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Effect of deficiency thyroid hormone on superoxide dismutase activity enzyme and their related metals in hypothyroid patients in Basrah Governorate/Iraq.

Bushra A.M. AL-Slem Abbas D.M AL- Maliki Kamel Al-Sowdani
Chemistry Department - Education College for pure sciences - Basrah University
Basrah-Iraq

Abstract

The maintenance of optimal health requires an adequate supply of carbohydrates, proteins and lipids, and macronutrients, micronutrients, and trace elements. The present study evaluates the lack secretion of thyroid hormones (hyporthyroidism) on antioxidant enzyme which is **(**superoxide dismutase**)** and levels of zinc and copper in serum of Iraqi patients with hypothyroid .The results showed a highly significant decrease ($p<0.001$) in erythrocyte superoxide dismutase(SOD) activity in patients as compared to control .The level of zinc decrease significantly in hypothyroid patients compared with control while the level of copper decreased in patient group compared with control group but no insignificant ($p>0.05$) . These results indicated that hypothyroidism increased the free radicals due to decreasing the free radicals scavengers.

Keywords: Hypothyroidism, Superoxide dismutase enzyme, Zinc, Copper

تأثير نقص هرمونات الغدة الدرقية على نشاط انزيم فوق اوكسيد ديسميوتيز والفلزات المرتبطة به في مرضى قصور الغدة الدرقية في محافظة البصرة /العراق

بشرى عبد المحسن عبد العزيز السالم عباس دواس مطر المالكي كامل حسن علوان السوداني
قسم الكيمياء – كلية التربية للعلوم الصرفة – جامعة البصرة
البصرة–العراق

الملخص

يحتاج الجسم الى كميات كافية من الكاربوهيدرات ,البروتينات ,الدهون والعناصر النزرة للحفاظ على الصحة .الدراسة الحالية تضمنت تأثير نقص افراز هرمونات الغدة الدرقية على احد مضادات الاكسدة الانزيمية المتمثلة بفوق اوكسيد ديسميوتيز وعلى بعض العناصر النزرة النحاس والزنك في دم المرضى الذين يعانون من قصور نشاط الغدة الدرقية. اظهرت النتائج انخفاض عالي المعنوية في نشاط انزيم فوق اوكسيد ديسميوتيز المقاس في كريات الدم الحمراء للمرضى الذين يعانون من خمول الدرقية مقارنة بأشخاص اصحاء.كما اظهرت النتائج

انخفاض مستوى الزنك والنحاس في مصل دم المرضى مقارنة بالاصحاء وكان الانخفاض عالي معنوية في مستوى الزنك بينما كان الانخفاض غير معنوي في مستوى النحاس .

الهدف من الدراسة الحالية تقييم نشاط كاسحات الجذور الحرة في مرضى يعانون من قصور الغدة الدرقية وتقييم دور العناصر النزرة في عملية الايض سواء كانت مرافقات انزيمية او مغذيات اساسية وهذة النتائج اثبتت ان قصور نشاط الغدة الدرقية يزيد الجذور الحرة بسبب نقصان كاسحات الجذور الحرة.

Introduction

Thyroid hormones are necessary for the normal development of body organs. Decreased thyroid hormones biochemical synthesis and low levels of circulating thyroid hormones result in biochemical and/or clinical hypothyroidism. Deficiency of thyroid hormones causes many metabolic processes to slow down. Thyroid hormones are among the
most important humoral factors involved in setting the basal metabolic rate on a long-term basis in target tissues such as liver, heart, kidney and brain (1) Decreased thyroid hormone synthesis and low levels of circulating thyroid hormones result in biochemical and/or clinical hypothyroidism (2).In the aerobic cells, active oxygen species like superoxide and hydrogen peroxide are generated as by products of oxidative metabolism in mitochondria (3). Reactive oxygen species (ROS) including partially reduced forms of oxygen; i.e. superoxide anion, hydrogen peroxid, and hydroxyl radical, as well as organic counterparts such as lipid peroxidation, are produced as natural consequences of oxidative cell metabolism(4).Under physiological conditions, ROS generation is controlled by a large number of antifree radical systems which act as protective mechanisms. These systems consist of antioxidant enzymes such as superoxide dismutase, catalase, glutathione peroxidase, and glutathione reductase as well as non-enzymatic antioxidants, among which the most important are vitamins C and E, carotenoids, glutathione and uric acid (5). The disturbance of the oxidants / antioxidant balance resulting from the increased production of ROS, inactivation of detoxification systems or excessive consumption of antioxidants is a causative factor in the oxidative damage of cellular structures and molecules, such as lipids, proteins and nucleic acids (6, 7).Superoxide dismutase one of the antioxidant enzymes, it is catalyzes the reaction between two superoxide radicals to yield one molecule each of oxygen and hydrogen peroxide (8). Two superoxide dismutase isoenzymes have so far been described in vertebrates i.e Cu/Zn-SOD (Copper Zinc Superoxide dismutase) and Mn-SOD (Manganese Superoxide dismutase). Cu/Zn- SOD has been demonstrated in the cytoplasm and also in the intermembrane space in mitochondria. Mn-SOD is found in the matrix space in mitochondria (9). Trace elements serve a variety of functions including catalytic, structural and regulatory activities in which they interact with macromolecules such as enzymes; pro-hormones.Zinc has important roles in thyroid metabolism (10); and a fundamental role in protein synthesis (11). It involves in triiodothyronine (T_3) binding to its nuclear receptor (12).while copper is necessary for proper iodine metabolism and Synthesis (13),Copper plays an important role in thyroid metabolism, especially in hormone production and consequently of proper thyroid hormone absorption. Copper stimulates the production of the thyroxine hormone (T_4) and prevents over-absorption of T_4 in the blood cells by controlling the body's calcium levels (Calcium is required for the stabilization of cell membranes and reduces) (14). Copper is a central component of the antioxidant superoxide dismutase molecule.
Hypothyroidism-associated oxidative stress is the consequence of both increased production of free radicals and reduced capacity of the antioxidative defense (15,16).
The present study aims to investigate the free radical scavenging activity, in hypothyroid patients

and the role of trace elements in many metabolic process either as essential nutrients or as cofactors.

Materials and methods

Subject:

Blood samples were collected from 30 patients with hypothyroid (15 females and 15 males),Their age between (16-63)years and 30 euthyroid subjects(15females and 15 males) their age between (15-62) years .The patients who attended to the endocrinology center in AL-Mawani hospital/Basrah governorate in Iraq were diagnosed depending on the results of the following examinations clinical , examinations serum hormones level triiodothyronine (T_3),thyroxine(T_4),thyroid stimulating hormone (TSH). All individuals who were smokers, diabetes mellitus, pregnancy, liver or kidney disorders were excluding.

Samples Collection and Preparation

Ten milliliters of venous blood from fasting subjects were drawn,part from blood allowed to clot and centrifuged at 4000 rpm for 10 minutes serum were separated and stored at -20 $^{\circ}$C.until analysis ,while the remaining from blood collected in heparinized tubes.Blood samples were centrifuged at 3000 rpm for 10 minutes; in order to separated the plsma. The remaining erythrocytes were washed three times with 0.9% NaCl, and lysate in1:1 (v/v) of double-deionised water, which was lysates used for determination superoxide dismutase activity using a kit (RANSOD) from Randox Laboratories.U.K.,Cat NO.SD.125. based on Woolliams *etal* .procedure (17).Serum thyroid hormones (T_3, T_4) and TSH level were determined by mini-VIDS assay using kit supplied by Biomerieux Marcy-I~ Etoile/France. Serum zinc and copper were determined by Spectrophotometric method by using a kit from LTA. Italian and Spectrum, Egypt.

Statistical analysis

The results of the present study were analyzed by univarate analysis of variance using SPSS version 9 was used to analyse the result in the study the data were expressed as mean±SD. least significant different test (LSD) was used to test the difference between groups.

Results

The levels of Serum T_3, T_4, TSH, Zn, Cu and erythrocyte superoxide dismutase activity (SOD) were in subjects with hypothyroidism and euthyroid are listed in table (1) which expressed as mean ±standard deviation.

Table (1): Biochemical characteristics in patients and control groups

Parameter	n=30 Hypothyroidism	n=30Control
T_3(nmol/L)	0.6863***±0.4331	1.724±0.3208
T_4(nmol/L)	52.379***±25.484	86.915±10.9616
TSH(µIU/ml)	33.007***±25.7407	1.377±0.6166
SOD(units/ml)	140.667***±32.263	190.333±45.142
serumZn(µg/dl)	56.582***±23.259	101.53±15.989
serumCu(µg/dl)	132.597 ±30.905	142.861±55.844

***significantly differences between patients and control group ($p<0.001$) respectively.

The results indicated that a highly significant decrease in the levels T_3 and T_4 and increased inTSH in hypothyroidism patients ($p<0.001$) comparing with control group respectively.

SOD shows a highly significant decrease in hypothyroidism compared with control ($p<0.001$). Serum zinc level of hypothyroidism patients are significantly lower ($p<0.01$), while decrease serum copper level but no significant (

p>0.05) when comparing with control group. Table (2) shows the correlation coefficient (r) between SOD and biochemical parameter in hypothyroid patients. The results indicate that there is a significant negative correlation between erythrocyte SOD and serum T_3 and no significant with T_4 respectively .Also serum Zn, Cu and TSH show a positive correlation with SOD in the patients group.

Table (2) Correlation coefficient (r) between SOD and biochemical parameter in hypothyroid patients.

Biochemical	Correlation coefficient(r)
T_3(nmol/L)	- 0.421*
T_4(nmol/L)	- 0.228
TSH(µIU/ml)	0.272
serumZn(µg/dl)	0.164
serumCu(µg/dl)	0.255

*correlation is significant at the 0.05

Discussion

The results in this study illustrate that significant decrease in the activity of SOD in hypothyroid patients in comparsion to that of normal subjects which are observed in other different researches (18,19).Also supported the suggestion that thyroid hypo function in patients with intellectual disability in some way is linked to the low levels of the major antioxidant molecules found in these patients. The depletion of antioxidants observed in hypothyroidism individuals may display by the increasing free radicals production at the electron transport chain on the mitochondrial inner membrane .The increase of free radicals was not compensated as expecting, by the decrease of antioxidants (18).

The effect of lack thyroid hormone on serum zinc levels were significantly lower with hypothyroidism patients comparing with control was found in this study, this agreement with the results obtained previously.(20,21).

These results can be thought due to firstly that gastrointestinal absorption of zinc is severely impaired in hypothyroidism subjects. Secondly a change in zinc distribution. The low serum zinc level may reflect sequestration of zinc by the liver or other tissues (22). And finaly due to the significant influence of TSH in the variation of the concentration of iodine, selenium and zinc in normal and altered human thyroid tissues (23). Also, the serum copper concentration decreased but not significant in patients with hypothyroidism as compare with normal subjects this result is agreement with previously reported (24). The statistics treatment to the results optained in this study show a positive correlation between serum Zn ,Cu ,TSH ,and activity SOD but SOD showed significant negative correlation with T_3 also negative correlation no significant withT_4

In conclusion, the present study suggests a very high production of ROS and oxidative stress in patients with hypothyroidism and with failure of antioxidant defense mechanisms.

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