Study of Some Trace Elements in Hyperthyroidism Patients

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ABSTRACT:

BACKGROUND:

The objective of this study is to shed more light on the role of trace metals and their mode of action in hyperthyroidism. The content of the trace elements (Zn, Cu, Mn, and Se) in the serum of patients was determined and compared to that of normal subjects.

METHODS:

Ninety eight (98) patients with hyperthyroidism were participated in this study and fifty normal healthy persons were taken as control. Serum zinc and copper were determined using flame atomic absorption spectrophotometer while serum manganese and selenium were estimated using flameless atomic absorption spectrophotometer technique.

RESULTS:

The study showed that serum zinc and selenium level of hyperthyroidism patients were significantly lower ($p<0.05$) than the level in normal subjects. While a significant increase in serum copper level was demonstrated in patients as compared with that of the normal subjects. The results showed no significant difference between the groups ($p>0.05$) in serum manganese.

CONCLUSION:

The present study confirmed a significant changes in the levels of serum Zn, Cu, and Se in hyperthyroidism patients and these changes may be related to pathophysiology of thyroid disease

KEY WORDS: hyperthyroidism, Copper, Manganese, Selenium, and Zinc

INTRODUCTION:

The thyroid hormones T3 and T4 act in many tissues to increase the basal metabolic rate, partly by regulating mitochondrial ATP synthesis. In addition, they promote embryonic development [(1)]. Hyperthyroidism is the constellation of clinical, physiological, and biochemical alterations that results when tissues are exposed to increased concentrations of thyroid hormones [(2)]. Hyperthyroidism may result in functional and therefore clinical abnormalities involving virtually every organ system [(3)]. The annual incidence of hyperthyroidism is three per 1,000 in the general population, and the condition is eight times more common in women. Hyperthyroidism may result from generalized thyroid gland over-activity or from causes other than over-activity of the gland, it is important to distinguish between these since the prognosis and treatment will be different [(4)].

In most patients with hyperthyroidism, the thyroid gland is increased to two to three times of its normal size. Furthermore, each cell increase its rate of secretion several folds [(3)]. The cause of hyperthyroidism in an individual patient can usually be identified by history and physical Examination; particularly attention should be paid to the duration of symptoms, and to palpation of the thyroid gland [(5, 6).]

Occasionally hyperthyroidism is found in patients who seek care for thyroid enlargement or infiltrative opthalmopathy but who are otherwise asymptomatic. Because the actions of thyroid hormone are in a broad sense stimulatory, the manifestations of hyperthyroidism usually reflect increased functioning of various organ systems to meet the demands imposed by hyperthyroidism [(7, 8, and 9)]. The maintenance of optimal health requires an adequate supply of macronutrients, micronutrients, and trace elements [(10)]. Trace elements are known to influence hormones at levels of action, including hormone secretion and activity and binding to target tissue. Conversely, hormones influence trace metals metabolism at several levels of action, including excretion and transport of trace metals [(11)]. Hence, trace elements assay in biological fluids can be used as diagnostic or prognostic aid with other biochemical parameters in patients with different hormonal disorders [(12, 13, 14, 15, and 16)].

PATIENTS AND METHODS:

Patients: Ninety-eighty (98) patients with hyperthyroidism were participated in this study. Their age ranges were between (19-69) years, 58 females and 40 males. The patients diagnosed depending on the results of the following examinations: clinical examinations, serum

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hormones (T3,T4) and TSH, computed tomography (CT scan), Pathological examination, and fine needle aspiration (If needed).

Normal Controls: Fifty normal healthy persons aged (18-55) years (29 females and 21 males) were used as control.

Samples Collection and Preparation:

About Five milliliters of venous blood from fasting subjects were drawn by utilizing disposable plastic syringes in the morning and transferred into sterile test tube. The blood was allowed to clot and centrifuged at 4000g for10 minutes. Sera were separates and stored at -20ºC until analysis.

Analysis of Trace Elements:

Determination of Zinc and Copper:

Serum zinc and copper were determined using flame atomic absorption spectrophotometer (AA-646) **(**Shimadzu, Japan**).** Samples were diluted 1:10 with 6% n-butanol solution as diluents. This method achieved 30% increase in sensitivity compared to the use of deionized water only [17]. This effect is due to decrease viscosity and difference in droplet formation and this technique is widely used [18]. Level of sera zinc and copper were calculated after application of absorbencies on suitable calibration curve for each element made from standard solutions.

Determination of Manganese & Selenium:

Serum samples were diluted with equal volume of deionized water for estimation of serum manganese and diluted two fold with deionized water to estimate serum selenium. Flameless atomic absorption spectrophotometer (Perkin-Elmer Model 503) was used to estimate the level of these elements in the diluted sera. Levels of sera manganese and selenium were calculated after application of absorbencies on suitable calibration curve for each element from standard solutions**.**

RESULTS:

Table (1) showed the results of serum trace elements expressed as (mean±standard deviation). Serum zinc and selenium levels of hyperthyroidism patients are significantly lower ($p<0.05$) than the level in normal subjects as showed in Table (2). A significant increase in serum copper level was demonstrated in patients as compared with that of the normal subjects as shown in table(1). The results also showed no significant difference between the groups ($p>0.05$) in serum manganese (table 2).

Table (1): The serum concentration of trace elements in hyperthyroidism patients and normal controls expressed as (mean ± standard deviation).

Serum Trace Element	Normal Controls µmol/L	Hyperthyroidism µmol/L
Zinc	9.08±2.48	8.21±2.55
Copper	21.73±6.44	31.28±12.57
Manganese	0.7±0.37	0.79±0.16
Selenium	1.35±0.44	0.80±0.45

Table (2): Probability values and significance of difference for the comparison between hyperthyroidism patients and normal control groups in the serum concentration of the studied trace elements.

Trace Elements	P-value	Significance
Zinc	0.042	Significant
Copper	0.002	Significant
Manganese	0.534	Not-Significant
Selenium	0.00095	Significant

DISCUSSION:

The present study showed significantly decrease in zinc content in serum of hyperthyroidism. This result is in agreement with results of previous works performed on hyperthyroidism patients [19-23]. Maes *et al* [24] showed that serum zinc and albumin were significantly lower in hyperthyroidism patients than normal volunteers. Because it seems likely, that albumin acts as the major transporter protein for zinc in plasma.

It is suggested that lower serum zinc in hyperthyroidism patients may be secondary to sequestration of metallothionein in the liver, which may be related to increased production of interleukin-6 as a response for inflammation [24]. Furthermore, Varga *et al* (1994) [25] confirmed that there is a significantly decreased red-blood cell Zn-content in overt hyperthyroidism compared to euthyroid controls which may reflect the parallel changes in serum zinc [25].

Other factor is the influence of TSH in the variation of the concentration of iodine, selenium and zinc in normal and altered human thyroid tissues was significant [26].

In one study, interleukin-1 produced a transient depression in the serum zinc concentration and increase serum ceruloplasmin [27]. Metallothionein levels were increased in liver fourteen fold after the increased in interleukin-1. Interleukin-1 production is stimulated by infection, cellular injury, and inflammation [27] which may all associated with hyperthyroidism. In the present work, a highly significant decrease in selenium concentration was observed in serum of hyperthyroidism patients as compared to that of normal subjects.

Aihara *et al* (1984) [28] also found that the mean concentration of serum selenium was significantly lower in patients with hyperthyroidism than in control subjects, and a statistically significant negative correlation was found between serum selenium levels and serum T4 or T3 levels. This finding suggested that thyroid hormone affects selenium metabolism directly or indirectly, but the precise mechanism of selenium metabolism in thyroid disease is not known [29].

Selenium was decreased in subjects with different thyroid disorders including; hyperthyroidism, carcinomas, or adenomas in comparing with controls groups. According to the literature, Se has a protective effect on carcinogenity as well as on biochemical pathways in thyroid cells [30].

Iodothyronine 5'-deiodinase, which is mainly responsible for peripheral triiodothyronine (T3) production, has recently been demonstrated to be a selenium-containing enzyme [31].

A highly significant linear correlation between T4, T3/T4 and selenium was observed in the population as a whole group and in older subjects. It's concluded that selenium status influences thyroid hormones in the elderly, mainly modulating T4 levels [31].

Selenium deficiency in rats for a period of up to 6 weeks inhibited both the production of (T3) from (T4) and also the catabolism of T3 to 3, 3'-di-iodothyronine (5-deiodination) in liver homogenates. It is concluded that, since both T3 production and catabolism are inhibited by selenium deficiency, there is little change in hepatic T3 stores [31]. In the current study, there is a significant increase in copper concentration in serum of hyperthyroidism patients compared to that of the normal group. Our result is in agreement with the results of previous works performed on hyperthyroidism patients [28].

Most plasma Cu (approximately 93%) is bound to ceruloplasmin and a small fraction to albumin (6 to 7%) or is chelated to amino acids (<1%), which is diffusible [32]. Hence the increase in serum copper may be due to the increase in ceruloplasmin [33]. Plasma ceruloplasmin level was reported to be increased in patients with hyperthyroidism [34].

These findings may provide one explanation for the data. In addition, ceruloplasmin is one of the acute phase reactant that increases in response to inflammation that was previously shown.

In patients with hyperthyroidism, the serum Cu and Zn exhibited the significantly positive correlation with triiodothyronine (T3) and thyroxine (T4) although the serum Cu and Zn were differed significantly before and after the therapy [35].

The present study showed non significant difference in manganese concentration in serum of patients with hyperthyroidism in comparisons to normal subjects. There is a few reports about serum manganese in hyperthyroidism and need more attention. This finding disagreed with the observation reported by other workers [28], who found a significant decrease in manganese concentration in hyperthyroidism patients.

This finding suggested that the thyroid hormone may in part, also chronically affect manganese metabolism or vice versa.

CONCLUSION:

There is an abnormal change in the level of the studied trace elements, except manganese in hyperthyroidism patients as compared with control group. Further studies are required to obtain a complete picture about the changing in trace elements in hyperthyroidism as a treatment adjuvant.

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