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Levels of Serum Zinc and Manganese among Sudanese Patients with Thyroid Dysfunction

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ABSTRACT

The objective of this study is to shed more light on the role of trace metals and their mode of action in hyperthyroidism and hypothyroidism. The content of the trace elements Zinc and Manganese (Zn and Mn) in the serum of patients was determined (Forty patients with hyperthyroidism (26 females and 14 males) and hypothyroidism (23 females and 17 males) were participated in this study. Serum zinc and manganese were determined using flame atomic absorption spectrophotometer technique. The study showed that serum zinc and manganese levels of hyperthyroidism patients were significantly lower ($p<0.05$) compared to reference range (zinc level is (0.5 to 1.2, mean 0.85 mg/l) and manganese is (0.3 to 0.9, mean 0.6 mg/l), While a significant increase in serum manganese level and decrease in serum zinc levels in patients with hypothyroidism ($p<0.05$). The present study confirmed significant changes in the levels of serum Zn, Mn in hyperthyroidism and hypothyroidism patients and these changes may be related to pathophysiology of thyroid disease.

Key words: Hyperthyroidism, Hypothyroidism, Zinc and Manganese.

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INTRODUCTION

The maintenance of optimal health requires an adequate supply of carbohydrates, proteins, lipid, and macronutrients, micronutrients, and trace elements (Solomon's, 1993). Many trace elements play an essential role in number of biological processes through their action as activators or inhibitors of enzymatic reactions, by competing with other elements and proteins for binding sites, by influencing the permeability of cell membranes, or through other mechanisms. Trace elements are known to influence hormone at level 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 (Stands, 2000). Hence, trace elements assay in biological fluids can be used as diagnostic or prognostic aid in patients with different hormonal disturbances alongside with other biochemical parameters.

Thyroid hormones regulate the rate of metabolic processes and consequent development of organism, deficiency of thyroid hormones causes many metabolic processes to slow down (Tapiero, 2003). Zinc is an important element for numerous biochemical processes as well as for cell proliferation. Zinc is extensively studied by bioinorganic chemistry and it is known that there are many metalloproteins with specific enzymatic activity contain zinc. Carbonic anhydrase, liver alcohol dehydrogenase and alkaline phosphatase are some examples of zinc enzyme (Bertini, 1982). Prasad (1990) reported that thyroid hormones modulate zinc transport activity in rate renal and intestinal brush-border membrane (Prasad, 1999). Zinc has been shown to have an antioxidant effect and stabilized cell membrane (Powell, 2000). Zinc is a metal that affects thyroid hormone function at several levels. For example, zinc deficiency inhibits TRH synthesis, (Morley, 1980) and depresses plasma TSH, T4, T3 (triiodothyronine) (Pekary, 1987). It is necessary for extrathyroidal T4 to T3 conversion, (Pekary, 1991) and it plays a role in T3 binding to nuclear receptor as well as the binding of the receptor to DNA (Anselmet, 1983).

Thyroid hormone receptors require zinc ion, (Sustrova, 1994) which facilitate folding into active shape (Bucci, 1999). There are indications that zinc is also important for

Table 1. The serum concentration of trace elements in hypothyroidism, hyperthyroidism patients and reference values.

Serum Trace Elements	Hyperthyroidism	Hypothyroidism
Zinc mg/l (M±SD)	0.19±0.12	0.17±0.07
Manganese mg/l (M±SD)	0.15±0.11	1.72±1.36

normal thyroid homeostasis. Its roles are complex and may include effects on both the synthesis and mode of action of the hormones. Thyroid hormone binding transcription factors, which are essential for modulation of gene expression, contain zinc bound to cysteine residues (Civitareale, 1994). However, it is not known whether dietary zinc deficiency has a direct effect on this aspect of thyroid hormone metabolism. In cultured cells, very strong chelators of zinc are required to influence binding of transcription factors to DNA. In the thyroid gland itself, transcription factor 2, which interacts with the promoters for the thyroglobulin and thyro peroxidase genes, is a zinc-containing protein. The binding of transcription factor 2 is affected by redox state, but again it is not known whether this can be changed by dietary zinc intake (Kralik, 1996). Zinc is very important in Thyrotropin-releasing hormone synthesis (Pekary, 1991) essential for thyroxine (T4)-to-T3 conversion, (Chen, 1998) and is required for the biological functioning of the thyroid hormone and related receptors (Freake, 2001). Manganese may affect thyroid hormone homeostasis and neuro developmental processes as a result of both direct dysregulation at the level of the thyroid gland and thyroid hormones, or indirectly via alterations in dopaminergic control of the thyroid gland and its hormones. Dopamine is a known modulator of both TSH and TSH subunit secretion (Konig, 2002). An additional effect of manganese on thyroid hormones homeostasis may be mediated through their metabolizing enzymes. Current data suggests that manganese can affect thyroid hormones directly by regulating the deiodinase enzymes (Aihara, 1984).

MATERIALS AND METHODS

Patients

Forty patients with hyperthyroidism were participated in this study, 26 females and 14 males. Forty patients with hypothyroidism include 23 females and 17 males. The patients diagnosed depending on the results of the following examinations: clinical examinations, serum hormones (T3,T4) and TSH.

Samples Collection and Preparation

A volume of 3 ml of venous blood sample was collected from both cases using sterile disposable syringe and aseptic standard non traumatic vein puncture technique was applied, and emptied in a sterile plane containers. And then will centrifuged at 4000 rpm for 10 min, then the serum was separated and transferred in a plain container and processed. Sera were separates and stored at -20ºC until analysis.

Analysis of Trace Elements

Determination of Zinc and Manganese

Serum zinc and manganese were determined using flame atomic absorption spectrophotometer (Buck Scientific 210/211 VGP Atomic Absorption-England). Samples were diluted with deionized water. The analysis was performed against standard prepared in glycerol to approximate the viscosity characteristics of diluted samples. For determination of serum zinc, samples were diluted 1:5 with deionized water. The serum samples for manganese estimation were diluted 1:10.

Statistical Analysis

The results of serum element concentrations were expressed as mean± standard deviation. Data was analyzed using SPSS program, the level of significance was determined by employing pooled t-test. Only when p-value less than 0.05, considered as statistically significant.

RESULTS AND DISCUSSION

Table 1 showed the results of serum trace elements expressed as (mean ± standard deviation).

Serum zinc and manganese levels of hyperthyroidism patients are significantly low (P.value 0.000). A significant decrease in serum zinc level was demonstrated in patients with hypothyroidism while there is significant increase in serum manganese level (P.value 0.000). Reference range of serum zinc level is (0.5 to 1.2, mean 0.85 mg/l) and manganese is (0.3 to 0.9, mean 0.6 mg/l) (Rükguer, 1997). The present study showed significantly decrease in zinc and manganese content in serum of hyperthyroidism. This result is in agreement with results of previous works performed on hyperthyroidism patients (Vitoux, 1999). Zinc effects on thyroid hormones are complex and include both synthesis and mode of action (Arthur, 2007). Thyroid transcription factors which are essential form odulation of gene expression contain zinc at cysteine residues (Bucci, 1999). Manganese may affect thyroid hormone homeostasis and neurodevelopmental processes as a result of both direct dysregulation at the level of the thyroid gland and thyroid hormones, or indirectly via alterations in dopaminergic control of the thyroid gland and its hormones. Dopamine is a known modulator of both TSH and TSH subunit secretion (Freake, 2001).

An additional effect of manganese on thyroid hormones homeostasis may be mediated through their metabolizing enzymes. Current data suggest that manganese can affect thyroid hormones directly by regulating the deiodinase enzymes (Konig, 2002). This finding disagrees with observation reported by other workers that showed no significant difference in manganese concentration in serum of patients with hyperthyroidism (Ali, 2007). The significant decrease in the level of zinc in hypothyroidism patients are observed in other different researches (Buchinger, 1988). One of possible explanation for this finding, that gastrointestinal absorption of zinc is severely impaired in hypothyroidism subjects. Low zinc level may reflect sequestration of zinc by liver or other tissues (Yoshida, 1990). Another explanation is due to the significant influence of TSH in the variation of the concentration of human thyroid tissues (Bellisola, 1998). Zinc has important roles in thyroid metabolism, It involves in T3 binding to its nuclear receptor, and participates in the formation and mechanism of action of TRH (Morley, 1980). A significant increase in manganese levels of hypothyroidism patients was observed. Manganese is a cofactor of many important enzymes especially, manganese superoxide dismutase, which is the principal antioxidant enzyme that neutralizes the toxic effects of reactive oxygen species. Manganese may directly or indirectly affect the thyroid function by injuring the thyroid gland or dysregulating dopaminergic modulation of thyroid hormone synthesis (Freake, 2001).

CONCLUSION

This study showed there is decrease in levels of zinc and manganese of hyperthyroidism patient while in hypothyroidism patient there is increase in serum manganese levels with decreasing in zinc levels.

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