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Oxidative stress in thyroid dysfunction

Abstract

Thyroidal dysfunction is a risk factor for the development of many metabolic disorders and pathologies. In this work we evaluated the status of the oxidative stress in hypo- and hyperthyroidism, as a sign for developing associated diseases. A total of 44 participants have been recruited and distributed into three groups: Euthyroidism (6), Hypothyroidism (29) and hyperthyroidism (9). Their hematological and biochemical parameters were diagnosed. Free thyroxin 4 (FT4) and thyroid stimulating hormone (TSH) were determined using Elisa kits. Malondialdehyde (MDA), glutathione peroxidase (GPx), superoxide dismutase (SOD) and glutathione (GSH) were measured in plasma samples by spectrophotometric methods. Our results showed an increase in lipid peroxidation in both hypo- and hyperthyroidism (1.14 ±0.631 µmol. L-1 and 0.904 ±0.179 µmol. L-1 , respectively) in comparison to normal cases (0.821 ±0.173 µmol.L-1). Our findings highlight the misbalance of the oxidative stress occurrence in hypo- and hyper-thyroidism due to the subsequent metabolic rate disturbances.

Keywords: hypothyroidism, hyperthyroidism, oxidative stress

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Introduction

Thyroidal disorder is a worldwide common health problem. In general, three thyroidism's conditions are recognized: euthyroidism with normal levels of thyroid's hormones and hyperthyroidism or hypothyroidism that are respectively characterized by high or low range of thyroxines' productions. Etiology of the disease includes congenital abnormalities, autoimmune disorders and environmental risk factors among which iodine nutritional supply has been well studied.[1,2] Because of the key stone role of thyroid hormones in regulating growth, particularly in young people, thyroidal dysfunction is associated to many other pathological disorders, such as cardiovascular pathology,[3] ophthalmologic disorders,[4] diabetes[5] and nonalcoholic fatty liver disease.[6] Obviously, the oxidative stress misbalance is conceived as a cross-linking mechanism leading to the development of many associated diseases.[7,8] In this work, the oxidative stress condition was investigated in a sample of population with thyroidal disorder.

Patients and methods

This study did include 44 participants visiting the Polyclinic (Metlaoui, Tunisia) for diagnosis of thyroidal dysfunction. Euthyroidism, hypo- and hyperthyroidism were observed respectively in 6, 29 and 9 patients. Blood samples were collected by venipuncture after an overnight fasting in order to determine the hematological, biochemical and oxidative stress parameters. Blood cell counts were made using mindray (BC 5390) automated analyzer, on whole blood samples collected into ethylenediamine tetraacetic acid (EDTA) containing tubes. Plasma contents in glucose, cholesterol triglycerides, creatinine and uric acid were evaluated using Indiko plus (Thermo Fisher Scientific) apparatus. The free thyroxine 4 (FT4) and thyroid stimulating hormone (TSH) hormones were determined using Elisa kits according to the manufacturer's instructions. Malondialdehyde (MDA), glutathione (GSH) and glutathione peroxidase (GPx) and superoxide dismutase (SOD) activities, were respectively quantified using methods described by Buge and Aust,[9] Weckbecker and Cory,[10] Floe and Gunzler[11] and Beauchamp and Fridovich.[12] MDA evaluation is based on determining the amount of substances reacting with thiobarbituric acid in acidified milieu. The formed MDA was spectrophotometrically determined at 532 nm wavelength.[9] Plasma samples were mixed with sulfo-salicyclic acid and left to react with 5,5'- dinthio-2-2 nitrobenzoic acid (DTNB). The intensity of the obtained yellowish color was evaluated at 412 nm, and reflects the GSH concentration.[10] The GPX reducing GSH activity was measured as the disappearing GSH for the reactional milieu using DTNB probe.[11] SOD activity was determined as its capacity to reduce the nitro-blue tetrazolium in presence of riboflavin and methionine, under 20 W fluorescent lamp light. The reaction produces blue formazan metabolite that was detected at 580 nm wavelength.[12] The obtained results were compared between different groups using Anova test and non-parametric LSD test. The statistical analysis was performed using SPSS program for Windows 2017 (IBM corporation). Significant differences were retained at 5 % (Table 1).

Table 1 participants' description

	Euthyroidism	Hypothyroidism	Hyperthyroidism
Number	6	29	9
Age (yrs)	43.30±5.08	53.89±12.20	52.30±18.60
Sex ratio (M/F)	0.17	0.10	0.11
BMI (Kg.m^{-2})	30.60±7.39	27.09±4.82	25.18±4.68
Overweight	0.66	0.22	0.55
Chronic diseases	0.33	0.31	0.44
Diabetes (A)	0.16	0.08	0.33
Hypertension (B)	0.16	0.10	0.00
(A+B)	0.00	0.14	0.11

Results and discussion

Thyroidl dysfunction is an endocrine disorder more frequently affecting women than men.[13,14] In recognition of their physiological role in controlling growth, both low and high levels of thyroid hormones have been associated to many diseases including, cancer, infertility and digestive, reproductive, metabolic, cardiovascular and mental disorders.[15] Similarly, our findings showed that out of 44 participants, 38 women presented thryroidal disorders and that subclinical hypothyroidism was the most frequent in the studied sample (74.36 %). Among patients suffering thyroidal disorders 34.21 % have associated diabetes, hypertension or both chronic diseases, but no significant correlation was found between the occurrence of diabetes nor hypertension with thyroidal status (Table 1). Among hematological disturbances that could be found in thyroidal disorders,[16,17] our results revealed significant ($p = 0.04$) decrease of hemoglobin concentration in both hypo- (12.40±1.13 g.dL-1) and hyperthyroidism (11.76±1.79 g.dL-1) in comparison to euthyroidism 13.81±1.24 g.dL-1). Furthermore, white blood cell count (WBC) was augmented in hyperthyroidism in comparison to hypothyroidism ($p = 0.029$) (table 2). Thyroid stimulating hormone (TSH) showed a slight decrease in hypothyroidism (44.53 ±13.85 µmol.L-1) in comparison to euthyroidism (54.17 ±11.67 µmol.L-1) and hyperthyroidism (51.00 ±13.06 µmol.L-1). The level of free thyroxine 4 (FT4) was relatively higher in both hypo- and hyperthyroidism (5.25 ±5.1 ng.dL-1 and (5.21 ±8.87 ng.dL-1 , respectively) in comparison to normal cases (2.18 ±1.48 ng.dL-1) (Figure 1).

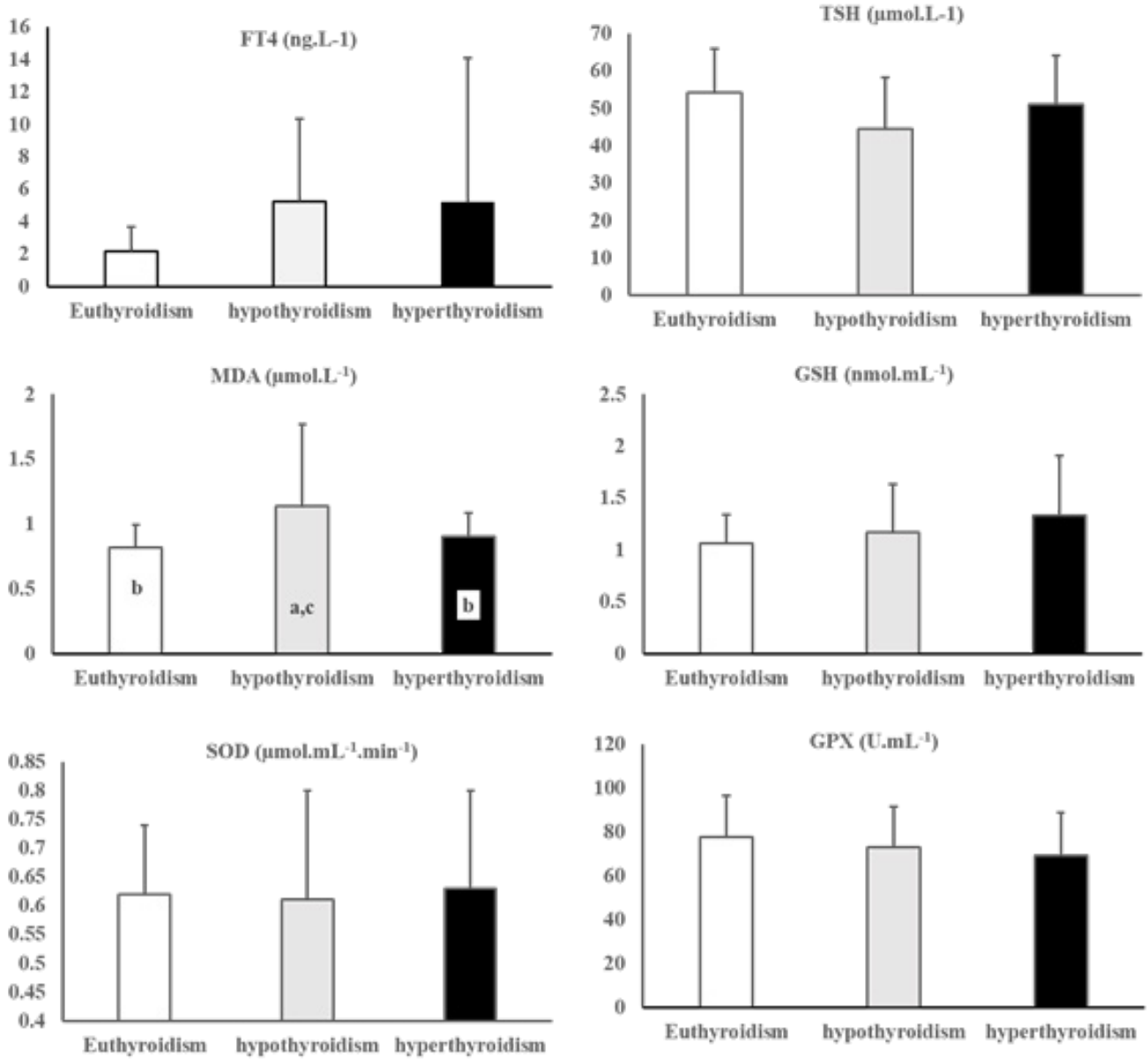

Figure 1 Levels (mean ± SD) of thyroids' hormones and of oxidative stress parameters in patients' peripheral blood. (a, b, and c designate significant differences respectively vs Eu-, Hypo- and Hyperthyroidism, at 0.05).

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Oxidative stress has been linked to the development and progression of diverse pathologies. In both hyperthyroidism and hypothyroidism, investigations revealed a misbalance of the oxidative/ anti-oxidative system.[7, 8,18] That imbalance may be due to changes in metabolic rates leading to excessive production of hydrogen peroxide and nitric oxide.[19] Owing to the excess production of free radicals, there are several tissues damages and inflammation[20] leading to instigation of associated diseases such as diabetes, hypertension and cancer.[7, 8,18] Accordingly, the recent work revealed a misbalance of the oxidative stress status in peripheral blood in thyroiditis. There was significant increase in lipid peroxidation metabolites in hypothyroidism (1.14 ±0.631 µmol. L-1) and hyperthyroidism (0.904 ±0.179 µmol.L-1) when compared to euthyroidism (0.821 ±0.173 µmol.L-1). Also, there was a slight decrease in glutathione peroxidase activity and increase in reduced glutathione levels in patients (Figure 1). The status of the oxidative stress might be reverted by treatment of the thyroid disorders[21,22] and antioxidants' supplementation such as vitamin E.[23, 24]

It is concluded that both hypothyroidism and hyperthyroidism induce a disequilibrium of the oxidative / anti-oxidative balance that can lead subsequent development of inflammation and many associated diseases. This can be prevented by the adequate management of the disease and supplementation with anti-oxidative dietetics (Table 2).

Table 2 blood hematology and biochemistry of participants a, b, and c designate significant differences respectively vs Eu-, Hypo- and Hyperthyroidism, at 0.05, using LSD test

	Euthyroidism	Hypothyroidism	Hyperthyroidism
Hematology			
RBC (10^{12}. L^{-1})	4.58±0.42	4.89±2.51	4.46±0.20
WBC (10^{12}. L^{-1})	6.07±1.54	5.64±1.55 (c)	7.5±2.44(b)
HGB ($g.dL^{-1}$)	13.81±1.24 (b,c)	12.40±1.13(a)	11.76±1.79(a)
HCT (%)	40.28±3.63	38.95±4.29	37.36±3.26
PLT (10^{3}. L^{-1})	288±70	270±80	342±99
Biochemistry			
Glucose ($g.L^{-1}$)	1.09±0.24	1.18±0.03	1.35±0.48
Cholesterol ($g.L^{-1}$)	2.01±0.45	1.92±0.38	2.14±0.81
Triglycerides ($g.L^{-1}$)	1.09±0.55	1.53±1.57	1.34±0.75
Uric acid ($g.L^{-1}$)	9.2±1.5	9.40±1.99	10±1.4
Creatinine ($mg.L^{-1}$)	9.25±1.15	9.49±1.90	10.22±1.14

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Conflicts of interests

Author declares there are no conflicts of interests.

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