (P>0.05) was observed between MDA and TSH and between MDA and serum electrolytes in hyperthyroid patients.

Table 3.Correlation coefficients and the significant levels of different serum chemical components in women patients with hyperthyroidism

Parameters	Hyperthyroid patients	
Component vs. MDA	R	P
TSH (mUI/l)	-0.522	0.229
GSH (nmol/l)	-0.998	0.045
Sodium (mmol/l)	-0.188	0.655
Potassium (mmol/l)	-0.520	0.187
Chloride (mmol/l)	-0.165	0.696

Discussion

It was the aim of the study to investigate the effects of thyroid dysfunction on blood glucose, hemoglobin concentration and serum electrolytes levels and stress oxidative state. According to differentcase reports in the literature someone could expect electrolyte disturbances in any sort of thyroid dysfunction. Our results shown that the level of blood glucose and hemoglobin are increased in hyperthyroid subjects compared to control. Thyroid hormones increase glycogen degradation and gluconeogenesis, resulting in increased blood glucose levels[15].The explanation of hemoglobin result is based on erythropoietin which is a natural glycopeptide hormone developed by the kidneys also by the liver which stimulates erythropoiesis, the process of production of erythrocytes (red blood cells), [16]. Among the hormonal factors regulating erythropoiesis that elevate the secretion of erythropoietin is thyroxin which explains the occurrence of polycythemia in hyperthyroidism [17], this is probably reflected in the hemoglobin and causes their elevation.Impairment in the oxidant/antioxidant equilibrium creates a condition known as oxidativestress. Oxidative stress is defined as an imbalance in the balance between antioxidants and pro-oxidants in favor of antioxidants [18]. There is a complex interaction between antioxidants and oxidants such as reactiveoxygen species, which modulates the generation of oxidative stress [19]. As per figure 1 concentration of serum MDA is increased bat the GSH concentration is significantly decreased in hyperthyroidism patients as compared to the control group which generate oxidative stress .Oxidative stress is caused by a relative overload of oxidants, reactive oxygen species[20]. Similar types of findings were observed in a study conducted by Dipaket al. (2005) [21]. Glutathione (GSH) participate in the cellular defense system against oxidative stress by scavenge free radicals and reactive oxygen intermediates [22].Hyperthyroidism is a hyper metabolic state accompanied by increased oxygen utilization, increased production of reactive oxygen species and consequently measurable changes in anti-oxidative factors [23].Because thyroid hormones modulate many functions, if thyroid hormone levels change, many cellular processes could be altered, including modifications in the REDOX environment. Because one of the most studied effects of the thyroid hormone is the control of the basal metabolic rate, a hypermetabolic state produces a modification of the REDOX environment [24]. It is well-known that a higher T_3 level, a hyper metabolic state, causes calori genesis in two ways. The first is a short-term signaling mechanism with the allosteric activation of cytochrome-C oxidase and the second is a long-term pathway producing nuclear and mitochondrial gene transcription through T_3 signaling, thus stimulating basal thermogenesis [25].In rat liver, T_3-induced hyperthyroidism was found to be associated with altered lipid-peroxidation indices, including elevated levels of thiobarbituric acid reactive substances (TBARS) and hydroperoxides[26]. One of the major effects of thyroid hormone is to increase mitochondrial respiration by many complex changes in the number and activity of mitochondria respiratory chain components[27]. Accelerated mitochondrial electron transport, brought about by a thyroid hormone-induced hypermetabolicstate, results in the increased generation of superoxide at the site of ubiquinone.Superoxide radical can lead to the formation of many other reactive species, including hydroxyl radicals, which can readily start the free radical process of lipid peroxidation[28].Results of this study indicate that in women hyperthyroidpatients an increase in sodium; level and descrease in potassium concentrationand no significantly difference of Serum chloride compared to the controls. Hypernatremia is a common electrolyte problem and is defined as a rise in serum sodium concentration to a value exceeding 145 mmol/L.Thyroid hormones are involved in controlling various metabolisms, more importantly lipid metabolism and that of various electrolytes, the hypothyroid patient generally suffers from a slow metabolism resulting in electrolyte disturbances [29]. Sodium and potassium are important components of the enzyme Na-K ATPase, which

is an enzyme on the cell membrane that helps in the transport of water and nutrients across the cell membrane. Thyroid hormones regulate the activity of sodium potassium pumps in most of the tissues [30]. Sodium and chloride are interdependent and changes in sodium ions will also be reflected in the chloride ions. it is postulated that hormones which are involved in ECFV (Extracellular Fluid Volume) regulation act on renal sodium transporters may also modulate the renal chloride transporters[31].As plasma water decreases, increases in plasma sodium concentration and osmolality are sensed by nuclei in the hypothalamus, with a resultant increase in production of ADH by the supraoptic and paraventricular nuclei. ADH acts to increase renal free water reabsorption in the collecting tubule to restore plasma water, resulting in a correction of plasma sodium concentration back towards the normal range [32]. The non-significant variations in potassium and chloride concentrations during the hypothyroid disease and the non-significant correlation with MDA level suggest that neither the dysthyroidism nor stress oxidative had any significant effect on these serum electrolyte levels during the hypothyroid in female patients. The correlation between MDA and GSH in patients with hypothyroidism represents the direct effect of MDA on antioxidant components level. Reduced glutathione functions as a direct free radical scavenger as a co-substrate for glutathione peroxide (GPx), which explained decreased GSH concentration with increased oxidative stresss [33].

Conclusion

In conclusion, the present study suggests a very high production of ROS and oxidative stress in patients with hyperthyroidism, with enhanced lipid peroxidation and concomitant failure of antioxidant defense mechanism, can eventually led to many other complications. Also, blood glucose, hemoglobin and electrolytes disturbances need to be monitored and treated appropriately to avoid the ill effects resulting from the changes in the blood levels of these parameters.

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Conflict of Interest: None

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