Studies on the Relationship Between Chromium(III) ion and Thyroid Peroxidase Activity in Sera of Patients with Thyroid Dysfunction

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Abstract

The objective of this study was to determine the concentration of trace element chromium(III) and thyroid peroxidase activity in human serum , and to find a relationship between the concentration of chromium(III) and thyroid peroxidase activity in serum of patients with hypothyroidism, hyperthyroidism and healthy subjects. Serum thyroid peroxidase was measured by enzyme linked radioimmunoassay(ELISA) method and chromium determination was by atomic absorption spectrophotometer .Comparing the values of chromium concentration and thyroid peroxidase activity in both samples showed that there were significant positive correlations between chromium levels and thyroid peroxidase activity($P<0.01$, $r=0.11$). The results showed that Serum thyroid peroxidase activity and chromium levels were significantly higher in hyperthyroidism patients (152.0±4.6 IU/L) (2.159±0.15 ppb) respectively than normal (51.0±1.8 IU/L) (0.378±0.024 ppb) respectively and lower than normal in hypothyroidism patients (35.0±0.31 IU/L)(0.099±0.011 ppb) respectively.

Key word : Chromium(III), Thyroid peroxidase, thyroid dysfunction

Introduction

The biosynthesis of thyroid hormone from thyroglobulin is catalyzed by thyroid peroxidase (TPO), an integral membrane protein. TPO is also a major autoantigen in autoimmune thyroid diseases [1]. Large quantities of purified TPO are essential for elucidating its structure and understanding its role in diseases activity [2]. Failure of organification could result from deficient thyroglobulin accepter, peroxidase enzyme defect and lack of H_2O_2. Altaration in the process of iodide organification has been detected in almost all thyroid diseases [3]. The qualitative abnormalities in the enzyme TPO system have been proved in patients with congenital thyroid diseases, and quantitative disturbances were observed in multinodular goiter, toxic adenoma, thyroiditis, and carcinoma [4]. Trace elements are known to influence hormones at levels of action, including hormone secretion and activity and binding to target tissue [5]. Conversely, hormones influence trace element metabolism at several levels of action, including excretion and transports of trace metals [6,7,8]. Hence trace elements assay in biological fluid can be used as diagnostic or prognostic aid in patients with different hormonal disturbance alongside with other biochemical parameters[9]. Chromium(III) is an essential trace element for human. Chromium(III) is an ion needed for nutritional support for the thyroid gland to help insulin through reducing body

weight since insulin blocks phosphorylation and therefore opposes the action of epinephrine and can impede thyroid hormone production [10,11]. Chromium(III) also helps to control cholesterol levels that often elevate in hypothyroidism patients as well as control blood sugar levels which are challenged by poor adrenal and thyroid gland health [12]. Serum chromium concentration are likely to be increased above the reference range in patients with metallic joint prosthesis, longevity, increased lipid quantity, impaired glucose metabolism, hyperglycemia, and glycosuria [13,14]. The aim of this study was conducted to verify the relation of the thyroid dysfunction and TPO activity together with Cr (III) ion.

Material and Method

Subjects

92 patients with hyperthyroidism and 82 patients with hypothyroidism for both sexes were involved in the study they were 27-68 years of age. 92 healthy person for both sexes aged 19-54 years were participated in this study and represented the control group.

Samples Collection and preparation

Volume of five milliliters of venous blood from patients and healthy subjects were drawn by utilizing disposable plastic syringes and transferred into sterile test tube. The blood was allowed to clot and centrifuged at 4000 rpm for 10 minutes. Sera were separated and stored at 20 C° until analysis .

Estimation of trace element chromium

Serum chromium was determined using Flame Atomic Absorption Spectrophotometer .Standards. Samples and blanks for estimation of chromium were aspirated into a (Perkin Elmer 6000) atomic absorption spectrophotometer utilizing along-path air/acetylene burner and cathode lamp for chromium metal. Each sample was read three times at 1 second. The concentration of chromium was found by standard addition method[15,16].

Estimation of thyroid peroxidase (TPO) activity

Serum thyroid peroxidase activity was measured by Enzyme Linked Immunosorbent Assay (ELISA) using ORGENTEC thyroid peroxidase (TPO) (ELISA) kit. The activity of TPO was assayed from calibration curve by interpolation .

Results and Discussion

The results and comparisons of serum chromium levels and TPO activity between hyperthyroidism, hypothyroidism and control groups were demonstrated in Table (1,2).There was positive correlation between serum chromium levels and TPO activity. The results of the present study revealed that serum chromium levels of hypothyroidism patients were significantly lower (0.099±0.011 ppb) than the levels in normal subjects (0.378±0.024 ppb) as shown in Table (1). A significant increase in serum chromium levels was demonstrated in hyperthyroidism patients (2.159±0.15 ppb) as compared with that of normal subjects.

Chromium is an essential mineral that is required in the maintenance of our health and it is essential to the metabolism of lipids, proteins, carbohydrates and insulin regulation [17,18]. Thyroid activity may directly or indirectly affect chromium status, low thyroid function may allow increased insulin secretion resulting in chromium loss or increased insulin production suppress thyroid function[19,20].

In this study significant decrease in the levels of Cr in hypothyroidism patients were observed .One possible explanation for these finding, that gastrointestinal absorption of chromium is severely impaired in hypothyroidism subjects [21,22,23,24]. Another explanation is due to the significant influence of TSH in the variation of the concentration of chromium in normal and altered human thyroid tissue [25]. High serum chromium levels have been reported in hyperthyroidism and serum chromium concentrations have been noted to correlate well with thyroid gland activity [26]. Data obtained showed an increased serum chromium levels in patients with hyperthyroidism and positively correlation between serum chromium levels and TPO activity. Changes in body metabolic rate have been shown to be reflected in altered chromium metabolism [27].

The increase in serum chromium levels in hyperthyroidism patients is in agreement with the studies of other researchers indicating the important role of chromium in controlling the thyroid gland function [28,29,30]. Goncharo and Ametov [31], studied the effect of chromium supplementation on the function of thyroid gland in experiment on albino male rats.

The results of their study illustrated that chromium supplementation (3Mg/body weight) improve thyroid activity in albino rats .

Table (2), showed that the TPO activity in hypothyroidism patients was significantly decreased (35±0.31 IU/L), probably due to a destruction that could occurs in thyroid tissue and replacement with fibroblast and lymphocyte [32]. It has been reported that serum TPO activity decreases in patients with hypothyroidism [33]. In hashimotos thyroiditis a variable degree of infiltration with lymphocytes and fibroblalsts is commonly seen in the thyroid gland, therefore, the activity of tissue enzyme is probably affected by the degree of tissue damage. The slight decrease of enzyme activity in the thyroid gland is somewhat intriguing considering the degree of tissue destruction which caused hypothyroidism [34] .

Defects of TPO are both quantitative and qualitative the alter include impaired binding to heme, impaired binding to thyrogobuline or iodine substrate, abnormal localization in the erythrocyte, and abnormal susceptibility to inhibition [35]. Thyroid peroxidase gene mutations have been identified causing either abnormal thyroid peroxidase or absent enzymatic activity or complete absence of TPO protein formation [36].

As shown in table (1), TPO activity in hyperthyroidism patients was significantly elevated (152±4.6 IU/L) in comparison with the normal subjects (51±1.8 IU/L). One possible explanation for these finding , that chronic TSH stimulation leads to increased iodide binding because of increased gland peroxidase content [37], increased iodide trapping , and presumably increased H_2O_2 generation [38]. hence increase TPO activity [39].

Another explanation is due to the significant influence of TSH in the concentration of iodine and chromium in normal and altered thyroid tissue. Thyroid peroxidase activity was grossly elevated in toxic goiter. This may be of significance in the pathogenesis of graves diseases [40].

The relation between TPO activity and serum chromium levels is shown in Figure (2). A significant positive correlation was obtained between TPO activity and serum chromium levels in hyperthyroidism and hypothyroidism (r=0.11), when chromium levels were decreased by more than (70 %) the TPO activity was markedly decreased .

Statistically significant correlation were found among indexes of chromium status and indexes of TPO. Concomitants deficiency of both key parameters are especially dangerous. In other studies, using animals chromium deficiency in rats inhibited the production of T3 and T4 [41].

Another studies revealed that chromium deficiency in animals can exert both a direct effect on the metabolic process and an indirect one disturbing iodine metabolism. The results of this study indicated that chromium deficiency in animals enhances the effect of hypothyroidism [42].

As shown in figure (3), from a total of 260 patients with thyroid diseases the most common genders are females. It can be seen from figure (2), that 92 persons were male and 170 were females. High level of chromium was found in females. Our results are consistent with other studies such as who found by Lien et al [43], that they proved thyroid disease affects female three times more than male .

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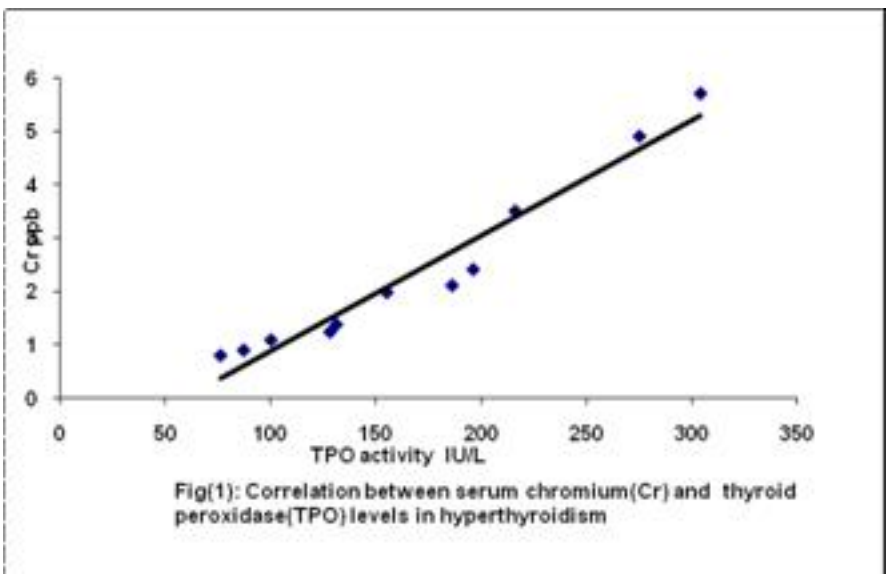
Table (1): The mean ± SE of serum levels of chromium and Thyroid peroxidase(TPO) activity In hyperthyroidism patients and normal subjects

Parameters	hyperthyroidism patients	normal subjects	P-value
Thyroid peroxidase (TPO) IU/L	152.0± 4.6	51.0 ±1.8	0.001
Chromium ppb	2.159±0.15	0.35±0.0241	0.003

Table(2): The mean ± SE of serum levels of chromium and Thyroid peroxidase(TPO) activity In hypothyroidism patients, and normal subjects

Parameters	Hypothyroidism patients	normal subjects	P-value
Thyroid peroxidase (TPO) IU/L	35.0± 0.31	51.0 ±1.8	0.006
Chromium ppb	0.09±0.011	0.35±0.0241	0.001

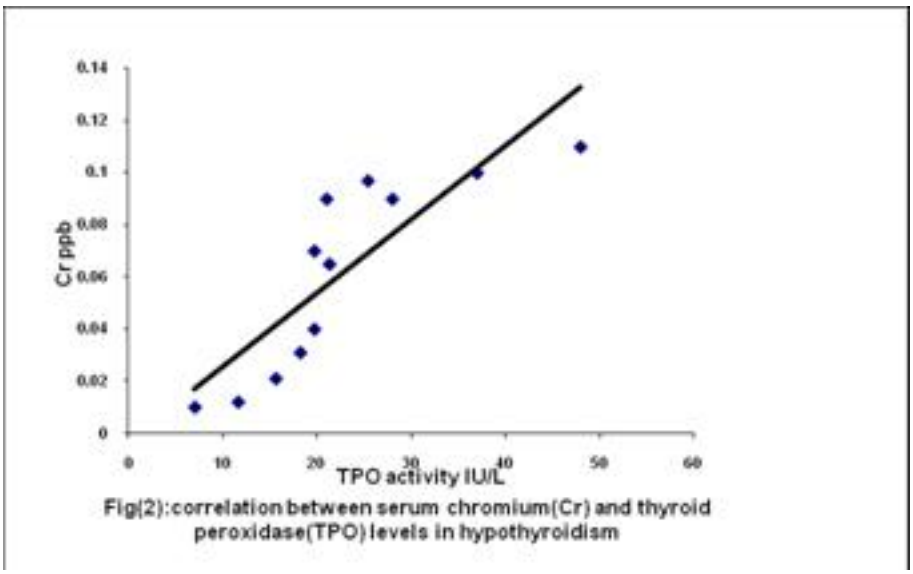
Y=0.0216X – 1.2734
r =0.12



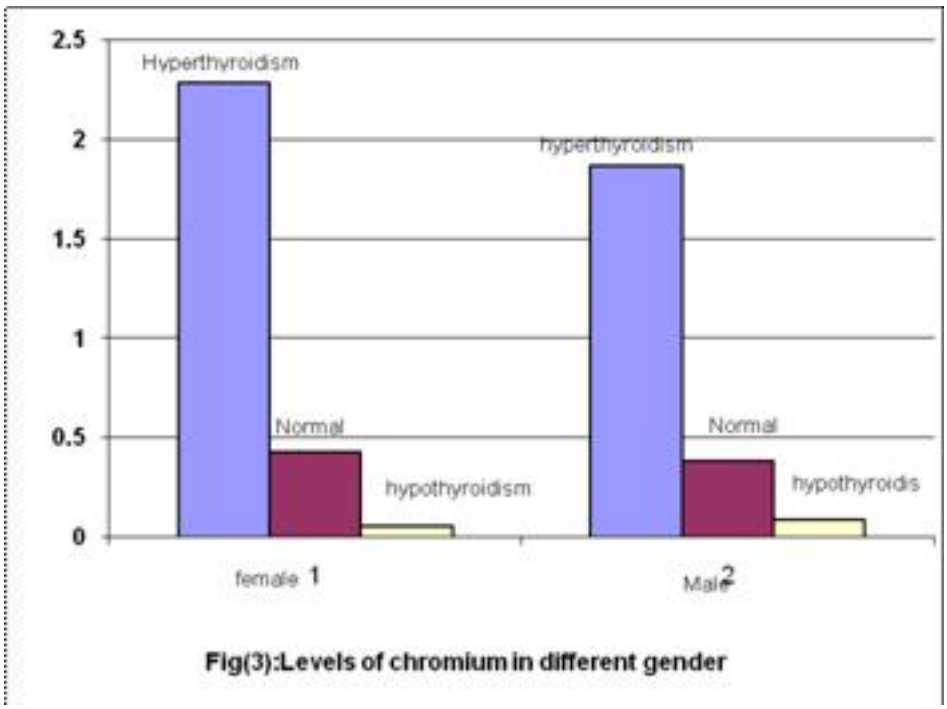
Fig(1): Correlation between serum chromium(Cr) and thyroid peroxidase(TPO) levels in hyperthyroidism

$$Y=0.0028X - 0.0027$$

$$r=0.11$$



Fig(2):correlation between serum chromium(Cr) and thyroid peroxidase(TPO) levels in hypothyroidism



Fig(3):Levels of chromium in different gender

دراسة عن العلاقة ما بين تركيز ايون الكروم الثلاثي وفعالية انزيم بيروكسيديز الدرقي في امصال المصابين باختلال الوظيفة الدرقية

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الخلاصة

تتلخص اهداف هذه الدراسة في تقدير تركيز ايون العنصر الضئيل الكروم الثلاثي وكذلك تقدير فعالية انزيم البيروكسيديز الدرقي في مصول الاشخاص المصابين بمرض اختلال الوظيفة الدرقي، ومن ثم ايجاد علاقة تربط ما بين الاثنين. استعملت طرائق مطيافية الامتصاص الذري في تقدير تركيز الكروم في عينات المصول المرضية والطبيعية كما واستعملت تقنية ال ELISA في تقدير فعالية انزيم البيروكسيديز الدرقي. اوجدت النتائج ان هناك زيادة معنوية وارتفاعا ملحوظين في مستويات الكروم وفعالية البيروكسيديز (2.159±0.15 ppb) (152.0±4.6 IU/L) على التوالي في مصول المرضى المصابين بالفرط الدرقي عنه في المصل الطبيعي (0.378±0.024 ppb) (51.0±1.8 IU/L). كما بينت النتائج ان تركيز الكروم وفعالية البيروكسيديز قد انخفضا انخفاضا ملحوظا في مصول قصور الدرقية (0.099±0.011 ppb) (35.0±0.31 IU/L) وعلى التوالي ومقارنة في امثالها عند الطبيعيين. كما بينت النتائج العلاقة المعنوية والايجابية ($P<0.001, r=0.11$) عند مقارنة تركيزالكروم وفعالية البيروكسيديز عند المرضى والطبيعيين.