Effect of Some Heavy Metal on Hyperthyroidism

Ahmed Jawad Kadhim[1], Maysaa Jalal Majeed[2], Muqdad Abd Al-Hassan[3]

[1]Scholar Researcher, Al-Sadr General Hospital/Baghdad Health Department Al-Rusafa, Ministry of Health, Iraq, [2]Scholar Researcher, Department of Biochemistry, College of Medicine, University of Baghdad, Iraq, [3]Scholar Researcher, Specialized Center for Endocrinology and Diabetes /Baghdad Health Department Rusafa, Ministry of Health, Iraq

Abstract

Background: The thyroid gland is one of the important glands that play an important role in the body and has many functions that the human body needs. Chronic toxicity of some heavy metals (lead, cadmium, copper, zinc and chromium) can damage the thyroid gland by recruiting antibodies to attack the thyroid gland, and this process may contribute to the development of autoimmune thyroid diseases such as Graves' disease, or an increase or decrease in some of these minerals may affect Thyroid hormone synthesis. **Methods:** The study involved 60 subjects, 24 female and 8 male in each group with age range (25-65 years) divided into two groups, the first group included 30 healthy subjects and the second group included 30 patients with hyperthyroidism. The laboratory investigation included measurement of S.TSH, Total S.T3, and Total S.T3 was depended on enzyme-linked fluorescent immunoassay (ELFA), S.TPO concentration was calculated by enzyme-linked immune sorbent assay (ELISA), serum heavy metal which involves (S.Pb, S.Cd, S.Cr, S.Cu and S.Zn) was determined by Flame Atomic Absorption Spectrophotometry(FAAS)and Graphite Furnace Atomic Absorption Spectrophotometry(GFAAS).Liver and kidney function tests were measured to exclude subjects with liver and kidney dysfunction in addition to smokers and cancer patients. **Results:** In this study, high concentrations of lead, cadmium and copper were obtained (with p.value≤0.05), and significantly lower concentrations (p.value≤0.05) of chromium and zinc were obtained in hyperthyroid patients compared to healthy subjects. An inverse relationship between some elements (lead and cadmium) was observed with TSH (r =-0.41, p≤0.05) and (r=-0.56, p≤0.05) consequently in hyperthyroid patients. No correlation was observed between thyroid hormones (T3 and T4) and TPO-Ab with the lead, cadmium, chromium, copper and zinc (with P.value >0.05) in hyperthyroid patients. Conclusion: Hyperthyroidism is associated with changes in heavy metals (Pb, Cd, Cr, Cu and Zn)

Keywords: *Hyperthyroidism, Lead (Pb), Cadmium (Cd), Chromium (Cr), Copper (Cu) and Zinc (Zn)*

Introduction

The thyroid gland is an essential hormone gland with essential role in the development, growth and metabolism of the human body. The thyroid gland helps control multiple bodily functions through continuous release into the bloodstream of a stable number of thyroid hormones. In some conditions, for example, when it be cold or when the body requires more energy, or during pregnancy, it releases more hormones [(1)]. The main Thyroid hormone Thyroxine (T4) is a prohormone, secreted by the thyroid that is converted to triiodothyronine (T3) the active hormone biologically in peripheral tissues[(2)]. Hyperthyroidism (overactive) is a situation in which the thyroid produces and supplies more hormones to the body than you require[(3)]. Graves' disease is the most common cause of hyperthyroidism. It is an autoimmune disease caused by the production of TSH receptor antibodies that stimulate thyroid gland

Corresponding author:
Ahmed Jawad Kadhim
Emil: labalsader@gmail.com

growth and thyroid hormone release. Patients will have abnormally increased T4 and T3 levels and a decrease in TSH[4]. Heavy metals are referred to by a variety of meanings in natural, biological, and toxicological contexts; the human body contains more than 70 trace elements. While they are very low in the body, their biological effects are important[5]. Heavy metal deposition in the body has been shown to harm human health by destroying the major metabolic processes in the body and causes an antioxidant imbalance. Similarly, different hormones' behaviour and the action of essential enzymes are influenced[6]. The study looked for the role and the effect of some heavy metals (cadmium, lead, chromium, zinc and copper) on the condition of the thyroid gland (Hyperthyroidism), and whether it is necessary to conduct them as routine tests.

Material and Methods

Statistical analysis were measured using a program MedCalc version 19.6.1, the results of comparison were expressed as mean ±SE depending on student t-test. Pearson correlation coefficient which also referredas Pearson's r, which was used to determine the study's variables correlations or association .the level of adopted significance during the study was 0.05, more than 0.05 was consider as not significant, while lesser or equal 0.05 consider as significant level The work was done during period from November 2020 to January2021 the subjects were selected from Baghdad Health Department Rusafa / Specialized Center for Endocrinology and Diabetes, and Al-Sadr General Hospital. The 60 subjects selected with age range (25-65 years) lived in Baghdad, Renal and liver function tests were checked and no one of the subjects takes special treatment of heavy metals poisoning. The subjects divided into two groups: First group: 30 healthy subjects documented by physician clinical exam and laboratory tests (serum TSH, Total T4 and Total T3) consider as a control group. Second group: 30 patients who previously diagnosis by Specialized Center for Endocrinology and Diabetes and Al-Sadr General Hospital as hyperthyroidism patients and they had a period (3-20 years) of treatment (Carbimazole 5 mg). It is worth noting that all thyroid gland measurements were made after treatment, due to the difficulty in obtaining patients in initial diagnosis stage before treatment, and this is part of limitations of the current study.

Blood Samples:

From the vein using a disposable syringe(10 ml) blood was drawn and divided into two parts the first part (7 mL)of the blood keep in gel tubes and centrifuged for five min then the serum was divided and used in the determined concentration of Serum TSH, Serum T4. Serum T3, Serum TPOAb, Serum Copper(Cu), serum Chromium(Cr), Serum Zn, S.AST, S.ALT, S.ALP, S. Urea and S. Creatinine . In the second part (3 ml) of the blood collected keep in an EDTA tube, which was used to Lead (Pb) and Cadmium (Cd) tests.

Results

Table (1) represent the general characterization of hyperthyroidism patients and healthy subjects demonstrate the Age, BMI, concentration of TPO and thyroid hormones (in basal level and after treatment) in serum without any statistical comparison.

Table (1) General Characterization of study's subject of Age, BMI expressed S.TPO and S.TSH, S.T4 and S.T3 (In basal and after treatment) expressed as mean ± Standard error (SE) without any statistical comparison

Parameters	Healthy subjects Mean ± SE No. =30	Hyperthyroidism Patients Mean ± SE No. =30
Age Years	46.87 ±2.20	47.07 ±2.22
BMI Kglm²	30.44 ±0.93	31.17 ±1.10

Cont... **Table (1) General Characterization of study's subject of Age, BMI expressed S.TPO and S.TSH, S.T4 and S.T3 (In basal and after treatment) expressed as mean ± Standard error (SE) without any statistical comparison**

S.TPO pg/ml	442 ±11.30	489.7 ±19.87
S.TSH basal (μIU/ml)	1.83 ±0.15	0.38 ±0.18
S.T4 basal (nmol/l)	103.83 ±4.30	155.2 ±10.51
S.T3 basal (nmol/l)	1.38 ±0.05	3.25 ±0.37
S.TSH after treatment (μIU/ml)		1.10±0.33
S.T4after treatment (nmol/l)		129.6±10.14
S.T3 after treatment (nmol/l)		2.03±0.16

The successful matching of Age and BMI was obtained by the chosen of the subjects with hyperthyroidism patients and healthy subjects represented by independent (not significant) difference between them with P>0.05. While S.TPO show a significant difference with P≤0.05 between these subjects (Table 2).

Table (2) Mean ± Standard error (SE) Age and BMI for hyperthyroidism patients and healthy subjects.

Parameters	**Healthy subject Mean ± SE No.=30**	**Hyperthyroidism Patient Mean ± SE No.=30**	**T-TEST Sig.**
Age years	46.87 ±2.20	47.07 ±2.22	P >0.05 N. Sig.
BMI Kg/m²	30.44 ±0.93	31.17 ±1.10	P >0.05 N. Sig.
S.TPO pg/ml	442 ±11.30	489.7 ±19.87	P ≤ 0.05 Sig.

sig. = significant, N.sig. = no significant

Hyperthyroidism patient show a significant (with p≤0.05) elevation when compare with healthy subjects in the level of each serum Copper (Cu)(141.60 ±8.75 µg/dl vs. 110.67 ± 11.57 µg/dl), serum Lead(Pb) (27.50±3.04 µg/dl vs. 14.60 ± 1.30 µg/dl) and serum Cadmium(Cd)(0.32 ±0.05 µg/dl vs. 0.13± 0.03 µg/dl). While show a significant (with p≤0.05) decrease when compare with healthy subject in the level of serum Zinc (Zn)(76.77±10.79 vs. 98.77±7.63 µg/dl) and serum Chromium(Cr)(0.14 ± 0.03 vs. 0.17±0.03 µg/dl) (Table 3).

Table (3) The heavy metals (Cu, Pb, Cd, Cr, Zn) status of hyperthyroidism patients compared to healthy subjects represent as Mean ± Standard error (SE).

Elements	Healthy subject Mean ± SE No.=30	Hyperthyroidism Patient Mean ± SE No.=30	T-TEST Sig.
S.Cu µg/dl	110.67±2.11	141.60±1.60	P ≤ 0.05 Sig.
S.Zn µg/dl	98.77±1.39	76.77±1.97	P ≤ 0.05 Sig.
S.Pb µg/dl	14.60±0.24	27.50±0.55	P ≤ 0.05 Sig.
S.Cd µg/dl	0.13±0.01	0.32±0.01	P ≤ 0.05 Sig.
S.Cr µg/dl	0.17±0.01	0.14±0.01	P ≤ 0.05 Sig.

sig. = significant, N.sig. = no significant

Correlation between serum heavy metals (Cu , Pb ,Cd, Cr ,Zn),S.TSH, S.TPO, S.T4 and S.T3 in hyperthyroidism patients, the only approved significant correlation in hyperthyroidism patients are negative correlation between S.TSH and each of S.Pb (r=-0.41, p≤0.05) and S.Cd (r=-0.56, p≤0.05) while the rest correlation are not approved is in hyperthyroidism patients between S.TSH and each of S.Cu (with r=0.19 , p>0.05), S.Cr (with r=0.16, p>0.05) and S.Zn(r=-0.26, p>0.05) . also There is no significant correlation between S.TPO and each of S.Cu (with r=-0.11 , p>0.05),S.Cr (with r=-0.13, p>0.05),S.Cd (with r=0.05, p>0.05), S.Pb (with r=-0.06, p>0.05)and S.Zn (with r=-0.21, p>0.05) in hyperthyroidism patients. it found there is no significant correlation between S.T4 and each of S.Cu (with r=-0.16 , p>0.05),S.Cr (with r=0.15, p>0.05),S. Cd (with r=0.10, p>0.05), S.Pb (with r=0.15, p>0.05)and S.Zn (with r=0.12, p>0.05) ,and no significant

correlation between S.T3 and each of S.Cu (with r=-0.02 , p>0.05),S.Cr (with r=0.16, p>0.05),S.Cd (with r=0.16, p>0.05), S.Pb (with r=0.35, p>0.05)and S.Zn (with r=-0.03, p>0.05) consequently in hyperthyroidism patients.

Discussion

In this study, TPO showed a significant increase in hyperthyroidism patients, this moderately increased level of TPO-Ab maybe give rise to the cause Graves' disease (an autoimmune disease) in hyperthyroidism[7,8]. On follicular cell, the TSH receptor activates after stimulated the thyroid gland by the antibodies which be mimic the TSH action but are not the same as TSH produced by the pituitary gland. So the patient produces much more thyroid gland hormones, resulting in thyrotoxicosis like Graves' disease[9] which give a possible explanation for these finding, that Chronic TSH stimulation causes an increase in iodide binding due to an increase in the content of gland peroxidase, iodine trapping, and likely increased peroxide production, causing an increase in the activity of TPO[10].

The Zn levels show a significant decrease in hyperthyroidism patients which can see in previous researches like Rezaei et al., and Abdrabo [11,12].

In previous research by Baltaci et al.on 34 people with hyperthyroidism, two conclusions were reached regarding low zinc in these patients, the first being low zinc absorption and secondly, zinc excretion through the kidneys, while Liu et al., suggested that the high concentration of thyroid hormone led to inhibition synthesis in of the carbonic anhydrase-I zinc enzyme in erythrocytes[1314]. Hyperthyroid patients had significantly elevated plasma Cu concentrations according to their controls subjects which agreement with Khadem-Ansari et al, and Sinha et al. In associated higher Cu levels with hyperthyroidism. In contrast, Rezaei et al reported a low level of cu in hyperthyroidism patients against control subjects. [15,16]. There are two reasons for this case the first possible explanation is that the zinc deficiency leads to increased absorption of copper from the intestine which agreement with AKÇAY et al.,[17] and the second, about 90% of Cu is transported in the bloodstream via ceruloplasmin and the ceruloplasmin increases significantly in hyperthyroid patients[16] Hence, increased ceruloplasmin and slow excretion of Cu from the body can explain elevated Cu level in hyperthyroidism. Some researchers have also recorded higher blood lead concentrations in hyperthyroidism patients relative to controls [11,18,19]. Lead (Pb) can influence the human body's antioxidant status by oxygen radical's generation, which is responsible for the creation of multiple complications, which can be associated with systemic damage led to dysfunction of the thyroid gland. A negative correlation between Cd and Pb with TSH agreement with Christensen et al,[20]. The detrimental impact of Pb and Cd toxicity on cell enzymatic processes results from the replacement of other important metal ions in metalloenzymes, as well as their extreme affinities for biological structures with (SH) group, like nucleic acids, enzymes, and proteins. [21] Indeed, one of the many mechanisms suggested to explain the impact of lead on the function of the thyroid; is secondary dysfunction of the thyroid as a result of pituitary disease owing to toxic lead effects on the HPT (hypothalamic-pituitary-thyroid) axis[22].

Chromium (III) is an important trace element that acts in a range of biochemical processes, including glucose, lipids and amino acids. As in the present study findings, abnormal Cr levels can affect thyroid hormone synthesis and functions physiologically. Although the level of chromium is within acceptable level, the moderate Decrease level of chromium concentration in hyperthyroidism patients is may be the result of the impaired chromium absorption in the gastrointestinal or the effect of the carbimazole treatment.

Conclusion

It can say that hyperthyroidism is associated with changes in heavy metals (Pb, Cd, Cr, Cu and Zn) some of them elevated such as (Pb, Cd and Cu) while other decreased (Cr and Zn) and this is evident through the results obtained from comparing them with healthy subjects, but the fact of relying on it and examining it as

a routine in the case of thyroid dysfunction needs more accurate studies and a larger number of samples. .

Recommendations

1- In the subsequent studies, measure the concentration of iodine and iron maybe give vision for the causes of thyroid dysfunction and the effect of the heavy metals on hyperthyroidism diseases.

2- Obtaining patients before starting treatment may give more accurate results through which we can know the causes of accumulation and decrease of these elements in the body.

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